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RHYTHM PHARMACEUTICALS, INC. INDEX TO FINANCIAL STATEMENTS

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As filed with the Securities and Exchange Commission on September 5, 2017

Registration No. 333-

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM S-1

REGISTRATION STATEMENT
UNDER
THE SECURITIES ACT OF 1933

RHYTHM PHARMACEUTICALS, INC.

(Exact name of Registrant as specified in its charter)

Delaware	**2834**	**46-2159271**
(State or Other Jurisdiction of Incorporation or Organization)	(Primary Standard Industrial Classification Code Number)	(I.R.S. Employer Identification Number)

500 Boylston Street
11th Floor
Boston, MA 02116
(857) 264-4280
(Address, including zip code, and telephone number, including area code, of Registrant's principal executive offices)

Keith M. Gottesdiener, M.D.
Chief Executive Officer and President
Rhythm Pharmaceuticals, Inc.
500 Boylston Street
11th Floor
Boston, MA 02116
(857) 264-4280
(Name, address, including zip code, and telephone number, including area code, of agent for service)

Please send copies of all communications to:

Julio E. Vega	**Steven D. Singer**
Laurie A. Cerveny	**Lisa Firenze**
Morgan, Lewis & Bockius LLP	**Wilmer Cutler Pickering Hale and Dorr LLP**
One Federal Street	**7 World Trade Center**
Boston, MA 02110	**New York, NY 10007**
(617) 951-8000	**(212) 230-8000**

Approximate date of commencement of the proposed sale to the public:
As soon as practicable after the effective date of this Registration Statement.

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act, check the following box. o

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. o

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. o

If this Form is a post-effective amendment filed pursuant to Rule 462(d) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. o

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer" "smaller reporting company" and "emerging growth company" in Rule 12b-2 of the Exchange Act. (Check one):

Large accelerated filer o	Accelerated filer o	Non-accelerated filer ☒ (Do not check if a smaller reporting company)	Smaller reporting company o Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. o

CALCULATION OF REGISTRATION FEE

Title of Each Class of Securities to be Registered	Proposed Maximum Aggregate Offering Price[(1)(2)]	Amount of Registration Fee[(3)]
Common Stock, $0.001 par value per share	$115,000,000	$13,328.50

(1) Includes a base offering of $100,000,000 of shares of common stock and $15,000,000 of shares of common stock that the underwriters have the option to purchase.

(2) Estimated solely for the purpose of calculating the registration fee pursuant to Rule 457(o) under the Securities Act of 1933, as amended.

(3) Calculated pursuant to Rule 457(o) based on an estimate of the proposed maximum aggregate offering price.

The Registrant hereby amends this Registration Statement on such date or dates as may be necessary to delay its effective date until the Registrant shall file a further amendment which specifically states that this Registration Statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933, as amended, or until the Registration Statement shall become effective on such date as the Securities and Exchange Commission, acting pursuant to said Section 8(a), may determine.

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SUBJECT TO COMPLETION, DATED SEPTEMBER 5, 2017

PRELIMINARY PROSPECTUS

The information in this preliminary prospectus is not complete and may be changed. We may not sell these securities until the registration statement filed with the Securities and Exchange Commission is effective. This preliminary prospectus is not an offer to sell these securities and it is not soliciting an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

Shares

Rhythm Pharmaceuticals, Inc.

Common Stock

Rhythm Pharmaceuticals, Inc. is offering shares of common stock. This is our initial public offering, and no public market currently exists for our common stock. We anticipate that the initial public offering price will be between $ and $ per share of common stock.

We have applied to have the common stock listed on the NASDAQ Global Market under the symbol "RYTM."

We are an "emerging growth company" under the federal securities laws and will be subject to reduced public company reporting requirements. Investing in our common stock involves risks. See "Risk Factors" beginning on page 16.

	Per Share	***Total***
Initial Public Offering Price	*$*	*$*
Underwriting Discount and Commissions[(1)]	*$*	*$*
Proceeds, before expenses, to us	*$*	*$*

(1) *We refer you to "Underwriting" beginning on page 211 for additional information regarding underwriting compensation relating to reimbursement of FINRA-related expenses.*

We have granted the underwriters an option for a period of up to 30 days to purchase up to additional shares of common stock.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

The underwriters expect to deliver the shares to purchasers on or about , 2017.

MORGAN STANLEY *BofA MERRILL LYNCH* *COWEN*

NEEDHAM & COMPANY

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We and the underwriters have not authorized anyone to provide any information or to make any representations other than those contained in this prospectus or in any free writing prospectuses we have prepared. We and the underwriters take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may provide you. We are offering to sell, and seeking offers to buy, shares of common stock only in jurisdictions where offers and sales are permitted. The information contained in this prospectus is accurate only as of the date of this prospectus, regardless of the time of delivery of this prospectus or of any sale of the common stock.

PROSPECTUS SUMMARY

This summary highlights information contained elsewhere in this prospectus and does not contain all of the information that you should consider in making your investment decision. Before investing in our common stock, you should carefully read this entire prospectus, including our financial statements and the related notes included elsewhere in this prospectus. You should also consider, among other things, the matters described under "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations," in each case appearing elsewhere in this prospectus. Unless otherwise stated, all references to "us," "our," "RYTM," "we," the "Company" and similar designations refer to Rhythm Pharmaceuticals, Inc. or our predecessor company, as the context may require. See "Corporate Reorganization."

Overview

We are a biopharmaceutical company focused on the development and commercialization of peptide therapeutics for the treatment of rare genetic deficiencies that result in life-threatening metabolic disorders. Our lead peptide product candidate is setmelanotide, a potent, first-in-class melanocortin-4 receptor, or MC4R, agonist for the treatment of rare genetic disorders of obesity. We believe setmelanotide, for which we have exclusive worldwide rights, has the potential to serve as replacement therapy for the treatment of melanocortin-4, or MC4, pathway deficiencies. MC4 pathway deficiencies result in the disruption of satiety signals and energy homeostasis in the body, which, in turn, leads to intense feelings of hunger and to obesity. Our development efforts are initially focused on obesity related to six single gene-related, or monogenic, MC4 pathway deficiencies—pro-opiomelanocortin, or POMC, leptin receptor, or LepR, Bardet-Biedl syndrome, Alström syndrome, POMC heterozygous, and POMC epigenetic disorders—for which there are currently no effective or approved treatments. We believe that the MC4 pathway is a compelling target for treating these genetic disorders because of its critical role in regulating appetite and weight by promoting satiety and weight control, and that peptide therapeutics are uniquely suited for activating this target.

We have demonstrated proof of concept in Phase 2 clinical trials in POMC deficiency obesity, LepR deficiency obesity, and Bardet-Biedl syndrome, three genetic disorders of extreme and unrelenting appetite and obesity, in which setmelanotide dramatically reduced both weight and hunger. The U.S. Food and Drug Administration, or FDA, has acknowledged the importance of this preliminary clinical evidence by giving setmelanotide breakthrough therapy designation for the treatment of obesity associated with genetic defects upstream of the MC4 receptor in the leptin-melanocortin pathway, which includes both POMC deficiency obesity and LepR deficiency obesity. Setmelanotide is currently in Phase 3 development for POMC deficiency obesity and LepR deficiency obesity. We are currently enrolling patients in our POMC deficiency obesity Phase 3 clinical trial. We expect to complete enrollment by the end of 2017 and to report Phase 3 data in the first half of 2019. We expect to enroll the first patient in our LepR deficiency obesity Phase 3 clinical trial in the second half of 2017, and to complete enrollment in 2018. We recently demonstrated preliminary proof of concept in our Phase 2 clinical trial in Bardet-Biedl syndrome, indicating that this is also a setmelanotide-responsive, upstream MC4 pathway disorder. We are continuing to enroll patients in this trial and expect to report preliminary Phase 2 results in the fourth quarter of 2017. We expect to initiate a Phase 3 clinical trial in Bardet-Biedl syndrome in 2018. We have also initiated Phase 2 clinical trials in Alström syndrome, POMC heterozygous deficiency obesity and POMC epigenetic disorders, and expect to enroll patients in these trials in the second half of 2017. We anticipate reporting preliminary results in these additional Phase 2 indications in the first half of 2018.

Obesity is epidemic in the United States and current treatment approaches have demonstrated limited long-term success for most obese patients. We are taking a different approach to obesity drug development by leveraging new understanding of the genetic causes of severe obesity to develop innovative therapies that we believe have the potential for compelling efficacy. We believe we are at the forefront of improving treatment outcomes in subtypes of severe obesity that are caused by genetically-defined defects in the MC4 pathway.

Our Product Pipeline

The following chart depicts key information regarding the development of setmelanotide, including the indications we are pursuing within MC4 pathway deficiencies, the current state of development and our expected upcoming milestones:

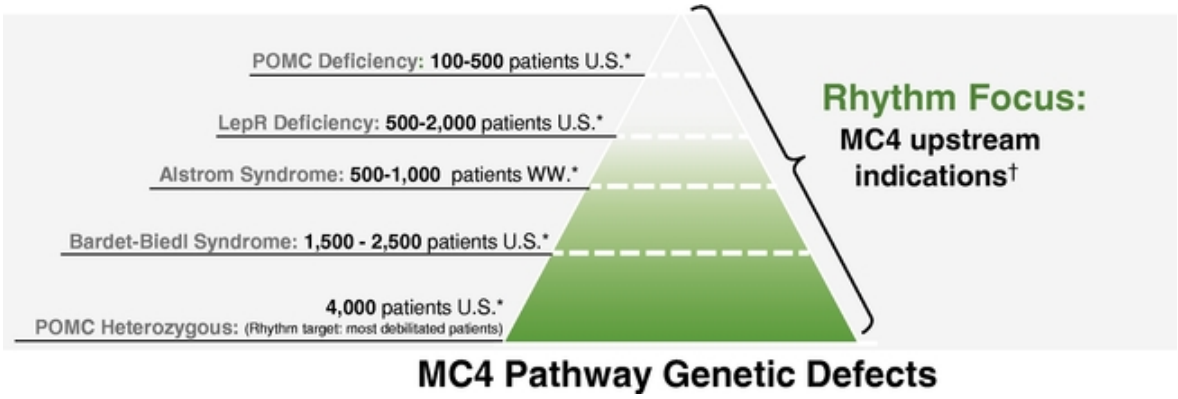
Setmelanotide: A First-in-Class MC4 Agonist

Setmelanotide is a potent, first-in-class, MC4R agonist peptide administered by daily subcutaneous, or SC, injection. Setmelanotide activates MC4R, which is part of the key pathway that can independently regulate energy homeostasis, which refers to the body's energy balance, and appetite. The critical role of the MC4 pathway in weight regulation was validated with the discovery that single genetic defects along this pathway result in early onset and severe obesity. An expanding set of severe obesity genetic defects are now identified that involve genes in the pathway which are either upstream of MC4R—for example POMC deficiency obesity and LepR deficiency obesity—or genes that are downstream of MC4R or affect MC4R itself. We are focusing setmelanotide clinical development on patients with monogenic upstream genetic defects in which obesity is life-threatening but the downstream MC4 pathway is fully functional. We believe setmelanotide has the potential to restore lost activity in the MC4 pathway by bypassing the defects upstream of MC4R, and activating the MC4 pathway below such defects. In this way, setmelanotide may serve as replacement therapy to reestablish weight and appetite control in patients with these genetic disorders.

The first generation MC4R agonists were small molecules that failed in clinical trials primarily due to safety issues, particularly increases in blood pressure, as well as limited efficacy. In contrast, setmelanotide is a peptide that retains the specificity and functionality of the naturally occurring hormone that activates MC4R. Approximately 275 obese subjects and patients have been treated with setmelanotide in previous and ongoing clinical trials in which setmelanotide demonstrated statistically significant weight loss with good tolerability.

Clinical Development in Rare Genetic Disorders of Obesity Caused by MC4 Pathway Deficiencies

The figure below summarizes the indications on which we are focusing for the development of setmelanotide, including our estimates for the addressable patient populations within these indications.



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* The patient numbers above are based on company estimates.

† Epidemiological estimates are not yet available for POMC epigenetic disorders.

We believe that the patient populations in the European Union are at least as large as those in the United States. However, we do not have comparable epidemiological data from the European Union and these estimates are therefore based solely on applying relative population percentages to the Company-derived estimates described above.

POMC Deficiency Obesity

POMC deficiency obesity is a life-threatening, ultra-rare orphan disease, with approximately 50 patients reported to date. Ultra-rare orphan diseases are generally categorized as those that affect fewer than 20 patients per million. We estimate that our addressable patient population for this disorder is approximately 100 to 500 patients in the United States. Patients with POMC deficiency have unrelenting hunger, or hyperphagia, that begins in infancy and they develop severe, early onset obesity. POMC deficiency obesity is caused by the loss of both genetic copies of either the gene for POMC or the gene for proprotein convertase subtilisin/kexin 1, or PCSK, both upstream of MC4R, which results in loss of function in the MC4 pathway. Currently, there is no approved treatment for the obesity and hyperphagia associated with this genetic disorder.

We have initiated a Phase 3 open label, single arm, multinational trial to evaluate the safety and efficacy of setmelanotide for POMC deficiency obesity, with setmelanotide administered once daily by SC injection for 12 months. We are currently enrolling patients in this trial. We expect to complete enrollment by the end of 2017 and to report Phase 3 data in the first half of 2019. Previously, we completed a positive Phase 2 clinical trial in which two patients were enrolled and received treatment. The first patient in this trial lost 146.6 lbs over 118 weeks, from a baseline weight of 341.7 lbs, and the second patient lost 89.3 lbs over 64 weeks, from a baseline weight of 336.9 lbs. Both patients experienced substantial reductions in hunger, with hunger scores falling to one to two from baseline scores of nine to 10. Hunger scores were measured using a Likert score of zero to 10, where zero represents no hunger and 10 represents extreme hunger. Setmelanotide was generally well tolerated in this Phase 2 trial.

Leptin Receptor Deficiency Obesity

LepR deficiency obesity is an ultra-rare orphan disease that results in hyperphagia and severe early-onset obesity, with an estimated prevalence of 1% of subjects with severe, early-onset obesity. We estimate

that our addressable patient population for this disorder is approximately 500 to 2,000 patients in the United States. Like other deficiencies upstream in the MC4 pathway, LepR deficiency results in loss of function in the MC4 pathway. Therefore, patients with this indication also manifest hyperphagia and severe obesity from early childhood. Currently, there is no approved treatment for the obesity and hyperphagia associated with this genetic disorder.

We have initiated a Phase 3 open label, single arm, multinational trial to evaluate the safety and efficacy of setmelanotide for LepR deficiency obesity, with setmelanotide administered once daily by SC injection for 12 months. We expect to enroll the first patient in our LepR deficiency obesity Phase 3 clinical trial in the second half of 2017, and to complete enrollment in 2018. Previously, we completed a positive Phase 2 clinical trial in which three patients were enrolled and received treatment in this trial each experiencing significant weight loss and substantial reductions in hunger. Setmelanotide was generally well tolerated in this Phase 2 trial.

Bardet-Biedl syndrome

Bardet-Biedl syndrome is a life-threatening, ultra-rare orphan disease with a prevalence of approximately one in 100,000 in North America. We estimate that our addressable patient population for Bardet-Biedl syndrome obesity is approximately 1,500 to 2,500 patients in the United States. Bardet-Biedl syndrome is a monogenic disorder that causes severe obesity and hyperphagia as well as vision loss, polydactyly, kidney abnormalities, and other signs and symptoms. Currently there are no approved or effective therapies for Bardet-Biedl syndrome.

We recently demonstrated preliminary proof of concept in our Phase 2 clinical trial in Bardet-Biedl syndrome, indicating that this is also a setmelanotide-responsive, upstream MC4 pathway disorder. We are continuing to enroll patients in this trial and expect to report preliminary Phase 2 results in the fourth quarter of 2017. We expect to initiate a Phase 3 clinical trial in Bardet-Biedl syndrome in 2018.

Other Upstream Genetic Defects in the MC4 Pathway

We are also focusing on additional monogenic, upstream MC4 pathway deficiencies for which setmelanotide can function as replacement therapy and provide activation of the pathway downstream of the defect, promoting satiety and weight control. We have initiated Phase 2 trials for Alström syndrome, a life-threatening, ultra-rare orphan disease, for which we estimate our addressable population is approximately 500 to 1,000 patients worldwide, for POMC heterozygous deficiency obesity, for which we estimate our addressable population is approximately 4,000 patients in the United States, and for POMC epigenetic disorders. For these patients, hyperphagia and obesity can have significant health consequences for which there is currently no approved treatment. We expect to enroll patients with Alström syndrome, POMC heterozygous deficiency obesity, and POMC epigenetic disorders in the second half of 2017 and to report preliminary results from these trials in the first half of 2018.

Expanding Attention to the Diagnosis of Genetic Obesity

We are supporting several initiatives to expand the diagnosis of genetic obesity, including The Genetic Obesity Project. The Genetic Obesity Project has initiated a genotyping study, or GO-ID genotyping study, and a patient registry, or GO-ID registry, both focusing initially on identifying people with POMC deficiency obesity and LepR deficiency obesity, and we are currently including other MC4 pathway deficiencies. Our preliminary results in 560 genotyped patients suggest we can successfully identify these patients. We have also conducted a genetic obesity epidemiology analysis of MC4 pathway genetic defects in a large representative sample of the U.S. population. Based on preliminary findings from this analysis, we believe the prevalence of these MC4 pathway deficiencies within the U.S. population could be substantially larger than our current estimates. We plan to continue our work in analyzing and assessing the epidemiology for these rare genetic disorders of obesity.

Breakthrough Therapy and Orphan Designations

Based on our POMC deficiency obesity and LepR deficiency obesity Phase 2 results, the FDA granted setmelanotide breakthrough therapy designation for the treatment of obesity associated with genetic defects upstream of the MC4 receptor in the leptin-melanocortin pathway, which includes both POMC deficiency obesity and LepR deficiency obesity, enabling an expedited path to approval of setmelanotide for these two indications. In April 2016, the FDA granted our orphan drug designation request for setmelanotide for the treatment of POMC deficiency obesity.

Company History

Our company was founded in November 2008 by former biopharmaceutical executives who have successfully developed, commercialized and in-licensed innovative pharmaceutical products, and we have subsequently expanded our senior management team to further broaden our team's experience in developing, registering and commercializing new drugs. In addition, our scientific advisory board, or SAB, members have extensive clinical expertise in obesity, endocrinology and metabolic diseases. We intend to leverage the experience of our senior management team and SAB to develop and commercialize setmelanotide. Through our senior management team's network of industry contacts, we will continue to evaluate additional product candidate licensing and acquisition opportunities. We are backed by strong and dedicated investors that include both private equity venture capital funds and public healthcare investment funds. Our investors include MPM Capital, New Enterprise Associates, Third Rock Ventures, Ipsen, Pfizer Venture Investments, OrbiMed, Deerfield Management and two public healthcare investment funds.

Our patent portfolio includes composition of matter patents for setmelanotide that expire in the United States in 2027, with possible patent term extension to 2032 under the Hatch-Waxman Act.

Our Strategy

Our goal is to be a leader in developing and commercializing targeted therapies for genetic deficiencies that result in life-threatening metabolic disorders. The key components of our strategy are:

- **Rapidly develop setmelanotide for rare genetic disorders of obesity caused by MC4 pathway deficiencies.** We are aiming to dramatically improve patient outcomes in severe obesity by targeting setmelanotide's mechanism of action to the treatment of patients with genetically-defined defects in the MC4 pathway. We are focusing setmelanotide clinical development on monogenic upstream genetic defects in which obesity is life-threatening but where the downstream MC4 pathway is fully functional.

- **Advance setmelanotide for POMC deficiency obesity and LepR deficiency obesity as our first indications in upstream MC4 pathway deficiencies.** We currently have a Phase 3 trial underway for POMC deficiency obesity and expect to report Phase 3 data in the first half of 2019. We have also initiated a Phase 3 trial for LepR deficiency obesity. We expect to enroll the first patient in our LepR deficiency obesity Phase 3 clinical trial in the second half of 2017, and to complete enrollment in 2018.

- **Expand setmelanotide development to additional upstream MC4 pathway deficiencies, including Bardet-Biedl syndrome, Alström syndrome, POMC heterozygous deficiency obesity, and POMC epigenetic disorders.** We have initiated Phase 2 clinical trials in these rare genetic disorders, and have obtained preliminary proof of concept in Bardet-Biedl syndrome demonstrating that this is also a setmelanotide-responsive, upstream MC4 pathway disorder. We anticipate reporting these preliminary results for Bardet-Biedl syndrome in the fourth quarter of 2017, starting Phase 3 clinical trials in 2018, and obtaining preliminary results for the other Phase 2 indications in the first half of 2018.

- **Commercialize setmelanotide for rare disease indications in core strategic markets.** We intend to establish our own commercial sales and marketing organization in the United States and other core strategic markets. We may also selectively establish partnerships in markets outside the United States for sales, marketing and distribution.

- **Leverage the broad experience of our team in clinical and commercial drug development, and product acquisitions.** We will apply our team's extensive experience in developing and commercializing innovative medicines to the development and launch of setmelanotide. In addition, we intend to identify and acquire new pipeline programs in related diseases.

Risks Associated with Our Business

Our business is subject to a number of risks of which you should be aware before making an investment decision. These risks are discussed more fully in the "Risk Factors" section beginning on page 16 of this prospectus. These risks include the following:

- We are a development stage biopharmaceutical company with a limited operating history and have not generated any revenue from product sales. We have incurred significant operating losses since our inception, anticipate that we will incur continued losses for the foreseeable future and may never achieve profitability. As of June 30, 2017, we had an accumulated deficit of $89.7 million.

- Even if this offering is successful, we will need to raise additional funding, which may not be available on acceptable terms, or at all. Failure to obtain this necessary capital when needed may force us to delay, limit or terminate our product development efforts or other operations.

- We have only one product candidate and we may not be successful in any future efforts to identify and develop additional product candidates.

- Positive results from early clinical trials of setmelanotide may not be predictive of the results of later clinical trials of setmelanotide. If we cannot generate positive results in our later clinical trials of setmelanotide, we may be unable to successfully develop, obtain regulatory approval for and commercialize setmelanotide.

- The number of patients suffering from each of the MC4 pathway deficiencies is small and has not been established with precision. If the actual number of patients with any of these conditions is smaller than we had estimated, our revenue and ability to achieve profitability will be materially adversely affected.

- Failures or delays in the commencement or completion of our planned clinical trials of setmelanotide could result in increased costs to us and could delay, prevent or limit our ability to generate revenue and continue our business.

- Changes in regulatory requirements, FDA guidance or unanticipated events during our clinical trials of setmelanotide may occur, which may result in changes to clinical trial protocols or additional clinical trial requirements, which could result in increased costs to us and could delay our development timeline. Additionally, it may be necessary to validate different or additional instruments for measuring subjective symptoms, and to show that setmelanotide has a clinically meaningful impact on those endpoints in order to obtain regulatory approval.

- Even if we complete the necessary clinical trials, the regulatory and marketing approval process is expensive, time consuming and uncertain and may prevent us from obtaining approvals for the commercialization of setmelanotide. We depend almost entirely on the success of setmelanotide, which is still in clinical development. We cannot be certain that we will be able to obtain regulatory approval for, or successfully commercialize setmelanotide. If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals, we will not be able to commercialize setmelanotide and our ability to generate revenue will be materially impaired.

- If we experience delays or difficulties in the enrollment of patients in clinical trials, our receipt of necessary regulatory approvals could be delayed or prevented.
- Setmelanotide may cause undesirable side effects that could delay or prevent its regulatory approval, limit the commercial profile of an approved labeling or result in significant negative consequences following marketing approval, if any.
- Even if approved, reimbursement policies could limit our ability to sell setmelanotide.
- Competing products and technologies could emerge, adversely affecting our opportunity to generate revenue from the sale of setmelanotide.
- If we are unable to obtain and maintain patent protection for setmelanotide and its related technology, or if the scope of the patent protection obtained is not sufficiently broad, our competitors could develop and commercialize technology and products similar or identical to ours, and our ability to successfully commercialize our technology and setmelanotide may be impaired.
- Since we have only a limited history of operating as an independent company, we may incur unforeseen expenses associated with doing so.

Corporate Reorganization and Other Information

We are a Delaware corporation organized in February 2013 under the name Rhythm Metabolic, Inc. and as of October 2015, under the name Rhythm Pharmaceuticals, Inc. Prior to our organization and the Corporate Reorganization referred to below, we were part of Rhythm Pharmaceuticals, Inc., a Delaware corporation which was organized in November 2008 and which commenced active operations in 2010. We refer to this corporation as the Predecessor Company.

In March 2013, the Predecessor Company underwent a corporate reorganization, which we refer to as the Corporate Reorganization, pursuant to which all of the outstanding equity securities of the Predecessor Company were exchanged for units of Rhythm Holding Company, LLC, a newly-organized limited liability company, which we refer to as the LLC entity. After the consummation of this exchange and as part of the Corporate Reorganization, the Predecessor Company contributed setmelanotide and the MC4R agonist program to us and distributed to the LLC entity all of the then issued and outstanding shares of our stock. The result of the Corporate Reorganization was that we and the Predecessor Company became wholly-owned subsidiaries of the LLC entity and the two product candidates and related programs that were originally held by the Predecessor Company were separated, with relamorelin and the ghrelin agonist program being retained by the Predecessor Company and setmelanotide and the MC4R agonist program being held by us. We refer to the Predecessor Company after consummation of the Corporate Reorganization as the Relamorelin Company. The Predecessor Company filed the IND for setmelanotide in October 2011 and conducted the setmelanotide clinical trials up until the Corporate Reorganization, after which all clinical trials have been conducted by us.

In October 2014, the LLC entity granted to Actavis plc, now owned by Allergan, Inc., or Allergan, an exclusive option to acquire the Relamorelin Company. The transaction was limited to the acquisition of the Relamorelin Company and did not include our company. In October 2016, the option to acquire the Relamorelin Company was exercised and the sale to Allergan closed on December 15, 2016.

In August 2015, we effected a 93,500-for-1 forward stock split of our then-outstanding common stock. Also in August 2015, December 2015, January 2017 and August 2017, we sold 25,000,000 shares, 15,000,000 shares, 20,475,001 shares and 20,474,998 shares, respectively, of our series A preferred stock to certain investors. Following the stock split and the closing of our series A preferred stock financings, the LLC entity remained our largest stockholder, with the balance of our stock being owned by our series A investors. In August 2017, the LLC entity exchanged 78,666,209 of its shares of our common stock for an equal number of newly-issued shares of our series A-1 junior preferred stock and the LLC entity

distributed all of its shares of our series A-1 junior preferred stock to the holders of its preferred units and the remaining 14,833,791 shares of our common stock to the holders of its common units. We refer to the exchange and distribution as the Distribution. The series A-1 junior preferred stock will convert into shares of our common stock on a one to one basis upon the closing of this offering. Following the Distribution, the LLC entity no longer owns any of our common stock.

On October 13, 2015, the Relamorelin Company changed its name to Motus Therapeutics, Inc. and we changed our name to Rhythm Pharmaceuticals, Inc.

Our principal executive offices are located at 500 Boylston Street, 11th Floor, Boston, MA 02116, and our telephone number is (857) 264-4280. Our corporate website address is www.rhythmtx.com. Information contained on or accessible through our website is not a part of this prospectus, and the inclusion of our website address in this prospectus is an inactive textual reference only.

This prospectus contains references to our trademarks and to trademarks belonging to other entities. Solely for convenience, trademarks and trade names referred to in this prospectus, including logos, artwork and other visual displays, may appear without the ® or ™ symbols, but such references are not intended to indicate, in any way, that we will not assert, to the fullest extent under applicable law, our rights or the rights of the applicable licensor to these trademarks and trade names. We do not intend our use or display of other companies' trade names or trademarks to imply a relationship with, or endorsement or sponsorship of us by, any other companies.

Implications of Being an Emerging Growth Company

We are an "emerging growth company" as defined in the Jumpstart Our Business Startups Act of 2012. We will remain an emerging growth company until the earlier of (1) the last day of the fiscal year (a) following the fifth anniversary of the completion of this offering, (b) in which we have total annual gross revenue of at least $1.07 billion, or (c) in which we are deemed to be a large accelerated filer, which means the market value of our common stock that is held by non-affiliates exceeds $700 million as of the prior June 30th, and (2) the date on which we have issued more than $1.0 billion in non-convertible debt securities during the prior three-year period. We refer to the Jumpstart Our Business Startups Act of 2012 in this prospectus as the "JOBS Act," and references in this prospectus to "emerging growth company" shall have the meaning ascribed to it in the JOBS Act.

An emerging growth company may take advantage of reduced reporting requirements that are otherwise applicable to public companies. These provisions include, but are not limited to:

- the ability to present only two years of audited financial statements and only two years of related Management's Discussion and Analysis of Financial Condition and Results of Operations in this prospectus;
- an exemption from the requirements to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, as amended;
- reduced disclosure obligations regarding executive compensation in our periodic reports, proxy statements and registration statements; and
- exemptions from the requirement to hold a nonbinding advisory vote on executive compensation and to obtain stockholder approval of any golden parachute payments not previously approved.

We may use these provisions until such time as we cease to be an emerging growth company.

We have elected to take advantage of certain of the reduced disclosure obligations in the registration statement of which this prospectus forms a part and may elect to take advantage of other reduced reporting requirements in future filings. As a result, the information that we provide to our stockholders

may be different from the information that you might receive from other public reporting companies in which you hold equity interests.

The JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. We have irrevocably elected not to avail ourselves of this exemption and, therefore, we will be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

THE OFFERING

Common stock offered by us	shares
Common stock to be outstanding after this offering	shares
Option to purchase additional common stock offered by us	shares
Use of proceeds	We estimate that our net proceeds from this offering will be approximately $ million at an assumed initial public offering price of $ per share, which is the midpoint of the price range set forth on the cover page of this prospectus, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. We intend to use the net proceeds from this offering, together with our existing cash resources, as follows: • approximately $ million to fund the development and manufacturing of setmelanotide through completion of our Phase 3 clinical trial for the treatment of POMC deficiency obesity; • approximately $ million for the development and manufacturing of setmelanotide through completion of enrollment of our Phase 3 clinical trial for the treatment of LepR deficiency obesity; • approximately $ million for the development of setmelanotide through proof of concept in our Phase 2 clinical trials for Bardet-Biedl syndrome, Alström syndrome, POMC heterozygous deficiency obesity and POMC epigenetic disorders; • preparation for commercialization of setmelanotide, including initiatives to expand the diagnosis of genetic obesity; and • the remainder for working capital purposes and other general corporate purposes.
Risk factors	See "Risk Factors" beginning on page 16 and the other information included in this prospectus for a discussion of factors you should carefully consider before deciding to invest in our common stock.
Proposed NASDAQ Global Market Symbol	"RYTM"

The number of shares of our common stock to be outstanding after this offering is based on shares of our common stock outstanding as of June 30, 2017 and assumes:

- a for reverse stock split of our common stock, to be effective immediately prior to the effectiveness of the registration statement of which this prospectus forms a part;
- the conversion of all our outstanding preferred stock into 159,616,208 shares of our common stock upon the completion of this offering;

- no exercise by the underwriters of their option to purchase additional shares of common stock; and
- the filing of our amended and restated certificate of incorporation upon the closing of this offering.

In this prospectus, unless otherwise indicated, the number of shares of common stock outstanding and the other information based thereon does not reflect:

- shares of common stock reserved for future issuance under our amended and restated 2015 equity incentive plan, as amended and in effect from and after the closing of this offering, or the post-offering Plan;
- shares of common stock reserved for future issuance under our 2017 employee stock purchase plan; and
- shares of common stock issuable upon the exercise of stock options outstanding as of under the post-offering Plan at a weighted average exercise price of $.

SUMMARY FINANCIAL DATA

The following summary financial data for the years ended December 31, 2015 and 2016 are derived from our audited financial statements included elsewhere in this prospectus. The summary financial data as of June 30, 2017 and for the six months ended June 30, 2016 and 2017 have been derived from our unaudited financial statements included elsewhere in this prospectus. These unaudited financial statements have been prepared on a basis consistent with our audited financial statements and, in our opinion, contain all adjustments, consisting only of normal and recurring adjustments, necessary for a fair presentation of such financial data. You should read this data together with our audited financial statements and related notes included elsewhere in this prospectus and the information under the captions "Selected Financial Data" and "Management's Discussion and Analysis of Financial Condition and Results of Operations." Our historical results are not necessarily indicative of our future results, and our operating results for the six-month period ended June 30, 2017 are not necessarily indicative of the results that may be expected for the fiscal year ending December 31, 2017 or any other interim periods or any future year or period.

Our financial statements for the periods presented include allocations of costs from certain shared functions provided to us by the Relamorelin Company. These allocations were made based on either a specific identification basis or, when a specific identification is not practicable, a proportional cost allocation method which allocates expenses based on the percentage of employee time and research and development efforts expended on our business as compared to total employee time and research and development efforts, and have been included in our financial statements for the periods presented.

The financial statements included in this prospectus may not necessarily reflect our financial position, results of operations and cash flows as if we had operated as an independent company during all of the periods presented. See "Corporate Reorganization."

	Year Ended December 31,		Six Months Ended June 30,	
	2015	2016	2016	2017
	(in thousands, except share and per share data)			
Operating expenses:				
Research and development	$ 7,148	$ 19,594	$ 8,544	$ 10,270
General and administrative	3,425	6,311	2,585	2,873
Total operating expenses	10,573	25,905	11,129	13,143
Loss from operations	(10,573)	(25,905)	(11,129)	(13,143)
Other income (expense):				
Revaluation of Series A Investor Right/Obligation and Series A Investor Instrument	(500)	—	—	(82)
Interest income, net	—	33	14	63
Total other income (expense):	(500)	33	14	(19)
Net loss and comprehensive loss	$ (11,073)	$ (25,872)	$ (11,115)	$ (13,162)
Net loss attributable to common stockholders	$ (12,000)	$ (29,074)	$ (12,711)	$ (15,534)
Net loss attributable to common stockholders per common share, basic and diluted[1]	$ (0.13)	$ (0.31)	$ (0.14)	$ (0.17)
Weighted average common shares outstanding, basic and diluted	93,500,000	93,500,000	93,500,000	93,500,000
Pro forma net loss attributable to common stockholders per common share, basic and diluted (unaudited)[1]		$ (0.19)		$ (0.09)
Pro forma weighted average common shares outstanding, basic and diluted (unaudited)[1]		133,500,000		153,409,393

	As of June 30, 2017		
	Actual	Pro Forma[2]	Pro Forma As Adjusted[3]
	(unaudited in thousands)		
Balance Sheet Data:			
Cash, cash equivalents and short-term investments	$ 17,740	$ 38,215	
Working capital	13,619	34,094	
Total assets	20,404	40,879	
Convertible preferred stock	60,147	—	
Accumulated deficit	(89,705)	(89,705)	
Total stockholders' equity (deficit)	$ (45,266)	$ 35,766	

(1) See Note 2 within the notes to our financial statements appearing elsewhere in this prospectus for a description of the methods used to calculate basic and diluted net loss per share and pro forma basic and diluted net loss per share.

(2) Pro forma to reflect the issuance of 78,666,209 shares of our series A-1 junior preferred stock in exchange for an equal number of shares of our common stock in connection with the Distribution, the issuance of 20,474,998 shares of series A preferred stock in August 2017 (see Note 12 within the notes to our financial statements appearing elsewhere in this prospectus) and the conversion of all of our outstanding preferred stock into 159,616,208 shares of common stock upon the closing of this offering.

(3) Pro forma as adjusted to further reflect the issuance and sale of shares of our common stock in this offering, at an assumed initial public offering price of $ per share, the midpoint of the price range set forth on the cover of this prospectus, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

CORPORATE REORGANIZATION

We are a Delaware corporation organized in February 2013 under the name Rhythm Metabolic, Inc. and as of October 2015, under the name Rhythm Pharmaceuticals, Inc. Prior to our organization and the Corporate Reorganization referred to below, we were part of Rhythm Pharmaceuticals, Inc., a Delaware corporation which was organized in November 2008 and which commenced active operations in 2010. We refer to this corporation as the Predecessor Company.

In March 2013, the Predecessor Company underwent a corporate reorganization, which we refer to as the Corporate Reorganization, pursuant to which all of the outstanding equity securities of the Predecessor Company were exchanged for units of Rhythm Holding Company, LLC, a newly-organized limited liability company, which we refer to as the LLC entity. After the consummation of this exchange and as part of the Corporate Reorganization, the Predecessor Company contributed setmelanotide and the MC4R agonist program to us and distributed to the LLC entity all of the then issued and outstanding shares of our stock. The result of the Corporate Reorganization was that we and the Predecessor Company became wholly-owned subsidiaries of the LLC entity and the two product candidates and related programs that were originally held by the Predecessor Company were separated, with relamorelin and the ghrelin agonist program being retained by the Predecessor Company and setmelanotide and the MC4R agonist program being held by us. We refer to the Predecessor Company after consummation of the Corporate Reorganization as the Relamorelin Company. The Predecessor Company filed the IND for setmelanotide in October 2011 and conducted the setmelanotide clinical trials up until the Corporate Reorganization, after which all clinical trials have been conducted by us.

In October 2014, the LLC entity granted to Actavis plc, now owned by Allergan, Inc., or Allergan, an exclusive option to acquire the Relamorelin Company. The transaction was limited to the acquisition of the Relamorelin Company and did not include us. In October 2016, the option to acquire the Relamorelin Company was exercised and the sale to Allergan closed on December 15, 2016.

In August 2015, we effected a 93,500-for-1 forward stock split of our then-outstanding common stock. Also in August 2015, December 2015, January 2017 and August 2017, we sold 25,000,000 shares, 15,000,000 shares, 20,475,001 shares and 20,474,998 shares, respectively, of our series A preferred stock to certain investors. Following the stock split and the closing of our series A preferred stock financings, the LLC entity remained our largest stockholder, with the balance of our stock being owned by our series A investors. In August 2017, the LLC entity exchanged 78,666,209 of its shares of our common stock for an equal number of newly-issued shares of our series A-1 junior preferred stock and the LLC entity distributed all of its shares of our series A-1 junior preferred stock to the holders of its preferred units and the remaining 14,833,791 shares of our common stock to the holders of its common units. We refer to the exchange and distribution as the Distribution. The series A-1 junior preferred stock will convert into shares of our common stock on a one to one basis upon the closing of this offering. Following the Distribution, the LLC entity no longer owns any of our common stock.

Prior to the sale of the Relamorelin Company to Allergan, we had an Amended and Restated Payroll Services Agreement with the Relamorelin Company, which we refer to as the Payroll Services Agreement. Pursuant to the Payroll Services Agreement, the Relamorelin Company provided us certain employee and consultant services. We had five employees whose services were provided to us pursuant to this agreement. We also shared certain costs with the Relamorelin Company, including finance, accounting, research and development and operations. As part of the sale of the Relamorelin Company, these employees became our employees and have employment agreements with us.

On October 13, 2015, the Relamorelin Company changed its name to Motus Therapeutics, Inc. and we changed our name to Rhythm Pharmaceuticals, Inc.

RISK FACTORS

Investing in our common stock involves a high degree of risk. You should carefully consider the following risks and uncertainties, together with all other information in this prospectus, including our financial statements and related notes, before investing in our common stock. Any of the risk factors we describe below could adversely affect our business, financial condition or results of operations. The market price of our common stock could decline if one or more of these risks or uncertainties actually occur, causing you to lose all or part of the money you paid to buy our common stock. Additional risks that we currently do not know about or that we currently believe to be immaterial may also impair our business. Certain statements below are forward-looking statements. See "Cautionary Note Regarding Forward-Looking Statements" in this prospectus.

Risks Related to Our Financial Position and Need for Capital

We are a clinical-stage biopharmaceutical company with a limited operating history and have not generated any revenue from product sales. We have incurred significant operating losses since our inception, anticipate that we will incur continued losses for the foreseeable future and may never achieve profitability.

We are a clinical-stage biopharmaceutical company with a limited operating history on which to base your investment decision. Biopharmaceutical product development is a highly speculative undertaking and involves a substantial degree of risk. We were incorporated in February 2013 in connection with the Corporate Reorganization. Our operations to date have been limited primarily to acquiring rights to intellectual property, business planning, raising capital, developing our technology, identifying potential product candidates, undertaking preclinical studies and conducting research and development activities, including clinical trials, for setmelanotide. We have never generated any revenue from product sales. We have not obtained any regulatory approvals for setmelanotide.

Since our inception, we have focused substantially all of our efforts and financial resources on the research and development of setmelanotide, which is currently in Phase 3 clinical development for two indications, POMC deficiency obesity and LepR deficiency obesity, and in various phases of development for other indications. We have funded our operations to date primarily through capital contributions from the Predecessor Company, the Relamorelin Company and the LLC entity and proceeds from sales of preferred stock and have incurred losses in each year since our inception.

Our net loss and comprehensive losses were $11.1 million, $25.9 million, $11.1 million and $13.2 million for the years ended December 31, 2015 and 2016 and the six months ended June 30, 2016 and 2017, respectively. As of June 30, 2017, we had an accumulated deficit of $89.7 million. Substantially all of our operating losses have resulted from costs incurred in connection with our development program and from general and administrative costs associated with our operations. Our prior losses, combined with expected future losses, have had and will continue to have an adverse effect on our stockholders' deficit and working capital. We expect our research and development expenses to significantly increase in connection with our additional clinical trials of setmelanotide and development of any other product candidates we may choose to pursue. In addition, if we obtain marketing approval for setmelanotide, we will incur significant sales, marketing and outsourced manufacturing expenses. Once we are a public company, we will incur additional costs associated with operating as a public company. As a result, we expect to continue to incur significant and increasing operating losses for the foreseeable future. Because of the numerous risks and uncertainties associated with developing pharmaceutical products, we are unable to predict the extent of any future losses or when we will become profitable, if at all. Even if we do become profitable, we may not be able to sustain or increase our profitability on a quarterly or annual basis.

Our ability to become profitable depends upon our ability to generate revenue. To date, we have not generated any revenue from setmelanotide, and we do not know when, or if, we will generate any revenue. We do not expect to generate significant revenue unless and until we obtain marketing approval for, and

begin to sell, setmelanotide. Our ability to generate revenue depends on a number of factors, including, but not limited to, our ability to:

- initiate and successfully complete later-stage clinical trials that meet their clinical endpoints;
- initiate and successfully complete all safety studies required to obtain U.S. and foreign marketing approval for setmelanotide as a treatment for obesity caused by genetic deficiencies affecting the MC4 pathway;
- successfully manufacture or contract with others to manufacture setmelanotide;
- commercialize setmelanotide, if approved, by building an internal sales force or entering into collaborations with third parties; and
- achieve market acceptance of setmelanotide in the medical community and with third-party payors.

Absent our entering into collaboration or partnership agreements, we expect to incur significant sales and marketing costs as we prepare to commercialize setmelanotide. Even if we initiate and successfully complete our pivotal clinical trials and setmelanotide is approved for commercial sale, and we incur the costs associated with these activities, setmelanotide may not be a commercially successful drug. We may not achieve profitability soon after generating product sales, if ever. If we are unable to generate product revenue, we will not become profitable and will be unable to continue operations without continued funding.

Even if this offering is successful, we will need to raise additional funding, which may not be available on acceptable terms, or at all. Failure to obtain this necessary capital when needed may force us to delay, limit or terminate our product development efforts or other operations.

We are currently advancing setmelanotide through clinical development. Developing peptide therapeutic products is expensive, and we expect our research and development expenses to increase substantially in connection with our ongoing activities, particularly as we advance setmelanotide in clinical trials. We intend to use the proceeds of this offering primarily for the clinical development and regulatory approval of setmelanotide. Depending on the status of regulatory approval and, if approved, commercialization of setmelanotide, as well as the progress we make in the sale of setmelanotide, we may still require significant additional capital to fund the continued development of setmelanotide and our operating needs thereafter. We may also need to raise additional funds if we choose to pursue additional indications and/or geographies for setmelanotide or otherwise expand more rapidly than we presently anticipate.

Through August 2015, we received capital contributions from the Predecessor Company, the Relamorelin Company and the LLC entity. In August 2015, December 2015, January 2017 and August 2017, we raised aggregate gross proceeds of $25.0 million, $15.0 million, $20.5 million and $20.5 million, respectively, through our issuance of series A preferred stock. As of June 30, 2017, our cash and cash equivalents and short-term investments were approximately $17.7 million and after giving effect, on a pro forma basis, to the aggregate gross proceeds from the sale of our series A preferred stock in August 2017, $38.2 million. We estimate that the net proceeds from this offering will be approximately $ million, assuming an initial public offering price of $ per share, the midpoint of the price range set forth on the cover page of this prospectus, after deducting estimated underwriting discounts and commissions and offering expenses payable by us. We expect that the net proceeds from this offering, together with our existing cash and cash equivalents, will be sufficient to fund our operating expenses into the first half of 2019. However, our operating plan may change as a result of many factors currently unknown to us, and we may need to seek additional funds sooner than planned, through public or private equity or debt financings, government or other third-party funding, marketing and distribution arrangements and other collaborations, strategic alliances and licensing arrangements, or a combination of these approaches. We will also require additional capital to obtain regulatory approval for, and to commercialize, setmelanotide. Raising funds in the current economic environment may present additional challenges. Even if we believe

we have sufficient funds for our current or future operating plans, we may seek additional capital if market conditions are favorable or if we have specific strategic considerations.

Any additional fundraising efforts may divert our management from their day-to-day activities, which may adversely affect our ability to develop and commercialize setmelanotide. In addition, we cannot guarantee that future financing will be available in sufficient amounts or on terms acceptable to us, if at all. Moreover, the terms of any financing may adversely affect the holdings or the rights of our stockholders and the issuance of additional securities, whether equity or debt, by us, or the possibility of such issuance, may cause the market price of our shares to decline. The sale of additional equity or convertible securities would dilute all of our stockholders. The incurrence of indebtedness would result in increased fixed payment obligations and we may be required to agree to certain restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell or license intellectual property rights, and other operating restrictions that could adversely impact our ability to conduct our business. We could also be required to seek funds through arrangements with collaborative partners or other third parties at an earlier stage than otherwise would be desirable and we may be required to relinquish rights to setmelanotide or technologies or otherwise agree to terms unfavorable to us, any of which may have a material adverse effect on our business, operating results and prospects.

If we are unable to obtain funding on a timely basis, we may be required to significantly curtail, delay or discontinue one or more of our research or development programs or the commercialization of setmelanotide or be unable to expand our operations or otherwise capitalize on our business opportunities, as desired, which could materially adversely affect our business, financial condition and results of operations.

Our auditors have issued a "going concern" audit opinion.

Our independent auditors have indicated in their report on our December 31, 2016 financial statements, that there is substantial doubt about our ability to continue as a going concern. A "going concern" opinion indicates that the financial statements have been prepared assuming we will continue as a going concern and do not include any adjustments to reflect the possible future effects on the recoverability and the classification of assets, or the amounts and classification of liabilities that may result if we do not continue as a going concern. Therefore, you should not rely on our balance sheet as an indication of the amount of proceeds that would be available to satisfy claims of creditors, and potentially be available for distribution to shareholders, in the event of a liquidation. The inclusion of a going concern explanatory paragraph by our auditors, our lack of cash resources and our potential inability to continue as a going concern may materially adversely affect our share price and our ability to raise new capital or to enter into critical contractual relationships with third parties.

Our very limited operating history may make it difficult for you to evaluate the success of our business to date and to assess our future viability.

We are an early-stage company. The Predecessor Company commenced active operations in February 2010, and we were incorporated as a separate company in February 2013. Our operations to date have been limited primarily to acquiring rights to intellectual property, business planning, raising capital, developing our technology, identifying potential product candidates, undertaking preclinical studies and, beginning in November 2010, conducting clinical trials. We have not yet demonstrated our ability to successfully complete a pivotal Phase 3 clinical trial, obtain marketing approvals, manufacture at commercial scale, or arrange for a third party to do so on our behalf or conduct sales, marketing and distribution activities necessary for successful product commercialization. Consequently, any predictions made about our future success or viability may not be as accurate as they could be if we had a longer operating history.

In addition, as a new business, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors. We will need to transition at some point from a company

with a research and development focus to a company capable of supporting commercial activities and we may not be successful in such a transition.

We expect our financial condition and operating results to continue to fluctuate significantly from quarter-to-quarter and year-to-year due to a variety of factors, many of which are beyond our control. Accordingly, you should not rely upon the results of any quarterly or annual periods as indications of future operating performance.

Our historical and pro forma financial information is not necessarily representative of the results we would have achieved as an independent company, and may not be a reliable indicator of our future results.

The historical financial and pro forma financial information we have included in this prospectus may not reflect what our results of operations, financial position and cash flows would have been had we been an independent company during the periods presented. This is primarily because:

- our historical financial information reflects allocations for services historically provided to us by the Predecessor Company and the Relamorelin Company, which allocations may not reflect the costs we now and in the future will incur for similar services as an independent company; and

- our historical financial information does not reflect changes that we have incurred and expect to continue to incur as a result of operating as an independent company and from reduced economies of scale, including changes in cost structure, personnel needs, financing and operations of our business.

In addition, the pro forma financial information included in this prospectus is based on the best information available, which in part includes a number of estimates and assumptions which may prove to be inaccurate. Accordingly, our pro forma financial information should not be assumed to be indicative of what our financial condition or results of operations actually would have been as an independent company, nor to be a reliable indicator of what our financial condition or results of operations may actually be in the future. See "Management's Discussion and Analysis of Financial Condition and Results of Operations."

Risks Related to the Development of Setmelanotide

Positive results from early clinical trials of setmelanotide may not be predictive of the results of later clinical trials of setmelanotide. If we cannot generate positive results in our later clinical trials of setmelanotide, we may be unable to successfully develop, obtain regulatory approval for, and commercialize setmelanotide.

Positive results from any of our Phase 1 and Phase 2 clinical trials of setmelanotide may not be predictive of the results of later clinical trials. The duration of effect of setmelanotide tested in our Phase 1 and Phase 2 clinical trials was often for shorter periods than that planned for testing in our current pivotal Phase 3 clinical trials. The duration of effect of setmelanotide has only been studied in long-term durations for a small number of patients in our Phase 2 clinical trials and safety or efficacy issues may arise when more patients are studied in longer trials. It is possible that the effects seen in short-term clinical trials will not be replicated in long-term or larger clinical trials. In addition, not all of our trials demonstrated statistically significant weight loss and there can be no guarantee that future trials will do so.

Positive results for one indication are not necessarily predictive of positive results for other indications. We have demonstrated proof of concept in Phase 2 clinical trials in POMC deficiency obesity, LepR deficiency obesity, and Bardet-Biedl syndrome, three genetic disorders of extreme and unrelenting appetite and obesity, in which setmelanotide dramatically reduced both weight and hunger. We hypothesize that patients with other upstream genetic defects in the MC4 pathway may also respond with reductions in weight and hunger after treatment with setmelanotide, however patients with other upstream genetic defects may not have a similar response to setmelanotide, and until we obtain more clinical data in other genetic defects, we will not be sure that we can achieve proof of concept in such indications. In addition, while we believe that proof of concept in Bardet-Biedl syndrome has been demonstrated by improvements in hunger and weight reduction, supporting that this is a setmelanotide-responsive, MC4 pathway disorder, the results of this trial are still at a preliminary stage.

We have or will have multiple clinical trials of setmelanotide ongoing, which are designed to include multiple genetically and clinically defined populations under one investigational protocol, although each population is enrolled and analyzed separately. A "basket" trial design could potentially decrease the time to study new populations by decreasing administrative burden, however, these trials do not overcome limitations to extrapolating data from the experience in one disease to other diseases, because safety and efficacy results in each indication are analyzed separately. Accordingly, clinical success in a basket trial, or any trial in one indication, may not predict success in another indication. In the event of an adverse safety issue, clinical hold or other adverse finding in one or more indications being tested, such event could adversely affect our trials in the other indications and may delay or prevent completion of the clinical trials.

Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in later stage clinical trials after achieving positive results in early stage development, and we cannot be certain that we will not face similar setbacks. These setbacks have been caused by, among other things, pre—clinical findings made while clinical trials were underway. We have completed the key toxicology studies that we believe the U.S. Food and Drug Administration, or the FDA, and the European Medicines Agency, or EMA, will require for approval, which include, among others, chronic toxicity studies, reproductive and developmental toxicity studies, and juvenile toxicology studies. Based on the totality of animal testing results to date, including the lack of any observed genotoxicity or tissue proliferative activity of setmelanotide in chronic toxicity studies, we have requested that the FDA permit us to defer carcinogenicity studies until after approval of a new drug application, or NDA, for setmelanotide. Accordingly, we believe that we will be able to defer all carcinogenicity studies until after we receive regulatory approval to market setmelanotide. However, the FDA has indicated that it will not make a decision on our request until after reviewing our final toxicology study reports. Accordingly, at this time, there can be no guarantee that we will be able to achieve this deferral which could impact the timing of any potential NDA approval as well as the time frame to achieve commercialization.

In addition to the foregoing issue, the FDA has requested that in our chronic rat and monkey studies we assess certain cells in brain, renal and liver tissues for the presence of vacuoles, which are common membrane-bound compartments. The recommendation was based on the FDA's review of a summary of a rat study that noted the presence of macrophage aggregates, which are groupings of specific white blood cells, in the choroid plexus, a network of blood vessels and epithelial tissue in the membrane lining outside the brain and spinal cord. The FDA noted that the existence of macrophage aggregates appears to be related to the polyethylene glycol vehicle in the product, rather than setmelanotide itself. We do not believe that the appearance of these aggregates raises any safety concerns, in part because of the localization of these aggregates. However, the FDA has not indicated that they agree with our position, and, accordingly, we are performing additional assessments for the presence of vacuoles, including assessments by an independent pathologist. Despite these additional assessments, the FDA may still not agree with our interpretation, and may require us to reflect these findings in the toxicological portion of the product labeling.

Additionally, setbacks may be caused by new safety or efficacy observations made in clinical trials, including previously unreported adverse events. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that believed their product candidates performed satisfactorily in preclinical studies and clinical trials nonetheless failed to obtain FDA approval or European Commission authorization. If we fail to obtain positive results in our Phase 3 clinical trials of setmelanotide, the development timeline and regulatory approval and commercialization prospects for setmelanotide,and, correspondingly, our business and financial prospects would be materially adversely affected.

The number of patients suffering from each of the MC4 pathway deficiencies we are targeting is small and has not been established with precision. If the actual number of patients is smaller than we estimate, our revenue and ability to achieve profitability may be materially adversely affected.

Due to the rarity of our target indications, there is no comprehensive patient registry or other method of establishing with precision the actual number of patients with MC4 pathway deficiencies. As a result, we have had to rely on other available sources to derive prevalence estimates for our target indications. Since the published epidemiology studies for these genetic deficiencies are based on relatively small population samples, and are not amenable to robust statistical analyses, it is possible that these projections may significantly exceed the addressable population, particularly given the need to genotype patients to definitively confirm a diagnosis.

We have estimated the potential addressable patient populations with these MC4 pathway deficiencies based on the following sources and assumptions:

- *POMC Deficiency Obesity.* There are approximately 50 patients with POMC deficiency obesity noted in a series of published case reports, each mostly reporting a single or small number of patients. However, we believe our addressable patient population for this deficiency may be approximately 100 to 500 patients in the United States, and a comparable addressable patient population in Europe, as most of the reported cases are from a small number of academic research centers, and because genetic testing for POMC deficiency is often unavailable and currently is rarely performed. Based on discussions with experts in rare diseases, we also believe the number of diagnosed cases could increase several-fold with increased awareness of this deficiency and the availability of new treatments.

- *LepR Deficiency Obesity and POMC Heterozygous Deficiency Obesity.* Our addressable patient population estimate for LepR deficiency obesity is approximately 500 to 2,000 patients in the United States, and for POMC heterozygous deficiency obesity is approximately 4,000 patients in the United States, with a comparable addressable patient population for both indications in Europe. Our estimates are based on:

  - epidemiology studies on LepR deficiency and POMC heterozygous deficiency in small cohorts of patients comprised of children with severe obesity and adults with severe obesity who have a history of early onset obesity;

  - U.S. Census Bureau figures for adults and children, and Centers for Disease Control and Prevention, or CDC, prevalence numbers for severe adult obese patients (BMI greater than 40 kg/ m^2) and for severe early onset obese children (99th percentile at ages two to 17 years old); and

  - with wider availability of genetic testing expected for LepR deficiency and POMC heterozygous deficiency and increased awareness of new treatments, our belief that up to 40% of patients with these disorders may eventually be diagnosed.

  Using these sources and assumptions, we calculated our estimates for addressable populations by multiplying (x) our estimate of the number of patients comprised of children with severe obesity and our estimate of a projected number of adults with severe obesity who have a history of early onset obesity, (y) the estimated prevalence from epidemiology studies of approximately 1% for LepR deficiency and 2% for POMC heterozygous, and (z) our estimated diagnosis rate of up to 40%.

- *Bardet-Biedl Syndrome.* Our addressable patient population estimate for Bardet-Biedl syndrome is approximately 1,500 to 2,500 patients in the United States based on:

  - Published prevalence estimates of one in 100,000 in North America, which projects to approximately 3,250 people in the United States. We believe the majority of these patients are addressable patients; and
  - We believe that with wider availability of genetic testing expected for Bardet-Biedl syndrome and increased awareness of new treatments, the number of patients diagnosed with this disorder will increase.

- *Alström Syndrome.* Our addressable patient population estimate for Alström syndrome is approximately 500 to 1,000 patients worldwide. This estimate is based on:

  - Published prevalence estimates of one in 1,000,000 in North America, which projects to approximately 325 people in the United States. We believe the majority of these patients are addressable patients; and
  - We believe that with wider availability of genetic testing expected for Alström syndrome and increased awareness of new treatments, the number of patients diagnosed with this disorder will increase.

- *POMC Epigenetic Disorders.* There is currently no epidemiology data that defines the prevalence of POMC epigenetic disorders.

We believe that the patient populations in the European Union are at least as large as those in the United States. However, we do not have comparable epidemiological data from the European Union and these estimates are therefore based solely on applying relative population percentages to the Company-derived estimates described above.

We are conducting additional clinical epidemiology studies to strengthen these prevalence projections. In parallel, we are also developing a patient registry for diagnosed patients with POMC deficiency and LepR deficiency which will further inform prevalence projections for these rare genetic orders.

Another method to estimate the size of these ultra-rare populations by genetic epidemiology is using newly available large genomic databases, containing full genome sequencing or exome sequencing. Ultra-rare orphan diseases are generally categorized as those that affect fewer than 20 patients per million. We have begun some substantial efforts with a series of such databases and/or collaborators. Much of our preliminary work has been with a database of approximately 140,000 genomes, which is representative of the U.S. population. These efforts generally are based on the prevalence of heterozygous mutations, as true null mutations are ultra-rare, and then standard scientific methods such as the Hardy-Weinberg equilibrium calculations, are applied to estimate the prevalence in the U.S. population. These methods make assumptions that may not be sufficiently robust for ultra-rare genetic disorders, and have the inherent variability of estimates for rare events. In addition, the databases currently available only provide limited clinical data, such as, age, weight and BMI, that would be needed to associate genetic defects with severe obesity. However, until these data are confirmed in further genetic epidemiology efforts in additional databases, we must continue to base our patient population estimates on clinical epidemiological information.

In addition, if any approval that we obtain is based on a narrower definition of these patient populations than we had anticipated, then the potential market for setmelanotide for these indications will be smaller than we originally believed. In either case, a smaller patient population in our target indications would have a materially adverse effect on our ability to achieve commercialization and generate revenues.

If the actual number of patients suffering from each of the MC4 pathway deficiencies we are targeting is smaller than we estimate or if any approval that we obtain is based on a narrower definition of these patient populations, including pediatric populations, our ability to recruit patients to our trials may be materially adversely affected.

If the actual number of patients with any of the MC4 pathway deficiencies we are targeting is lower than we believe, it may be difficult to recruit patients, and this may affect the timelines for the completion of clinical trials. If we experience delays or difficulties in the enrollment of patients in clinical trials, our receipt of necessary regulatory approvals could also be delayed or prevented.

The pediatric population is an important patient population for setmelanotide and our addressable patient population estimates include pediatric populations. However, it may be more challenging to conduct studies in this population, and to locate and enroll pediatric patients.

We currently are treating patients 12 years of age and older in our trials, but we aim to gain regulatory approval and labeling for patients six years of age and older. Accordingly, we have applied for permission from the FDA and other equivalent competent authorities in the EU member states to enroll these younger patients, aged six to 11, in our pivotal trials. However, there may be issues that preclude this approval including, but not limited to, potential disagreement on dose titration or delivery methods and suitability of patient reported outcomes in younger patients, as well as avoiding over-suppression of normal appetite in adolescents. In addition, the competent authorities in the EU member states may consider the polyethylene glycol vehicle in the product to carry additional risks in pediatric patients. We cannot guarantee that the FDA or other equivalent competent authorities in the EU member states will ultimately grant permission to enroll the younger pediatric patient population, nor can we predict whether they will require additional pre-clinical studies or estimate the timing for approval, if any, of including patients under 12 in our trials or for the use of setmelanotide for such patients at all. The inability to obtain permission from the FDA or other equivalent competent authorities in the EU member states to enroll these younger patients under age 12 may narrow our potential patient population such that we may experience delays in enrolling sufficient numbers of patients in our clinical trials. Furthermore, if the FDA or other equivalent competent authorities in the EU member states do not approve the enrollment of the younger patient population in clinical trials or does not approve the use of setmelanotide in this population, the product candidate will not be labeled for promotion for these patients, even if they approve an NDA for setmelanotide for patients 12 and older.

While we have no knowledge of competitors developing product candidates intended to treat MC4 pathway deficiencies, competitors may emerge. If that were to occur and competitors initiated clinical trials for product candidates that treat the same indications as setmelanotide, patients who would otherwise be eligible for our clinical trials may instead enroll in the clinical trials of our competitors' product candidates.

Patient enrollment is also affected by other factors including:

- the severity of the disease under investigation;
- the eligibility criteria for the clinical trial in question;
- the perceived risks and benefits of the product candidate under study;
- the success of efforts to facilitate timely enrollment in clinical trials;
- the patient referral practices of physicians;
- the ability to monitor patients adequately during and after treatment; and
- the proximity and availability of clinical trial sites for prospective patients.

Our inability to enroll a sufficient number of patients for our clinical trials would result in significant delays, could require us to abandon one or more clinical trials altogether and could delay or prevent our receipt of necessary regulatory approvals. Enrollment delays in our clinical trials may result in increased

development costs for setmelanotide, which would cause the value of our company to decline and limit our ability to obtain additional financing.

Failures or delays in the commencement or completion of our planned clinical trials of setmelanotide could result in increased costs to us and could delay, prevent or limit our ability to generate revenue and continue our business.

We completed Phase 2 clinical trials for setmelanotide in 2016 for POMC deficiency obesity and are currently enrolling Phase 3 clinical trials for setmelanotide for POMC deficiency obesity in 2017. We completed Phase 2 clinical trials for setmelanotide for LepR deficiency obesity, and we expect to enroll the first patient in our LepR deficiency obesity Phase 3 clinical trial in the second half of 2017. We have also initiated Phase 2 clinical trials for Bardet-Biedl syndrome, Alström syndrome, POMC heterozygous deficiency obesity, and POMC epigenetic disorders. Successful completion of such clinical trials is a prerequisite to submitting an NDA to the FDA, a marketing authorization application to the EMA, and other applications for marketing authorization to equivalent competent authorities in foreign jurisdictions, and consequently, the ultimate approval and commercial marketing of setmelanotide. We do not know whether our planned additional Phase 2 or Phase 3 clinical trials will begin or whether any of our clinical trials will be completed on schedule, if at all, as the commencement and completion of clinical trials can be delayed or prevented for a number of reasons, including but not limited to:

- the FDA or other equivalent competent authorities in foreign jurisdictions may deny permission to proceed with our planned Phase 3 clinical trials or any other clinical trials we may initiate, or may place a clinical trial on hold;
- delays in filing or receiving approvals or additional investigational new drug application, or IND, that may be required;
- negative results from our ongoing and planned preclinical studies, or the FDA or other equivalent competent authorities in foreign jurisdictions requiring additional preclinical studies;
- delays in commencing additional necessary preclinical studies, including carcinogenicity and juvenile toxicology studies;
- delays in reaching or failing to reach agreement on acceptable terms with prospective contract research organizations, or CROs, and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- since many already diagnosed patients are at academic sites, delays in conducting clinical trials at academic sites due to the particular challenges and delays typically associated with those sites;
- inadequate quantity or quality of setmelanotide or other materials necessary to conduct clinical trials, including delays in the manufacturing of sufficient supply of finished drug product;
- difficulties obtaining Institutional Review Board, or IRB, and/or ethics committee approval to conduct a clinical trial at a prospective site or sites;
- challenges in recruiting and enrolling patients to participate in clinical trials, including the size and nature of the patient population, the proximity of patients to clinical trial sites, eligibility criteria for the clinical trial, the nature of the clinical trial protocol, the availability of approved effective treatments for the relevant disease and competition from other clinical trial programs for similar indications;
- severe or unexpected drug-related side effects experienced by patients in a clinical trial, including side effects previously identified in our completed clinical trials;
- delays in identifying and recruiting patients with any of the genetic causes of obesity in indications that we are targeting;

- disagreement by the FDA, other regulatory agencies or the equivalent competent authorities in foreign jurisdictions with our clinical trial designs, which may in turn cause delays in initiating our clinical trials, or may lead to rejection of our interpretation of data from clinical trials or to changes in the requirements for approval even after it has reviewed and commented on the design for our clinical trials;

- the requirement to have a placebo controlled study even though the FDA and EMA did not impose one for POMC deficiency obesity, as we cannot be certain that this will be true for other indications or that the FDA or EMA, an advisory committee or the equivalent competent authorities in foreign jurisdictions will not change its guidance, as it has done so in the past for other open control trials;

- uncertainty related to the length of placebo-controlled intervals in clinical trials;

- the need to perform non-inferiority trials, which can be larger, longer and more costly, if treatment is approved for similar indications;

- potential delays in the initiation of our clinical trials of LepR deficiency obesity due to the fact that we have not yet had discussions with the FDA regarding clinical trials for LepR deficiency obesity and, accordingly, do not know if the FDA will disagree with our clinical trial design;

- POMC heterozygous deficiency may have additional challenges, including that the FDA the EMA, or the equivalent competent authorities in foreign jurisdictions may require that we show that setmelanotide works better in these patients than in the genetically normal population; other challenges associated with these patients may include additional delays in initiating clinical trials for this indication due to uncertainty about the subset of these patients who will respond effectively to setmelanotide and the lack of discussion for this indication with the FDA;

- reports from preclinical or clinical testing of other weight loss therapies may raise safety or efficacy concerns; and

- difficulties retaining patients who have enrolled in a clinical trial but may be prone to withdraw due to rigors of the clinical trial, lack of efficacy, side-effects, personal issues or loss of interest.

Clinical trials may also be delayed or terminated as a result of ambiguous or negative interim results. In addition, a clinical trial may be suspended or terminated by us, the FDA or other equivalent competent authorities in foreign jurisdictions, the IRBs or ethics committees at the sites where the IRBs or the ethics committees are overseeing a clinical trial, a data and safety monitoring board, or DSMB, or Safety Monitoring Committee, or SMC, overseeing the clinical trial at issue or other equivalent competent authorities due to a number of factors, including, among others:

- failure to conduct the clinical trial in accordance with regulatory requirements or our clinical trial protocols;

- inspection of the clinical trial operations or trial sites by the FDA or other equivalent competent authorities that reveals deficiencies or violations that require us to undertake corrective action, including the imposition of a clinical hold;

- unforeseen safety issues, adverse side effects or lack of effectiveness;

- changes in government regulations or administrative actions;

- problems with clinical trial supply materials; and

- lack of adequate funding to continue the clinical trial.

Changes in regulatory requirements, FDA or EMA guidance or unanticipated events during our clinical trials of setmelanotide may occur, which may result in changes to clinical trial protocols, changes to instruments for measuring subjective systems or additional clinical trial requirements, which could result in increased costs to us and could delay our development timeline.

Changes in regulatory requirements, FDA guidance, guidance published by the EMA or the other competent authorities in foreign jurisdictions, or unanticipated events during our clinical trials may force us to amend clinical trial protocols or the FDA, or the other competent authorities in foreign jurisdictions may impose additional clinical trial requirements. For instance, the FDA issued draft guidance on developing products for weight management in February 2007. In March 2012, the FDA's Endocrinologic and Metabolic Drugs Advisory Committee met to discuss possible changes to how the FDA evaluates the cardiovascular safety of weight-management drugs, and the FDA may require additional studies to support registration. In addition, the FDA is considering broader applicability of requirements for cardiovascular outcomes trials, or CVOTs, presenting the possibility of cardiovascular risk pre-approval, including for obesity products. While our Phase 3 discussions with the FDA have not resulted in a requirement for any of these activities, any future requirement for these activities could result in additional clinical requirements for setmelanotide, increase our costs and delay approval of setmelanotide.

Amendments to our clinical trial protocols would require resubmission to the FDA and IRBs or other competent authorities and ethics committees in foreign jurisdictions for review and approval, which may adversely impact the cost, timing or successful completion of a clinical trial. If we experience delays completing, or if we terminate, any of our clinical trials, or if we are required to conduct additional clinical trials, the commercial prospects for setmelanotide may be harmed and our ability to generate product revenue will be delayed.

In addition, as part of commencing our Phase 3 clinical trial for setmelanotide in POMC deficiency obesity, we sought FDA concurrence with, and received substantial input on, the use of Patient Reported Outcome, or PRO, and Observer Reported Outcome, or ORO questionnaires for measuring subjective endpoints for changes in hunger and/or food-seeking behavior and compulsions. A PRO is a measurement based on a report that comes from the patient about the status of a patient's health condition, without amendment or interpretation of the patient's response by a clinician or anyone else. An ORO is a measurement based on an observation by someone other than the patient or a health professional, such as a parent, spouse or other non-clinical caregiver who is in a position to regularly observe and report on a specific aspect of the patient's health. In our Phase 3 clinical trial for setmelanotide, based on the FDA feedback, we plan to measure the ability of setmelanotide to mitigate hunger and/or hyperphagia, the overriding physiological drive to eat, through PRO and ORO questionnaires. The questionnaires are designed to elicit feedback from patients on how well setmelanotide decreases their hunger, and from their family members or caregivers on the effect of setmelanotide on the patients' food seeking behavior.

To our knowledge, no sponsor of an approved drug has yet used PRO or ORO questionnaires to generate data on hyperphagia or hunger mitigating endpoints. Because we may be relying on clinical endpoints that have not previously been the subject of prior FDA approvals, there is a risk that the FDA or other equivalent competent authorities in foreign jurisdictions may not consider the endpoints to provide evidence of clinically meaningful results or that results may be difficult for the FDA to interpret, in particular for the pediatric age group. If we experience delays in our ongoing validation of our PRO or ORO questionnaires, or do not receive agreement with those proposed questionnaires based on the conceptual framework, content reliability, other measures of validity, or their ability to detect changes in hyperphagia or hunger, we may experience delays in our trials or in product approval as well as be unable to reference data on hyperphagia or hunger in our product labeling. Finally, our Phase 3 clinical trials will be assessing hunger using multiple methods, some of which were previously used in Phase 2, but some of which were initiated in Phase 3 trials and for which little data is available. Hence it is possible that the effects on hunger seen in Phase 2 trials may differ with some of the new methodologies for assessing hunger being used in Phase 3 trials, or may not support language in the proposed product labeling.

Setmelanotide may cause undesirable side effects that could delay or prevent regulatory approval, limit the commercial profile of an approved labeling, or result in significant negative consequences following marketing approval, if any.

First generation MC4R agonists were predominantly small molecules that failed in clinical trials due to significant safety issues, particularly increases in blood pressure, and had limited efficacy. Undesirable side effects caused by setmelanotide could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive labeling or the delay or denial of regulatory approval by the FDA or other equivalent competent authorities in foreign jurisdictions.

Setmelanotide is an MC4R agonist. Potential side effects of MC4R agonism, which have been noted either with setmelanotide or with other MC4R agonists in clinical trials and preclinical studies, may include:

- adverse effects on cardiovascular parameters, such as increases in heart rate and blood pressure;
- erections in males and similar effects in women, such as sexual arousal, clitoral swelling and hypersensitivity;
- nausea and vomiting;
- reduced appetite;
- effects on mood, depression, anxiety and other psychiatric manifestations; and
- other effects, specifically back pain, headaches, fatigue, diarrhea and joint pain, that have been seen numerically more frequently in setmelanotide-treated patients as compared with placebo patients.

Injection site reactions have been seen in subcutaneous, or SC injections with setmelanotide. In addition, setmelanotide has likely off-target effects on the closely-related MC1 receptor, which mediates tanning in response to sun exposure. Other MC1 mediated effects include darkening of skin blemishes, such as freckles and moles, and hair color change in one subject. These effects have generally been reversible in clinical trials, but it is still unknown if they will be reversible with long-term exposure. The MC1 mediated effects may also carry risks. The long-term impact of MC1 activation has not been tested in clinical trials, and could potentially include increases in skin cancer, excess biopsy procedures and cosmetic blemishes. These skin changes may also result in unblinding, which could make interpretation of clinical trial results more complex and possibly subject to bias.

The safety data we have disclosed to date represents our interpretation of the data at the time of disclosure and they are subject to our further review and analysis. The only serious adverse event possibly attributed to setmelanotide in our clinical trials was one report of atypical chest pain seen in our Phase 2 clinical trial with once daily SC injection, although there was no evidence of any serious respiratory or cardiac cause on careful examination. Overall, there have been five other serious adverse events in the overall clinical development program in addition to the serious adverse event described above: two others during treatment on setmelanotide, left arm numbness and influenza immunization reaction and three during treatment with placebo, including biliary dyskinesia, severe groin strain and pelvic inflammatory disease. None of these serious adverse events was considered related to setmelanotide.

We are also initiating trials of setmelanotide in potential new indications that include patients who might have more serious underlying conditions, such as Alström syndrome and lipodystrophy. It is possible that the underlying conditions in these patients, such as congestive heart failure and pancreatitis, may confound the understanding of the safety profile of setmelanotide.

In addition, our interpretation of the safety data from our clinical trials is contingent upon the review and ultimate approval of the FDA, other regulatory authorities or other equivalent competent authorities in foreign jurisdictions. The FDA or other equivalent competent authorities in foreign jurisdictions may

not agree with our methods of analysis or our interpretation of the results. In addition, the long-term effects of setmelanotide have only been tested in a limited number of patients.

Further, if setmelanotide receives marketing approval and we or others identify undesirable side effects caused by the product, or any other similar product, before or after the approval, a number of potentially significant negative consequences could result, including:

- regulatory authorities may request that we withdraw the product from the market or may limit their approval of the product through labeling or other means;
- regulatory authorities may require the addition of labeling statements, such as a "boxed" warning or a contraindication;
- the FDA and other equivalent competent authorities in foreign jurisdictions may require the addition of a Risk Evaluation and Mitigation Strategy, or REMS, or other specific obligations as a condition for marketing authorization due to the need to limit treatment to rare patient populations, or to safety concerns;
- we may be required to change the way the product is distributed or administered, conduct additional clinical trials or change the labeling of the product;
- we may decide to remove the product from the marketplace;
- we could be sued and held liable for injury caused to individuals exposed to or taking the product; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of setmelanotide and could substantially increase the costs of commercializing setmelanotide and significantly impact our ability to successfully commercialize setmelanotide and generate revenues.

Although we have been granted orphan drug designation for setmelanotide in treating POMC deficiency obesity, we may be unable to obtain orphan drug designation for other uses or to obtain exclusivity in any use. Even with exclusivity, competitors may obtain approval for different drugs that treat the same indications as setmelanotide.

The FDA may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act of 1983, or the Orphan Drug Act, the FDA may designate a product candidate as an orphan drug if it is intended to treat a rare disease or condition, which is defined under the Federal Food, Drug and Cosmetic Act, or FDCA, as having a patient population of fewer than 200,000 individuals in the United States, or a patient population greater than 200,000 in the United States where there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the United States.

Generally, if a product candidate with an orphan drug designation receives the first marketing approval for the indication for which it has such designation, the product is entitled to a period of seven years of marketing exclusivity, which precludes the FDA from approving another marketing application for a product that constitutes the same drug treating the same indication for that marketing exclusivity period, except in limited circumstances.

The exclusivity period in the United States can be extended by six months if the NDA sponsor submits pediatric data that fairly respond to a written request from the FDA for such data. Even under these circumstances, we may not be granted pediatric approval from the FDA for these indications. Orphan drug exclusivity may be revoked if the FDA determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the product to meet the needs of patients with the rare disease or condition. Other potential benefits of orphan drug designation and/or approval of a designated drug include eligibility for: exemption from certain prescription drug user fees, tax credits for

certain qualified clinical testing expenses, and waivers from the pediatric assessment requirements of the Pediatric Research Equity Act, or PREA.

Although we have been granted orphan drug designation for setmelanotide in treating POMC deficiency obesity, if we request orphan drug designation for setmelanotide for other uses, there can be no assurance that the FDA will grant such designation. For example, if the population of patients who would be appropriate candidates for a drug is 200,000 or more individuals, the drug may not qualify for orphan drug designation, even if the population for which the sponsor seeks approval is lower than 200,000. Additionally, the designation of setmelanotide as an orphan drug does not guarantee that the FDA will accelerate regulatory review of, or ultimately approve, setmelanotide.

Even if we obtain orphan drug exclusivity for setmelanotide, that exclusivity may not effectively protect setmelanotide from competition because different drugs can be approved for the same condition. In the United States, even after an orphan drug is approved, the FDA may subsequently approve another drug for the same condition if the FDA concludes that the latter drug is not the same drug or is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care.

On August 3, 2017, Congress passed the FDA Reauthorization Act of 2017, or the FDARA. FDARA, among other things, codified the FDA's pre-existing regulatory interpretation, to require that a drug sponsor demonstrate the clinical superiority of an orphan drug that is otherwise the same as a previously approved drug for the same rare disease in order to receive orphan drug exclusivity. The new legislation reverses prior precedent holding that the Orphan Drug Act unambiguously requires that the FDA recognize the orphan exclusivity period regardless of a showing of clinical superiority. The FDA may further reevaluate the Orphan Drug Act and its regulations and policies. We do not know if, when, or how the FDA may change the orphan drug regulations and policies in the future, and it is uncertain how any changes might affect our business. Depending on what changes the FDA may make to its orphan drug regulations and policies, our business could be adversely impacted.

Although we have obtained breakthrough therapy designation for setmelanotide for the treatment of obesity associated with genetic defects upstream of the MC4 receptor in the leptin-melanocortin pathway, which includes both POMC deficiency obesity and LepR deficiency obesity, the FDA may rescind the breakthrough designation and we may be unable to obtain breakthrough therapy designation for other uses. In addition, breakthrough therapy designation by the FDA may not lead to a faster development, regulatory review or approval process, and it does not increase the likelihood that setmelanotide will receive marketing approval in the United States.

Under the Food and Drug Administration Safety and Innovation Act, or FDASIA, the FDA is authorized to give certain products "breakthrough therapy designation." Breakthrough therapy product candidate is defined as a product candidate that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that such product candidate may demonstrate substantial improvement on one or more clinically significant endpoints over existing therapies. The FDA will seek to ensure the sponsor of breakthrough therapy product candidate receives intensive guidance on an efficient drug development program, intensive involvement of senior managers and experienced staff on a proactive, collaborative and cross-disciplinary review and a rolling review process whereby the FDA may consider reviewing portions of an NDA before the sponsor submits the complete application. Product candidates designated as breakthrough therapies by the FDA may be eligible for other expedited programs, such as priority review, if supported by clinical data.

Designation as breakthrough therapy is within the discretion of the FDA. Accordingly, even if we believe setmelanotide meets the criteria for designation as breakthrough therapy for other uses, the FDA may disagree. In any event, the receipt of breakthrough therapy designation for a product candidate, or acceptance for one or more of the FDA's other expedited programs, may not result in a faster development process, review or approval compared to products considered for approval under conventional FDA

procedures and does not guarantee ultimate approval by the FDA. Additionally, the FDA may later decide that the product candidate no longer meets the conditions for designation and may withdraw designation at any time or decide that the time period for FDA review or approval will not be shortened.

We may not be able to translate the current formulations of setmelanotide for methods of delivery that would be acceptable to the FDA or other equivalent competent authorities in foreign jurisdictions or commercially successful.

Setmelanotide is currently administered by SC injection using small insulin-type needles. SC injection is generally less well-received by patients than other methods of administration, such as oral administration. Considerable additional resources and efforts, including potential studies, may be necessary in order to translate the current formulations of setmelanotide into forms that will be well-received by patients.

We have entered into a license agreement with Camurus AB, or Camurus, for the use of Camurus' drug delivery technology, FluidCrystal, to formulate setmelanotide. This formulation, if successfully developed for setmelanotide, will be delivered subcutaneously, similar to our current formulation, except that we anticipate it will be injected once weekly.

While we plan to utilize the current formulation, or to develop new and useful formulations and delivery technology for setmelanotide, we cannot estimate the probability of success, nor the resources and time needed to succeed. If we are unable to utilize this formulation, or to develop new formulations, setmelanotide may not achieve significant market acceptance and our business, financial condition and results of operations may be materially harmed.

Our approach to treating patients with MC4 pathway deficiencies requires the identification of patients with unique genetic subtypes, for example, POMC genetic deficiency. The FDA or other equivalent competent authorities in foreign jurisdictions could require the approval or CE mark of an in vitro companion diagnostic device to ensure appropriate selection of patients as a condition of approving setmelanotide. The development and approval or CE mark of an in vitro companion diagnostic device would require substantial financial resources and could delay regulatory approval of setmelanotide.

We intend to focus our development of setmelanotide as a treatment for obesity caused by certain genetic deficiencies affecting the MC4 pathway. In order to assist in identifying this subset of patients, we employ a genetic diagnostic test, which is a test or measurement that evaluates the presence of genetic variants in a patient. The FDA has advised that for our clinical trial of setmelanotide to treat POMC deficiency obesity, it will be sufficient to use genetic diagnostic testing known as Sanger bi-directional nucleotide sequencing, as long as that testing is performed by laboratories meeting the standards of the Clinical Laboratory Improvement Amendments, or CLIA, for Laboratory Developed Tests, or LDTs. Currently the Centers for Medicare and Medicaid Services, or CMS, regulates LDTs and the laboratories that develop them, and enforces CLIA. CMS evaluates whether there is clinical utility for each specific test, and also performs postmarket oversight of laboratory operational processes. CMS coverage determinations of clinical utility measure the ability of the test to impact clinically meaningful health outcomes, such as mortality or morbidity, through the adoption of efficacious treatments. CMS's oversight through the CLIA program is designed to confirm that a lab assesses analytical validity, but does not confirm whether it had results from an analytical validity assessment that were sufficient to support the claimed intended use of the test. The FDA has issued guidance indicating, however, that in the future it intends to assert jurisdiction over LDTs and to increase regulatory requirements for LDTs. If the FDA does so, the burdens and costs of using LDTs to select patients for setmelanotide could increase, the availability of those LDTs could be negatively affected, and our development program for setmelanotide could be delayed, which in turn could delay or impair our ability to proceed to commercialization.

Although the FDA has advised us that an LDT is sufficient for identifying patients in our clinical trials, the agency also indicated that approval of an *in vitro* companion diagnostic device may be necessary should clinical results reveal that genetic testing is needed for the safe use of setmelanotide, such as to avoid significant toxicities in certain patients or because the drug might provide only marginal benefits except in a very clearly defined eligible population. *In vitro* companion diagnostic devices provide information that is essential for the safe and effective use of a corresponding therapeutic product. These companion diagnostic devices may be co-developed with a device manufacturer or with a laboratory, and generally require FDA approval as well.

Should the FDA or other equivalent competent authorities in foreign jurisdictions require the use of a companion diagnostic device, we may face significant delays or obstacles in obtaining approval of an NDA, or of comparable foreign marketing authorization for setmelanotide as the FDA or other equivalent competent authorities in foreign jurisdictions may take the position that a companion diagnostic is required prior to granting approval of setmelanotide. In addition, we may be dependent on the sustained cooperation and effort of third-party collaborators with whom we may partner in the future to develop *in vitro* companion diagnostic devices. We and our potential future collaborators may encounter difficulties in developing such tests, including issues relating to the selectivity and/or specificity of the diagnostic, analytical validation, reproducibility or clinical validation. Any delay or failure by us or our potential future collaborators to develop or obtain regulatory clearance or approval of, or to CE mark, such tests, if necessary, could delay or prevent approval of setmelanotide.

If the FDA deems setmelanotide to require an *in vitro* companion diagnostic device to accurately identify the patients who belong to the target subset, the FDA will require product labeling that limits use to only those patients who express the genetic variants identified by the device. Moreover, even if setmelanotide and an *in vitro* companion diagnostic device are approved together, the device itself may be subject to reimbursement limitations that could limit access to treatment and therefore adversely affect our business and financial results.

We have only one product candidate and we may not be successful in any future efforts to identify and develop additional product candidates.

We have only one product candidate and may seek to identify and develop additional product candidates, both within and outside of our current area of expertise. If so, the success of our business may depend primarily on our ability to identify, develop and commercialize these products. Research programs to identify new product candidates require substantial technical, financial and human resources. We may fail to identify other potential product candidates for clinical development for a number of reasons. Our research methodology may be unsuccessful in identifying potential product candidates or our potential product candidates may be shown to have harmful side effects or may have other characteristics that may make the products unmarketable or unlikely to receive marketing approval. We may focus our efforts and resources on potential programs or product candidates that ultimately prove to be unsuccessful. In addition, any such efforts could adversely impact our continued development and commercialization of setmelanotide.

If any of these events occur, we may be forced to abandon some or all of our development efforts for a program or programs, which would have a material adverse effect on our business and could potentially cause us to cease operations.

Prader-Willi syndrome, or PWS, is a complex disease, and companies have had difficulties in developing new therapies for PWS. In addition, PWS patients may carry special risks, due to the disease, which may add risk to clinical trials in these patients.

Although we have been granted orphan drug designation for setmelanotide in treating PWS, we are not moving directly towards a Phase 3 trial in PWS at this time, but instead will be assessing how to

proceed in another Phase 2 trial. We do not know the probability that we will be able to proceed to Phase 3 and/or approval, even when these efforts are completed. In addition, the experience by others suggests that PWS patients are high risk for adverse experiences and hence clinical trials in that population are extremely challenging. It may be both difficult to determine if adverse effects in this population are due to the disease, setmelanotide or some combination of both. PWS is a complex multigenic disease, and the hypothesis that PWS is an upstream MC4 pathway disorder is supported primarily on the role of only one of those genes, MAGEL2, in animal models of obesity. Our results may support that PWS is not an upstream MC4 pathway disorder. Alternatively, other design factors may have influenced the outcome of this trial, and we will be reassessing in 2018 the possibility of future Phase 2 trials in PWS that address the following potential factors: duration of treatment, younger age of population, improved setmelanotide pharmacokinetics, consideration of higher doses, and operational limitations of the completed Phase 2 trial. There can be no assurances that some of the factors that affected the results of the PWS trials will not also adversely impact the results of our trials for other indications.

Risks Related to the Commercialization of Setmelanotide

Even if approved, reimbursement policies could limit our ability to sell setmelanotide.

Market acceptance and sales of setmelanotide will depend on reimbursement policies and may be affected by healthcare reform measures. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels for those medications. Cost containment is a primary concern in the U.S. healthcare industry and in foreign jurisdictions. Government authorities and these third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. We cannot be sure that reimbursement will be available for setmelanotide and, if reimbursement is available, the level of such reimbursement. Reimbursement may impact the demand for, or the price of setmelanotide. If reimbursement is not available or is available only at limited levels, we may not be able to successfully commercialize setmelanotide.

In some foreign countries, particularly in Canada and in the EU member states, the pricing of prescription pharmaceuticals is subject to strict governmental control. In these countries, pricing negotiations with governmental authorities can take six to 12 months or longer after the receipt of regulatory approval and product launch. To obtain favorable reimbursement for the indications sought or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of setmelanotide with other available therapies. If reimbursement for setmelanotide is unavailable in any country in which we seek reimbursement, if it is limited in scope or amount, if it is conditioned upon our completion of additional clinical trials or if pricing is set at unsatisfactory levels, our operating results could be materially adversely affected.

In the European Union, in particular, each EU member state can restrict the range of medicinal products for which its national health insurance system provides reimbursement and can control the prices of medicinal products for human use marketed in its territory. As a result, following receipt of marketing authorization in an EU member state, through any application route, an applicant is required to engage in pricing discussions and negotiations with the competent pricing authority in the individual EU member states. Some EU member states operate positive and negative list systems under which products may only be marketed once a reimbursement price has been agreed upon. Other EU member states approve a specific price for the medicinal product or may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. The downward pressure on healthcare costs in general, particularly prescription drugs, has become more intense. As a result, increasingly high barriers are being erected to the entry of new products. In addition, we may face competition for setmelanotides from lower priced products in foreign countries that have placed price controls on pharmaceutical products.

Health Technology Assessment, or HTA, of medicinal products, however, is becoming an increasingly common part of the pricing and reimbursement procedures in some EU member states, including the United Kingdom, France, Germany, Ireland, Italy and Sweden. HTA is the procedure according to which the assessment of the public health impact, therapeutic impact and the economic and societal impact of use of a given medicinal product in the national healthcare systems of the individual country is conducted. HTA generally focuses on the clinical efficacy and effectiveness, safety, cost, and cost-effectiveness of individual medicinal products as well as their potential implications for the healthcare system. Those elements of medicinal products are compared with other treatment options available on the market. The outcome of HTA regarding specific medicinal products will often influence the pricing and reimbursement status granted to these medicinal products by the competent authorities of individual EU member states. The extent to which pricing and reimbursement decisions are influenced by the HTA of the specific medicinal product varies between EU member states. In addition, pursuant to Directive 2011/24/EU on the application of patients' rights in cross-border healthcare, a voluntary network of national authorities or bodies responsible for HTA in the individual EU member states was established. The purpose of the network is to facilitate and support the exchange of scientific information concerning HTAs. This may lead to harmonization of the criteria taken into account in the conduct of HTAs between EU member states and in pricing and reimbursement decisions and may negatively affect price in at least some EU member states.

If we are unable to establish sales and marketing capabilities or enter into agreements with third parties to market and sell setmelanotide, if approved, we may not be able to generate any revenue.

We do not currently have infrastructure in place for the sale, marketing or distribution of pharmaceutical products. In order to market setmelanotide, if approved by the FDA or other equivalent competent authorities in foreign jurisdictions, we must build our sales, marketing, managerial and other non-technical capabilities or make arrangements with third parties to perform these services. If we are unable to establish adequate sales, marketing and distribution capabilities, whether independently or with third parties, or if we are unable to do so on commercially reasonable terms, our business, results of operations, financial condition and prospects would be materially adversely affected.

Even if we receive marketing approval for setmelanotide in the United States, we may never receive regulatory approval to market setmelanotide outside of the United States.

We intend to pursue marketing approval for setmelanotide in the European Union and in other countries worldwide. In order to market any product outside of the United States, we must establish and comply with the numerous and varying safety, efficacy and other regulatory requirements of other countries. Approval procedures vary among countries and can involve additional setmelanotide testing and additional administrative review periods. The time required to obtain approvals in other countries might differ from that required to obtain FDA approval. The marketing approval processes in other countries may implicate all of the risks detailed above regarding FDA approval in the United States as well as other risks. In particular, in many countries outside of the United States, products must receive pricing and reimbursement approval before the product can be commercialized. Obtaining this approval can result in substantial delays in bringing products to market in such countries. Marketing approval in one country does not ensure marketing approval in another, but a failure or delay in obtaining marketing approval in one country may have a negative effect on the regulatory process or commercial activities in others. Failure to obtain marketing approval in other countries or any delay or other setback in obtaining such approval would impair our ability to market setmelanotide in such foreign markets. Any such impairment would reduce the size of our potential market share and could have a material adverse impact on our business, results of operations and prospects.

Even if we receive marketing approval for setmelanotide, we may not achieve market acceptance, which would limit the revenue that we generate from the sale of setmelanotide.

The commercial success of setmelanotide, if approved by the FDA or other equivalent competent authorities in foreign jurisdictions, will also depend upon the awareness and acceptance of setmelanotide within the medical community, including physicians, patients and third-party payors. If setmelanotide is approved but does not achieve an adequate level of acceptance by patients, physicians and third-party payors, we may not generate sufficient revenue to become or remain profitable. Before granting reimbursement approval, third-party payors may require us to demonstrate that, in addition to treating obesity caused by certain genetic deficiencies affecting the MC4 pathway, setmelanotide also provides incremental health benefits to patients. Our efforts to educate the medical community and third-party payors about the benefits of setmelanotide may require significant resources and may never be successful. All of these challenges may impact our ability to ever successfully market and sell setmelanotide.

Market acceptance of setmelanotide, if approved, will depend on a number of factors, including, among others:

- the ability of setmelanotide to treat obesity caused by certain genetic deficiencies affecting the MC4 pathway and, if required by any competent authority in connection with the approval for these indications, to provide patients with incremental health benefits, as compared with other available treatments, therapies, devices or surgeries;
- the relative convenience and ease of SC injections as the necessary method of administration of setmelanotide, including as compared with other treatments for obese patients;
- the prevalence and severity of any adverse side effects associated with setmelanotide;
- limitations or warnings contained in the labeling approved, as well as the existence of a REMS, for setmelanotide by the FDA or the specific obligations imposed as a condition for marketing authorization imposed by other equivalent competent authorities in foreign jurisdictions, particularly by the European Commission;
- availability of alternative treatments, including a number of obesity therapies already approved or expected to be commercially launched in the near future;
- the size of the target patient population, and the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the ability of setmelanotide to treat the maximum range of pediatric patients, and any limitations on its indications for use, such as if the labeling limits the approved population to patients ages 12 and above;
- the strength of marketing and distribution support and timing of market introduction of competitive products;
- publicity concerning setmelanotide or competing products and treatments;
- pricing and cost effectiveness;
- the effectiveness of our sales and marketing strategies;
- our ability to increase awareness of setmelanotide through marketing efforts;
- our ability to obtain sufficient third-party coverage or reimbursement;
- the willingness of patients to pay out-of-pocket in the absence of third-party coverage; and
- the likelihood that the FDA or other equivalent competent authorities in foreign jurisdictions may require development of a REMS as a condition of approval or post-approval, may not agree with

our proposed REMS or may impose additional requirements that limit the promotion, advertising, distribution or sales of setmelanotide.

Our industry is intensely competitive. If we are not able to compete effectively against current and future competitors, we may not be able to generate revenue from the sale of setmelanotide, our business will not grow and our financial condition and operations will suffer.

The biotechnology and pharmaceutical industries are intensely competitive and subject to rapid and significant technological change. We have competitors in a number of jurisdictions, many of which have substantially greater name recognition, commercial infrastructures and financial, technical and personnel resources than we have. Established competitors may invest heavily to quickly discover and develop compounds that could make setmelanotide obsolete or uneconomical. Any new product that competes with an approved product may need to demonstrate compelling advantages in efficacy, convenience, tolerability and safety to be commercially successful. Other competitive factors, including generic competition, could force us to lower prices or could result in reduced sales. In addition, new products developed by others could emerge as competitors to setmelanotide. If we are not able to compete effectively against our current and future competitors, our business will not grow and our financial condition and operations will suffer.

Currently, there are no approved or effective current treatments for regulating hunger and hyperphagia related behaviors of patients with POMC deficiency obesity, LepR deficiency obesity, Bardet-Biedl syndrome, Alström syndrome, POMC heterozygous deficiency obesity, or POMC epigenetic disorders. Bariatric surgery is not a treatment option for these genetic disorders of obesity because the severe obesity and hyperphagia associated with these disorders are considered to be risk factors for bariatric surgery. While we are unaware of any competitive products in development for the obesity and hyperphagia caused by MC4 pathway deficiencies specifically, new competitors may emerge which could limit our business opportunity in the future.

We face potential product liability exposure, and, if claims are brought against us, we may incur substantial liability.

The use of setmelanotide in clinical trials and the sale of setmelanotide, if approved, exposes us to the risk of product liability claims. Product liability claims might be brought against us by patients, healthcare providers or others selling or otherwise coming into contact with setmelanotide. For example, we may be sued if any product we develop allegedly causes injury or is found to be otherwise unsuitable during product testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design or a failure to warn of dangers inherent in the product, including as a result of interactions with alcohol or other drugs, negligence, strict liability and a breach of warranties. Claims could also be asserted under state consumer protection laws. If we become subject to product liability claims and cannot successfully defend ourselves against them, we could incur substantial liabilities. In addition, regardless of merit or eventual outcome, product liability claims may result in, among other things:

- withdrawal of patients from our clinical trials;
- substantial monetary awards to patients or other claimants;
- decreased demand for setmelanotide or any future product candidates following marketing approval, if obtained;
- damage to our reputation and exposure to adverse publicity;
- litigation costs;
- distraction of management's attention from our primary business;
- loss of revenue; and

- the inability to successfully commercialize setmelanotide or any future product candidates, if approved.

We maintain product liability insurance coverage for our clinical trials with a $10.0 million annual aggregate coverage limit. Our insurance coverage may be insufficient to reimburse us for any expenses or losses we may suffer. Moreover, in the future, we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses, including if insurance coverage becomes increasingly expensive. If and when we obtain marketing approval for setmelanotide, we intend to expand our insurance coverage to include the sale of commercial products. However, we may not be able to obtain this product liability insurance on commercially reasonable terms. Large judgments have been awarded in class action lawsuits based on drugs that had unanticipated side effects. The cost of any product liability litigation or other proceedings, even if resolved in our favor, could be substantial, particularly in light of the size of our business and financial resources. A product liability claim or series of claims brought against us could cause our stock price to decline and, if we are unsuccessful in defending such a claim or claims and the resulting judgments exceed our insurance coverage, our financial condition, business and prospects could be materially adversely affected.

Risks Related to Our Dependence on Third Parties

We rely, and expect that we will continue to rely, on third parties to conduct clinical trials for setmelanotide. If these third parties do not successfully carry out their contractual duties or meet expected deadlines, we may not be able to obtain regulatory approval for or commercialize setmelanotide and our business could be substantially harmed.

We enter into agreements with third-party CROs to provide monitors for and to manage data for our ongoing clinical trials. We rely heavily on these parties for the execution of clinical trials for setmelanotide and control only certain aspects of their activities. As a result, we have less direct control over the conduct, timing and completion of these clinical trials and the management of data developed through the clinical trials than would be the case if we were relying entirely upon our own staff. Communicating with outside parties can also be challenging, potentially leading to mistakes as well as difficulties in coordinating activities. However, we remain responsible for the conduct of these trials and are subject to enforcement which may include civil and criminal liabilities for any violations of FDA rules and regulations and the comparable foreign regulatory provisions during the conduct of our clinical trials. Outside parties may:

- have staffing difficulties;
- fail to comply with contractual obligations;
- devote inadequate resources to our clinical trials;
- experience regulatory compliance issues;
- undergo changes in priorities or become financially distressed; or
- form more favorable relationships with other entities, some of which may be our competitors.

These factors may materially adversely affect the willingness or ability of third parties to conduct our clinical trials and may subject us to unexpected cost increases that are beyond our control. Nevertheless, we are responsible for ensuring that each of our studies is conducted in accordance with the applicable protocol, legal, regulatory and scientific standards, and our reliance on CROs does not relieve us of our regulatory responsibilities. We and our CROs are required to comply with current Good Clinical Practices, or cGCPs, which are guidelines enforced by the FDA, the Competent Authorities of the EU member states and equivalent competent authorities in foreign jurisdictions for any products in clinical development. The FDA enforces these regulations and cGCP guidelines through periodic inspections of clinical trial sponsors, principal investigators and trial sites. If we or our CROs fail to comply with applicable cGCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or other equivalent competent authorities in foreign jurisdictions may require us to perform additional clinical trials before

approving our marketing applications. We cannot assure you that, upon inspection, the FDA will determine that any of our clinical trials comply with cGCPs. In addition, our clinical trials must be conducted with products produced under current Good Manufacturing Practices, or cGMPs. Our failure or the failure of our CROs to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process and could also subject us to enforcement action up to and including civil and criminal penalties.

If any of our relationships with these third-party CROs terminate, we may not be able to enter into arrangements with alternative CROs. If CROs do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain are compromised due to the failure to adhere to our clinical protocols, regulatory requirements or for other reasons, any such clinical trials may be extended, delayed or terminated, and we may not be able to obtain regulatory approval for, or successfully commercialize, setmelanotide. As a result, our financial results and the commercial prospects for setmelanotide in the subject indication would be harmed, our costs could increase and our ability to generate revenue could be delayed.

We rely completely on third-party suppliers to manufacture our clinical drug supplies of setmelanotide, and we intend to rely on third parties to produce commercial supplies of setmelanotide and preclinical, clinical and commercial supplies of any future product candidate.

We do not currently have, nor do we plan to acquire, the infrastructure or capability to internally manufacture our clinical drug supply of setmelanotide, or any future product candidates, for use in the conduct of our preclinical studies and clinical trials, and we lack the internal resources and the capability to manufacture any product candidate on a clinical or commercial scale. The facilities used by our contract manufacturing organizations, or CMOs, to manufacture the active pharmaceutical ingredient, or API, and final drug product must pass inspection by the FDA and other equivalent competent authorities in foreign jurisdictions pursuant to inspections that would be conducted after we submit our NDAs or relevant foreign regulatory submission to the other equivalent competent authorities in foreign jurisdictions. In addition, our clinical trials must be conducted with products produced under cGMP regulations. Our failure or the failure of our CROs or CMOs to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process and could also subject us to enforcement action, including civil and criminal penalties. If we import any drugs or drug substances, we would be subject to FDA and U.S. Bureau of Customs and Border Patrol, or CBP, import regulation requirements. Such enforcement for our failure or our CROs or CMOs' failure to comply with these regulations could result in import delays, detention of products, and, depending on criteria such as the history of violative activities, the FDA could place a foreign firm or certain drug substances or products on Import Alert and require that all such drug substances or products be subject to detention without physical examination, or DWPE, which could significantly impact the global supply chain for setmelanotide. FDARA provides that prescription drug products, with the exception of those on the FDA's drug shortage list or properly imported by individuals, may not be imported for commercial use if they were manufactured in a foreign country, unless they have been approved or are otherwise authorized to be marketed in the United States and are labeled accordingly.

We currently contract with a third party for the manufacture of setmelanotide and intend to continue to do so in the future. We have entered into a process development and manufacturing services agreement with Corden Pharma Brussels S.A, or Corden, formerly Peptisyntha SA prior to its acquisition by Corden, under which Corden will provide certain process development and manufacturing services in connection with the manufacture of setmelanotide. We have also entered into a process development and manufacturing services agreement with Recipharm Monts S.A.S, or Recipharm, under which Recipharm will provide certain process development and manufacturing services in connection with the manufacture of setmelanotide. Under our agreements, we pay both Corden and Recipharm for services in accordance with the terms of mutually agreed upon work orders, which we, Corden and Recipharm may enter into

from time to time. The agreement with Corden also provides that, subject to certain conditions, for a period following each product launch date, we will source from Corden a portion of our requirements for that product being sourced from non-affiliate third parties. We may need to engage additional third-party suppliers to manufacture our clinical drug supplies. In the future, if we approach commercialization of setmelanotide or any future product candidate, we will need to engage other third parties to assist in, among other things, labeling, packaging, distribution, post-approval safety reporting, and pharmacovigilance activities. We cannot be certain that we can engage third-party suppliers on terms as favorable as those that are currently in place.

We do not perform the manufacturing of any drug products, and are completely dependent on, our CMOs to comply with cGMPs for manufacture of both API and finished drug product. We recognize that we are ultimately responsible for ensuring that our drug substances and finished product are manufactured in accordance with cGMPs, and, therefore, the company's management practices and oversight, including routine auditing, are critical. If our CMOs cannot successfully manufacture material that conform to our specifications and the strict regulatory requirements of the FDA or other equivalent competent authorities in foreign jurisdictions, they may be subject to administrative and judicial enforcement for non-compliance and the drug products would be deemed misbranded or adulterated and prohibited from distribution into interstate commerce. Furthermore, all of our CMOs are engaged with other companies to supply and/or manufacture materials or products for such companies, which exposes our manufacturers to regulatory risks for the production of such materials and products. As a result, failure to satisfy the regulatory requirements for the production of those materials and products may affect the regulatory clearance of our CMOs' facilities generally. If the FDA or another equivalent competent foreign regulatory agency does not approve these facilities for the manufacture of setmelanotide or if it withdraws its approval in the future, we may need to find alternative manufacturing facilities, which would adversely impact our ability to develop, obtain regulatory approval for or market setmelanotide.

We are currently in the process of manufacturing finished drug product for use in our upcoming clinical trials. We believe we currently have a sufficient amount of finished setmelanotide, diluent and placebo to complete our planned clinical trials. However, these projections could change based on delays encountered with manufacturing activities, equipment scheduling and material lead times. Any such delays in the manufacturing of finished drug product could delay our planned clinical trials of setmelanotide, which could delay, prevent or limit our ability to generate revenue and continue our business.

We do not have long-term supply agreements in place with our contractors, and each batch of setmelanotide is individually contracted under a quality and supply agreement. If we engage new contractors, such contractors must be approved by the FDA and other equivalent competent authorities in foreign jurisdictions. We will need to submit information to the FDA and other equivalent competent authorities in foreign jurisdictions describing the manufacturing changes. If manufacturing changes occur post-approval, the FDA will have to approve these changes. We plan to continue to rely upon CMOs and, potentially, collaboration partners to manufacture commercial quantities of setmelanotide, if approved. Our current scale of manufacturing appears adequate to support all of our current needs for clinical trial supplies for setmelanotide. If setmelanotide is approved, we will need to identify CMOs or partners to produce setmelanotide on a larger scale.

Risks Related to Our Intellectual Property Rights

If we are unable to adequately protect our proprietary technology or maintain issued patents that are sufficient to protect setmelanotide, others could compete against us more directly, which would have a material adverse impact on our business, results of operations, financial condition and prospects.

Our commercial success will depend in part on our success in obtaining and maintaining issued patents and other intellectual property rights in the United States and elsewhere and protecting our proprietary technology. If we do not adequately protect our intellectual property and proprietary technology, competitors may be able to use our technologies and erode or negate any competitive advantage we may have, which could harm our business and ability to achieve profitability.

We cannot provide any assurances that any of our patents have, or that any of our pending patent applications that mature into issued patents will include, claims with a scope sufficient to protect setmelanotide. Other parties have developed technologies that may be related or competitive to our approach, and may have filed or may file patent applications and may have received or may receive patents that may overlap with our patent applications, either by claiming the same methods or formulations or by claiming subject matter that could dominate our patent position. The patent positions of biotechnology and pharmaceutical companies, including our patent position, involve complex legal and factual questions, and, therefore, the issuance, scope, validity and enforceability of any patent claims that we may obtain cannot be predicted with certainty.

Although an issued patent is presumed valid and enforceable, its issuance is not conclusive as to its validity or its enforceability and such patent may not provide us with adequate proprietary protection or competitive advantages against competitors with similar products. Patents, if issued, may be challenged, deemed unenforceable, invalidated or circumvented. U.S. patents and patent applications or the patents and patent application obtained or submitted pursuant to comparable foreign laws, may also be subject to interference proceedings, *ex parte* reexamination, *inter partes* review proceedings, post-grant review proceedings, supplemental examination and challenges in district court. Patents may be subjected to opposition or comparable proceedings lodged in various foreign, both national and regional, patent offices. These proceedings could result in either loss of the patent or denial of the patent application or loss or reduction in the scope of one or more of the claims of the patent or patent application. In addition, such proceedings may be costly. Thus, any patents that we may own or exclusively license may not provide any protection against competitors. Furthermore, an adverse decision in an interference proceeding can result in a third party receiving the patent right sought by us, which in turn could affect our ability to develop, market or otherwise commercialize setmelanotide.

Competitors may also be able to design around our patents. Other parties may develop and obtain patent protection for more effective technologies, designs or methods. The laws of some foreign countries do not protect our proprietary rights to the same extent as the laws of the United States, and we may encounter significant problems in protecting our proprietary rights in these countries. If these developments were to occur, they could have a material adverse effect on our sales.

In addition, proceedings to enforce or defend our patents could put our patents at risk of being invalidated, held unenforceable or interpreted narrowly. Such proceedings could also provoke third parties to assert claims against us, including that some or all of the claims in one or more of our patents are invalid or otherwise unenforceable. If any of our patents covering setmelanotide are invalidated or found unenforceable, our financial position and results of operations would be materially and adversely impacted. In addition, if a court found that valid, enforceable patents held by third parties covered setmelanotide, our financial position and results of operations would also be materially and adversely impacted.

The degree of future protection for our proprietary rights is uncertain, and we cannot ensure that:

- any of our patents, or any of our pending patent applications, if issued, will include claims having a scope sufficient to protect setmelanotide;
- any of our pending patent applications will issue as patents;
- we will be able to successfully commercialize setmelanotide, if approved, before our relevant patents expire;
- we were the first to make the inventions covered by each of our patents and pending patent applications;
- we were the first to file patent applications for these inventions;
- others will not develop similar or alternative technologies that do not infringe our patents;

- any of our patents will be found to ultimately be valid and enforceable;
- any patents issued to us will provide a basis for an exclusive market for our commercially viable products, will provide us with any competitive advantages or will not be challenged by third parties;
- we will develop additional proprietary technologies or product candidates that are separately patentable; or
- our commercial activities or products will not infringe upon the patents of others.

We rely upon unpatented trade secrets, unpatented know-how and continuing technological innovation to develop and maintain our competitive position, which we seek to protect, in part, by confidentiality agreements with employees, consultants, collaborators and vendors. We also have agreements with employees and selected consultants that obligate them to assign their inventions to us. It is possible that technology relevant to our business will be independently developed by a person who is not a party to such an agreement. We may not be able to prevent the unauthorized disclosure or use of our technical knowledge or trade secrets by consultants, collaborators, vendors, former employees and current employees. Furthermore, if the parties to our confidentiality agreements breach or violate the terms of these agreements, we may not have adequate remedies for any such breach or violation, and we could lose our trade secrets through such breaches or violations. Further, our trade secrets could otherwise become known or be independently discovered by our competitors.

We may be involved in lawsuits to protect or enforce our patents or the patents of our licensors, which could be expensive, time-consuming and unsuccessful.

Competitors may infringe our patents or the patents of our licensors. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time-consuming and divert the attention of our management and key personnel from our business operations. Even if we prevail in any lawsuits that we initiate, the damages or other remedies awarded may not be commercially meaningful. In addition, in an infringement proceeding, a court may decide that a patent of ours or our licensors is not valid, is unenforceable and/or is not infringed, or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation or defense proceedings could put one or more of our patents at risk of being invalidated or interpreted narrowly and could put our patent applications at risk of not issuing.

Interference proceedings provoked by third parties or brought by us may be necessary to determine the priority of inventions with respect to our patents or patent applications or those of our licensors. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms. Our defense of litigation or interference proceedings may fail and, even if successful, may result in substantial costs and distract our management and other employees. We may not be able to prevent, alone or with our licensors, misappropriation of our intellectual property rights, particularly in countries where the laws may not protect those rights as fully as in the United States.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. There could also be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a material adverse effect on the price of our common stock.

We may infringe the intellectual property rights of others, which may prevent or delay our product development efforts and stop us from commercializing or increase the costs of commercializing setmelanotide, if approved.

Our success will depend in part on our ability to operate without infringing the intellectual property and proprietary rights of third parties. We cannot assure you that our business, products and methods do not or will not infringe the patents or other intellectual property rights of third parties. For example, numerous third-party U.S. and non-U.S. patents and pending applications exist that cover melanocortin receptor analogs and methods of using these analogs.

The pharmaceutical industry is characterized by extensive litigation regarding patents and other intellectual property rights. Other parties may allege that setmelanotide or the use of our technologies infringes patent claims or other intellectual property rights held by them or that we are employing their proprietary technology without authorization. For example, we received a letter in January 2013 from a third party bringing to our attention several patents and patent applications, both U.S. and non-U.S. We responded in April 2013 and have not received any further correspondence since then. Although most of the patents and patent applications mentioned in the letter were abandoned or not in force at the time the letter was sent to us, and subsequent to our response, the third party has allowed three additional U.S. patents to lapse for non-payment of patent maintenance fees, we cannot assure you that the holder of these third-party patents will not attempt to assert these patents against us.

Patent and other types of intellectual property litigation can involve complex factual and legal questions, and their outcome is uncertain. Any claim relating to intellectual property infringement that is successfully asserted against us may require us to pay substantial damages, including treble damages and attorney's fees if we are found to be willfully infringing another party's patents, for past use of the asserted intellectual property and royalties and other consideration going forward if we are forced to take a license. In addition, if any such claim were successfully asserted against us and we could not obtain such a license, we may be forced to stop or delay developing, manufacturing, selling or otherwise commercializing setmelanotide.

If we are unable to avoid infringing the patent rights of others, we may be required to seek a license, defend an infringement action or challenge the validity of the patents in court, or redesign our products. Patent litigation is costly and time consuming. We may not have sufficient resources to bring these actions to a successful conclusion.

In addition, in order to avoid infringing the intellectual property rights of third parties and any resulting intellectual property litigation or claims, we could be forced to do one or more of the following, which may not be possible and, even if possible, could be costly and time-consuming:

- cease development and commercialization of setmelanotide;
- pay substantial damages for past use of the asserted intellectual property;
- obtain a license from the holder of the asserted intellectual property, which license may not be available on reasonable terms, if at all; and
- in the case of trademark claims, rename setmelanotide.

Any of these risks coming to fruition could have a material adverse effect on our business, results of operations, financial condition and prospects.

We may be subject to claims challenging the inventorship or ownership of our patents and other intellectual property.

We may also be subject to claims that former employees, collaborators or other third parties have an ownership interest in our patents or other intellectual property. Litigation may be necessary to defend against these and other claims challenging inventorship or ownership. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as

exclusive ownership of, or right to use, such intellectual property. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

The U.S. Patent and Trademark Office, or U.S. PTO, and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other provisions during the patent process. There are situations in which noncompliance can result in abandonment or lapse of a patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, competitors might be able to enter the market earlier than would otherwise have been the case.

Issued patents covering setmelanotide could be found invalid or unenforceable if challenged in court.

If we or one of our licensing partners threatened or initiated legal proceedings against a third party to enforce a patent covering setmelanotide, the defendant could claim that the patent covering setmelanotide is invalid and/or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace. Grounds for a validity challenge include alleged failures to meet any one of several statutory requirements, including novelty, non-obviousness and enablement. Grounds for unenforceability assertions include allegations that someone connected with prosecution of the patent withheld material information from the U.S. PTO, or made a misleading statement, during patent prosecution. Third parties may also raise similar claims before administrative bodies in the United States or abroad, even outside the context of litigation. Such mechanisms include re-examination, *inter partes* review, post grant review and equivalent proceedings in foreign jurisdictions, for example, opposition proceedings. Such proceedings could result in revocation or amendment of our patents in such a way that they no longer cover setmelanotide or competitive products. The outcome following legal assertions of invalidity and/or unenforceability is unpredictable. With respect to validity, for example, we cannot be certain that there is no invalidating prior art, of which we and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, we would lose at least part, and perhaps all, of the patent protection on setmelanotide. Such a loss of patent protection would have a material adverse impact on our business.

We do not seek to protect our intellectual property rights in all jurisdictions throughout the world and we may not be able to adequately enforce our intellectual property rights even in the jurisdictions where we seek protection.

Filing, prosecuting and defending patents on setmelanotide in all countries and jurisdictions throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States could be less extensive than those in the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and further, may export otherwise infringing products to territories where we have patent protection, but enforcement is not as strong as that in the United States. These products may compete with our product and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents and other intellectual property protection,

particularly those relating to biopharmaceuticals, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights generally. For example, an April 2017 report from the Office of the United States Trade Representative identified a number of countries, including India and China, where challenges to the procurement and enforcement of patent rights have been reported. Several countries, including India and China, have been listed in the report every year since 1989. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly, could put our patent applications at risk of not issuing and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

We are dependent on licensed intellectual property. If we were to lose our rights to licensed intellectual property, we may not be able to continue developing or commercializing setmelanotide, if approved.

We have licensed our rights to setmelanotide from Ipsen Pharma SAS, or Ipsen. Our license with Ipsen imposes various obligations on us, and provides Ipsen the right to terminate the license in the event of our material breach of the license agreement, our failure to initiate or complete development of a licensed product, or our commencement of an action seeking to have an Ipsen licensed patent right declared invalid. Termination of our license from Ipsen would result in our loss of the right to use the licensed intellectual property, which would materially adversely affect our ability to develop and commercialize setmelanotide, as well as harm our competitive business position and our business prospects.

We also have licensed from Camurus its drug delivery technology, FluidCrystal, to formulate setmelanotide. Our license with Camurus imposes various obligations on us, and provides Camurus the right to terminate the license in the event of our material breach of the license agreement. Termination of our license from Camurus would result in our inability to use the licensed intellectual property.

We may enter into additional licenses to third-party intellectual property that are necessary or useful to our business. Future licensors may also allege that we have breached our license agreement and may accordingly seek to terminate our license with them. In addition, future licensors may have the right to terminate our license at will. Any termination could result in our loss of the right to use the licensed intellectual property, which could materially adversely affect our ability to develop and commercialize setmelanotide, if approved, as well as harm our competitive business position and our business prospects.

We have not yet registered trademarks for a commercial trade name for setmelanotide and failure to secure such registrations could adversely affect our business.

We have not yet registered trademarks for a commercial trade name for setmelanotide. Any future trademark applications may be rejected during trademark registration proceedings. Although we would be given an opportunity to respond to those rejections, we may be unable to overcome them. In addition, in the U.S. PTO and in comparable agencies in many foreign jurisdictions, third parties are given an opportunity to oppose pending trademark applications and to seek to cancel registered trademarks. Opposition or cancellation proceedings may be filed against our trademarks, and our trademarks may not survive those proceedings. Moreover, any name we propose to use for setmelanotide in the United States must be approved by the FDA, regardless of whether we have registered it, or applied to register it, as a trademark. The FDA typically conducts a review of proposed product names, including an evaluation of potential for confusion with other product names. If the FDA objects to any of our proposed product names, we may be required to expend significant additional resources in an effort to identify a suitable

substitute name that would qualify under applicable trademark laws, not infringe the existing rights of third parties and be acceptable to the FDA.

If we do not obtain additional protection under the Hatch-Waxman Amendments and similar foreign legislation by extending the patent terms and obtaining product exclusivity for setmelanotide, our business may be materially harmed.

Depending upon the timing, duration and specifics of FDA marketing approval for setmelanotide, one or more of the U.S. patents we license may be eligible for limited patent term restoration under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent term restoration of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. However, we may not be granted an extension because of, for example, failure to apply within applicable deadlines, failure to apply prior to expiration of relevant patents or otherwise failure to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain patent term extension or restoration or the term of any such extension is less than we request, our competitors may obtain approval of competing products following our patent expiration, and our ability to generate revenues could be materially adversely affected.

While we believe that setmelanotide contains active ingredients that would be treated by the FDA as a new chemical entity, or a new drug product, and, therefore, if approved, should be afforded five years of marketing exclusivity, the FDA may disagree with that conclusion and may approve generic products within a period that is less than five years. Manufacturers may seek to launch these generic products following the expiration of the applicable marketing exclusivity period, even if we still have patent protection for setmelanotide. Competition that setmelanotide may face from generic versions could materially and adversely impact our future revenue, profitability and cash flows and substantially limit our ability to obtain a return on the investments we have made in setmelanotide.

If we fail to obtain an extension of patent protection under similar foreign legislation, where applicable, our competitors may obtain approval of competing products following our patent expiration, and our ability to generate revenues could be materially adversely affected in the foreign countries concerned.

Changes in U.S. patent law could diminish the value of patents in general, thereby impairing our ability to protect our product.

The United States has enacted and is currently implementing the America Invents Act of 2011, wide-ranging patent reform legislation. Further, the U.S. Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain future patents, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on decisions by the U.S. Congress, the federal courts and the U.S. PTO, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents or future patents.

We may be subject to damages resulting from claims that we or our employees have wrongfully used or disclosed alleged trade secrets of their former employers.

Our employees have been previously employed at other biotechnology or pharmaceutical companies, including our competitors or potential competitors. We may be subject to claims that these employees or we have inadvertently or otherwise used or disclosed trade secrets or other proprietary information of the former employers of our employees. Litigation may be necessary to defend against these claims. Even if we

are successful in defending against these claims, litigation could result in substantial costs and be a distraction to management. If we fail in defending such claims, in addition to paying money damages, we may lose valuable intellectual property rights or personnel. A loss of key personnel or their work product could hamper or prevent our ability to commercialize setmelanotide, which would materially adversely affect our commercial development efforts.

Risks Related to Regulatory Approval and Marketing of Setmelanotide and Other Legal Compliance Matters

Even if we complete the necessary clinical trials, the regulatory and marketing approval process is expensive, time consuming and uncertain and may prevent us from obtaining approvals for the commercialization of setmelanotide. We depend entirely on the success of setmelanotide, which is in Phase 3 clinical development for treatment of POMC deficiency obesity and LepR deficiency obesity. We cannot be certain that we will be able to obtain regulatory approval for, or successfully commercialize, setmelanotide. If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals, we will not be able to commercialize setmelanotide, and our ability to generate revenue will be materially impaired.

We currently have only one product candidate, setmelanotide, in clinical development, and our business depends entirely on its successful clinical development, regulatory approval and commercialization. We currently have no drug products for sale and may never be able to develop marketable drug products. Setmelanotide, which is currently in Phase 3 clinical development as a treatment for genetic deficiencies affecting the MC4 pathway, including POMC deficiency obesity and LepR deficiency obesity, will require substantial additional clinical development, testing and regulatory approval before we are permitted to commence commercialization. The clinical trials of setmelanotide are, and the manufacturing and marketing of setmelanotide will be, subject to extensive and rigorous review and regulation by numerous government authorities in the United States and in other countries where we intend to test and, if approved, market setmelanotide. Before obtaining regulatory approvals for the commercial sale of any product candidate, we must demonstrate through non-clinical testing and clinical trials that the product candidate is safe and effective for use in each target indication. This process can take many years and approval, if any, may be conditional on post-marketing studies and surveillance, and will require the expenditure of substantial resources beyond the proceeds we raise in this offering. When a sponsor relies exclusively or predominantly on foreign clinical data, the FDA may require a showing that those data are applicable to the U.S. population and U.S. medical practice, which in some cases may require bridging studies or other evidence. Of the large number of drugs in development in the United States and in other countries, only a small percentage will successfully complete the FDA regulatory approval process or the equivalent process in foreign jurisdictions and will be commercialized. In addition, we have not discussed all of our proposed development programs with the FDA of the competent authorities of foreign jurisdictions. Accordingly, even if we are able to obtain the requisite financing to continue to fund our development and clinical trials, we cannot assure you that setmelanotide will be successfully developed or commercialized.

We are not permitted to market setmelanotide in the United States until we receive approval of an NDA from the FDA, or in any foreign jurisdictions until we receive the requisite approval from such countries. We have two Phase 3 clinical trials underway, one each for the treatment of POMC deficiency obesity and LepR deficiency obesity. Under our current development program, we plan to conduct a single Phase 3 clinical trial for POMC deficiency obesity. To date, in our ongoing discussions with the FDA, the agency has not asked for additional Phase 3 trials in POMC deficiency obesity, but the agency could still require us to conduct additional Phase 3 clinical trials for this indication. Moreover, for POMC deficiency obesity, the FDA could alter its previous advice on many aspects of the trial—the small size, the open label design, the amount of past medical history available on individual patients, the statistical analysis plan, the definition of clinically-relevant success for the protocol, entry of patients ages 12 or over—all of which may impact the timing and ability to obtain FDA approval. There are other aspects of the trial for which we

have not received advice from the FDA, such as the number of U.S. versus non-U.S. patients and the number of patients with POMC gene defects versus the number of patients with PCSK1 defects, which could also impact the timing of and our ability to obtain FDA approval. We have not discussed the protocol for a Phase 3 program for LepR deficiency obesity with the FDA and thus we do not know if the FDA will provide advice on this trial that differs from the advice provided by the FDA for the trial in POMC deficiency obesity. Therefore, the timeline for enrollment, availability of data, and cost of conducting such trials are uncertain, and could be less favorable than those applicable to the POMC deficiency obesity program.

In addition, the FDA and other equivalent competent authorities in foreign jurisdictions will expect for there to be no introduction of bias in the open-label Phase 3 trials. Accordingly, we proposed to the FDA that little, if any, efficacy data will be available to us in any form until the Phase 3 trials are complete.

The FDA or other regulatory authorities and other equivalent competent authorities in foreign jurisdictions will also require that we conduct one or more pivotal trials for each other indication sought. In addition, we are not sure if one or more Phase 3 trials would be required for approval in each other indication. The need and length of placebo-controlled data in these pivotal trials and the number of patients required for these approvals is also unclear. We expect to seek an indication for obesity caused by monogenic deficiencies affecting the MC4 pathway. We are currently conducting Phase 3 trials for treatment of setmelanotide in POMC deficiency obesity and LepR deficiency obesity and Phase 2 trials for treatment of Bardet-Biedl syndrome, Alström syndrome, POMC heterozygous deficiency obesity, and POMC epigenetic disorders. If the clinical data meet key primary and secondary endpoints for safety and efficacy, our overall clinical program may be less time consuming and require fewer patients than might a program for a broader obesity indication.

In the European Union we are currently conducting the Phase 3 clinical trial RM-493-012 in Germany and the United Kingdom. In France, the clinical trial application has recently been approved by the competent authorities. On March 23, 2017, we received EMA scientific advice on the appropriateness and sufficiency of the non-clinical and clinical development programs to support an initial marketing authorization application in POMC deficiency obesity. The EMA scientific advice included preliminary advice on the clinical trial RM-493-012. The EMA expressed general support for the ongoing Phase 3 program in POMC deficiency obesity. The EMA, advised that the regulatory strategy for a rare disorder is supported, and that the EMA may have to rely on scarce data. The EMA advised, however, that we need to consider whether full approval, approval under conditional or exceptional circumstances would be the most appropriate pathway for application for POMC deficiency obesity.

Given the orphan status of setmelanotide for the treatment of POMC deficiency in the European Union the marketing authorization application for a POMC deficiency obesity indication will be submitted via the centralized procedure. In addition, we plan to submit a pediatric investigation plan for setmelanotide to the EMA Pediatric Development Committee in 2017.

We cannot assure you that the clinical trials we are conducting in the European Union will be completed within this timeline. Similar to the United States, we are subject to comprehensive regulatory oversight by the EMA and the competent authorities of the individual EU member states where we are conducting our clinical trials. Failure by us or by any of our third party partners to comply with EU laws and the related national laws of individual EU member states governing the conduct of clinical trials may result in the suspension of clinical trials and in other administrative, civil, or criminal penalties.

Our plan is to expand our internal clinical development operations and capabilities so that we can continue to enroll and manage our Phase 2 clinical trials, and enroll and manage our Phase 3 clinical trials, such that, if the clinical trials are successful, we can file an NDA for POMC deficiency obesity in the United States by 2019. We believe we have finalized the design, timing and size of our Phase 3 trial for POMC deficiency obesity with the FDA but we cannot assure you that the trial will not be subject to further modification or that it will be completed on time. In addition, obtaining approval of an NDA and

the approval of a marketing authorization application from the European Commission is a complex, lengthy, expensive and uncertain process, and the FDA, EMA or equivalent competent authorities in foreign jurisdictions may delay, limit or deny approval of setmelanotide for many reasons, including, among others:

- the FDA, the EMA, or other equivalent competent authorities in foreign jurisdictions may disagree with our interpretation of data from clinical trials, or may change the requirements for approval even after it has reviewed and commented on the design for our clinical trials;
- we may not be able to demonstrate to the satisfaction of the FDA, the EMA, or other equivalent competent authorities in foreign jurisdictions that setmelanotide is safe and effective in treating obesity caused by certain genetic deficiencies affecting the MC4 pathway;
- the results of our clinical trials may not be interpretable or meet the level of statistical or clinical significance required by the FDA, the EMA, or other equivalent competent authorities in foreign jurisdictions for marketing approval. For example, the potential unblinding of setmelanotide studies due to easily identifiable adverse events may raise the concern that potential bias has affected the clinical trial results;
- the FDA, the EMA, or other equivalent competent authorities in foreign jurisdictions may disagree with the number, size, conduct or implementation of our clinical trials;
- the FDA, the EMA, or other equivalent competent authorities in foreign jurisdictions may require that we conduct additional clinical trials or pre-clinical studies;
- the FDA, the EMA, or other equivalent competent authorities in foreign jurisdictions or the applicable foreign regulatory agency may identify deficiencies in our chemistry, manufacturing or controls of setmelanotide;
- the CROs that we retain to conduct our clinical trials may take actions outside of our control that materially adversely impact our clinical trials;
- the FDA, the EMA, or other equivalent competent authorities in foreign jurisdictions may find the data from preclinical studies and clinical trials insufficient to demonstrate that clinical and other benefits of setmelanotide outweigh its safety risks;
- the FDA, the EMA, or other equivalent competent authorities in foreign may disagree with our interpretation of data from our preclinical studies and clinical trials;
- the FDA, the EMA, or other equivalent competent authorities in foreign jurisdictions may not approve the formulation, labeling or specifications of setmelanotide;
- the FDA, the EMA, or other equivalent competent authorities in foreign may not accept data generated at our clinical trial sites;
- if and when our NDA or our marketing authorization application is submitted and reviewed by an advisory committee, the FDA, the EMA, or the equivalent competent authorities in foreign jurisdictions may have difficulties scheduling an advisory committee meeting in a timely manner or the advisory committee may recommend against approval of our application or may recommend that the FDA, the EMA, or the equivalent competent authorities in foreign jurisdictions require, as a condition of approval, additional preclinical studies or clinical trials, limitations on approved labeling or distribution and use restrictions;
- the FDA may require development of a REMS as a condition of approval or post-approval, or may not agree with our proposed REMS or may impose additional requirements that limit the promotion, advertising, distribution, or sales of setmelanotide. In addition, the European Commission may grant only conditional approval marketing authorization or impose specific obligations as a condition for marketing authorization, or may require us to conduct post authorization safety studies as a condition of grant of marketing authorization;

- the FDA or other equivalent competent foreign regulatory agency may deem our manufacturing processes or our facilities or the facilities of our CMOs inadequate to preserve the identity, strength, quality, purity, or potency of our product; or

- the FDA, the European Commission, or the equivalent competent authorities in foreign jurisdictions may change its approval policies or adopt new regulations and guidance.

Any of these factors, many of which are beyond our control, could jeopardize our ability to obtain regulatory approval for and successfully market setmelanotide. Moreover, because our business is entirely dependent upon setmelanotide, any such setback in our pursuit of regulatory approval would have a material adverse effect on our business and prospects.

Our failure to obtain marketing approval in foreign jurisdictions would prevent setmelanotide from being marketed abroad, and any approval we are granted for setmelanotide in the United States would not assure approval of setmelanotide in foreign jurisdictions.

In order to market and sell setmelanotide and any other product candidate that we may develop in the European Union and many other jurisdictions, we or our third-party collaborators must obtain separate marketing authorizations and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval may differ substantially from that required to obtain FDA approval. The regulatory approval process outside the United States generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside the United States, it is required that the product be approved for reimbursement before the product can be sold in that country. We or these third parties may not obtain approvals from competent authorities outside the United States on a timely basis, if at all. Approval by the FDA does not ensure approval by competent authorities in other countries or jurisdictions, and approval by one competent authority outside the United States does not ensure approval by competent authorities in other countries or jurisdictions or by the FDA. We may not be able to file for marketing approvals and may not receive necessary approvals to commercialize setmelanotide in any market. Additionally, on June 23, 2016, the electorate in the United Kingdom voted in favor of leaving the European Union, commonly referred to as Brexit. On March 29, 2017, the country formally notified the European Union of its intention to withdraw pursuant to Article 50 of the Lisbon Treaty. Since a significant proportion of the regulatory framework in the United Kingdom is derived from European Union directives and regulations, the referendum could materially impact the regulatory regime with respect to the approval of setmelanotide in the United Kingdom or the European Union. Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of Brexit or otherwise, would prevent us from commercializing setmelanotide in the United Kingdom and/or the European Union and restrict our ability to generate revenue and achieve and sustain profitability. If any of these outcomes occur, we may be forced to restrict or delay efforts to seek regulatory approval in the United Kingdom and/or European Union for setmelanotide, which could significantly and materially harm our business.

Even if we obtain marketing approval for setmelanotide, the terms of approval and ongoing regulation may limit how we manufacture and market setmelanotide and compliance with such requirements may involve substantial resources, which could materially impair our ability to generate revenue.

Even if we receive marketing approval for setmelanotide, regulatory authorities may impose significant restrictions on setmelanotide's indicated uses or marketing or impose ongoing requirements for potentially costly post approval studies. Setmelanotide will also be subject to ongoing requirements by the FDA, the EMA, and the competent authorities in the EU member states, governing labeling, packaging, storage advertising, promotion, marketing, distribution, importation, exportation, post-approval, manufacturing, recordkeeping, and submission of safety and other post market information. The FDA and the other competent foreign authorities haves significant post market authority, including, for example, the authority to require labeling changes based on new safety information and to require post market studies

or clinical trials to evaluate serious safety risks related to the use of a drug. The FDA also has the authority to require, as part of an NDA or post approval, the submission of a REMS, which may include Elements to Assure Safe Use, or ETASU. Any REMS required by the FDA may lead to increased costs to assure compliance with new post approval regulatory requirements and potential requirements or restrictions on the sale of approved products, all of which could lead to lower sales volume and revenue.

Manufacturers of drug products and their facilities are subject to continual review and periodic inspections by the FDA and other equivalent competent authorities for compliance with cGMPs and other regulations. If we or a regulatory agency discover problems with setmelanotide, such as adverse events of unanticipated severity or frequency, or problems with the facility where setmelanotide is manufactured, a regulatory agency may impose restrictions on setmelanotide, the manufacturer or us, including requiring withdrawal of setmelanotide from the market or suspension of manufacturing. If we, setmelanotide or the manufacturing facilities for setmelanotide fail to comply with applicable regulatory requirements, a regulatory agency may, among other things:

- issue warning letters or untitled letters;
- seek an injunction or impose civil or criminal penalties or monetary fines;
- suspend or withdraw marketing approval;
- suspend any ongoing clinical trials;
- refuse to approve pending applications or supplements to applications submitted by us;
- suspend or impose restrictions on operations, including costly new manufacturing requirements; or
- seize or detain setmelanotide, refuse to permit the import or export of setmelanotide, or request that we initiate a product recall.

Accordingly, assuming we receive marketing approval for setmelanotide, we and our CMOs will continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production, product surveillance and quality control. If we are not able to comply with post-approval regulatory requirements, we could have the marketing approvals for setmelanotide withdrawn by regulatory authorities and our ability to market any future products could be limited, which could adversely affect our ability to achieve or sustain profitability. Thus, the cost of compliance with post-approval regulations may have a negative effect on our operating results and financial condition.

Similar to the United States, both marketing authorization holders and manufacturers of medicinal products are subject to comprehensive regulatory oversight by the EMA and the competent authorities of the individual EU member states, both before and after grant of the manufacturing and Marketing Authorizations. This oversight includes control of compliance with cGMP rules, which govern quality control of the manufacturing process and require documentation policies and procedures. We and our third party manufacturers would be required to ensure that all of our processes, methods, and equipment are compliant with cGMP. Failure by us or by any of our third party partners, including suppliers, manufacturers, and distributors to comply with EU laws and the related national laws of individual EU member states governing the conduct of clinical trials, manufacturing approval, marketing authorization of medicinal products, both before and after grant of marketing authorization, and marketing of such products following grant of authorization may result in administrative, civil, or criminal penalties. These penalties could include delays in or refusal to authorize the conduct of clinical trials or to grant Marketing Authorization, product withdrawals and recalls, product seizures, suspension, or variation of the marketing authorization, total or partial suspension of production, distribution, manufacturing, or clinical trials, operating restrictions, injunctions, suspension of licenses, fines, and criminal penalties.

In addition, EU legislation related to pharmacovigilance, or the assessment and monitoring of the safety of medicinal products, provides that the EMA and the competent authorities of the EU member states have the authority to require companies to conduct additional post-approval clinical efficacy and

safety studies. The legislation also governs the obligations of marketing authorization holders with respect to additional monitoring, adverse event management and reporting. Under the pharmacovigilance legislation and its related regulations and guidelines, we may be required to conduct a labor intensive collection of data regarding the risks and benefits of marketed products and may be required to engage in ongoing assessments of those risks and benefits, including the possible requirement to conduct additional clinical studies, which may be time-consuming and expensive and could impact our profitability. Non-compliance with such obligations can lead to the variation, suspension or withdrawal of marketing authorization or imposition of financial penalties or other enforcement measures.

Recently enacted and future healthcare reform legislation or regulation may increase the difficulty and cost for us and any future collaborators to obtain marketing approval of and commercialize setmelanotide and may adversely affect the prices we, or they, may obtain and may have a negative impact on our business and results of operations.

In the United States and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could, among other things, prevent or delay marketing approval of setmelanotide, restrict or regulate post-approval activities and affect our ability, or the ability of any future collaborators, to profitably sell any products for which we, or they, obtain marketing approval. Among policy makers and payors in the United States and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and/or expanding access. In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives. We expect that current laws, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we, or any future collaborators, may receive for any approved products.

In March 2010, President Obama signed into law the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, or collectively the ACA. Among the provisions of the ACA of importance to our business, including, without limitation, our ability to commercialize and the prices we may obtain for any of setmelanotide and that are approved for sale, are the following:

- an annual, nondeductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government healthcare programs, although this fee does not apply to sales of certain products approved exclusively for orphan indications;

- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to certain individuals with income at or below 133% of the federal poverty level, thereby potentially increasing a manufacturer's Medicaid rebate liability;

- expansion of manufacturers' rebate liability under the Medicaid Drug Rebate Program by increasing the minimum rebate for both branded and generic drugs and revising the definition of "average manufacturer price," or AMP, for calculating and reporting Medicaid drug rebates on outpatient prescription drug prices and extending rebate liability to prescriptions for individuals enrolled in Medicare Advantage plans;

- introduction of a price reporting requirement for drugs that are inhaled, instilled, implanted, injected, or infused and not generally dispensed through retail community pharmacies;

- addition of more entity types eligible for participation in the Public Health Service the 340B drug pricing program, or the 340B program;

- established the Medicare Part D coverage gap discount program by requiring manufacturers to provide a 50% point-of-sale-discount off the negotiated price of applicable brand drugs to eligible beneficiaries during their coverage gap period as a condition for the manufacturers' outpatient drugs to be covered under Medicare Part D;

- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research;

- the Independent Payment Advisory Board, or IPAB, which has authority to recommend certain changes to the Medicare program to reduce expenditures by the program that could result in reduced payments for prescription drugs. However, the IPAB implementation has been not been clearly defined. ACA provided that under certain circumstances, IPAB recommendations or recommendations of the Secretary of Health and Human Services will become law unless Congress enacts legislation that will achieve the same or greater Medicare cost savings; and

- established the Center for Medicare and Medicaid Innovation within CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending.

In addition, other legislative changes have been proposed and adopted since the ACA was enacted. For example, beginning April 1, 2013, Medicare payments for all items and services, including drugs and biologics, were reduced by 2% under the sequestration (i.e., automatic spending reductions) required by the Budget Control Act of 2011, as amended by the American Taxpayer Relief Act of 2012. Subsequent legislation extended the 2% reduction, on average, to 2025. Sequestration may result in additional reductions in Medicare and other healthcare funding and, if we obtain regulatory approvals, may otherwise affect the prices we may obtain for setmelanotide or the frequency with which setmelanotide is prescribed or used if approved.

Legislative changes to or regulatory changes under the ACA remain possible and appear likely in the 115th U.S. Congress and under the Trump administration. The nature and extent of any legislative or regulatory changes to the ACA, including repeal and replacement initiatives, are uncertain at this time. It is possible that ACA repeal and replacement initiatives, if enacted into law, could ultimately result in fewer individuals having health insurance coverage or in individuals having insurance coverage with less generous benefits. The scope of potential future legislation to modify or repeal and replace ACA provisions is highly uncertain in many respects.

Additional changes that may affect our business include the expansion of new programs such as Medicare payment for performance initiatives for physicians under the Medicare Access and CHIP Reauthorization Act of 2015, or MACRA, which will be fully implemented in 2019. At this time, it is unclear how the introduction of the Medicare quality payment program will impact overall physician reimbursement. The costs of prescription pharmaceuticals in the United States has also been the subject of considerable discussion in the United States, and members of Congress and the Administration have stated that they will address such costs through new legislative and administrative measures. This focus has resulted in several Congressional inquiries and proposed bills designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drug products.

We expect that these and other healthcare reform measures that may be adopted in the future may result in more rigorous coverage criteria and in additional downward pressure on the price that we receive for any approved drug. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our drugs. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our drug candidates or additional pricing pressures.

The pricing of prescription pharmaceuticals is also subject to governmental control outside the United States. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain reimbursement or pricing approval in some

countries, we may be required to conduct a clinical trial that compares the cost effectiveness of setmelanotide to other available therapies. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our ability to generate revenues and become profitable could be impaired.

If we participate in the Medicaid Drug Rebate Program and fail to comply with our reporting and payment obligations under that program or other governmental pricing programs that we participate in, we could be subject to additional reimbursement requirements, penalties, sanctions and fines, which could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

We expect to participate in and have certain price reporting obligations to the Medicaid Drug Rebate program. Under the Medicaid Drug Rebate program, if we successfully commercialize setmelanotide, we would be required to pay a rebate to each state Medicaid program for our covered outpatient drugs that are dispensed to Medicaid beneficiaries and paid for by a state Medicaid program as a condition of having federal funds being made available to the states for our drugs under Medicaid and Medicare Part B. Those rebates are based on pricing data we would have to report on a monthly and quarterly basis to the Centers for Medicare and Medicaid Services, or CMS, the federal agency that administers the Medicaid Drug Rebate program. These data include the average manufacturer price and, in the case of innovator products, the best price for each drug which, in general, represents the lowest price available from the manufacturer to any entity in the U.S. in any pricing structure, calculated to include all sales and associated rebates, discounts and other price concessions. Our failure to comply with these price reporting and rebate payment obligations if we participate in the program could negatively impact our financial results.

Federal law requires that any company that participates in the Medicaid Drug Rebate program also participate in the 340B program in order for federal funds to be available for the manufacturer's drugs under Medicaid and Medicare Part B. The 340B program requires participating manufacturers to agree to charge statutorily defined covered entities no more than the 340B "ceiling price" for the manufacturer's covered outpatient drugs. These 340B covered entities include a variety of community health clinics and other entities that receive health services grants from the Public Health Service, as well as hospitals that serve a disproportionate share of low-income patients. The ACA expanded the list of covered entities to include certain free-standing cancer hospitals, critical access hospitals, rural referral centers and sole community hospitals, but exempts "orphan drugs" from the ceiling price requirements for these covered entities. The 340B ceiling price is calculated using a statutory formula based on the average manufacturer price and rebate amount for the covered outpatient drug as calculated under the Medicaid Drug Rebate program, and in general, products subject to Medicaid price reporting and rebate liability are also subject to the 340B ceiling price calculation and discount requirement. Any additional future changes to the definition of average manufacturer price and the Medicaid rebate amount under the ACA or other legislation or regulation could affect our 340B ceiling price calculations and negatively impact our results of operations if we successfully commercialize setmelanotide. In addition, legislation may be introduced that, if passed, would further expand the 340B program to additional covered entities or would require participating manufacturers to agree to provide 340B discounted pricing on drugs used in an inpatient setting.

In order to be eligible to have our products that we successfully commercialize paid for with federal funds under the Medicaid program and purchased by certain federal agencies and grantees, we also would have to participate in the U.S. Department of Veterans Affairs, or VA, Federal Supply Schedule, or FSS, pricing program. As part of this program, we would be obligated to make our products available for procurement on an FSS contract under which we must comply with standard government terms and conditions and charge a price that is no higher than the statutory Federal Ceiling Price, or FCP, to four federal agencies (VA, U.S. Department of Defense, or DOD, Public Health Service, and U.S. Coast Guard).

Civil monetary penalties can be applied if we participate in these programs and if we are found to have knowingly submitted any false price information to the government or if we fail to submit the required price data on a timely basis. Such conduct also could be grounds for CMS to terminate the Medicaid drug rebate agreement pursuant to which we would participate in the Medicaid drug rebate program, in which case federal payments may not be available under Medicaid for our covered outpatient drugs. We cannot assure you that our submissions will not be found by CMS or another government agency to be incomplete or incorrect.

If we obtain marketing approval for setmelanotide, we will be subject to strict enforcement of post-marketing requirements and we could be subject to substantial penalties, including withdrawal of our product from the market, if we fail to comply with all regulatory requirements.

If we obtain marketing approval for setmelanotide, we will be subject to continual requirements of and review by the FDA and equivalent competent authorities in foreign jurisdictions. These requirements may include, but are not limited to, post-approval studies to be conducted which may include carcinogenicity studies, a QT interval prolongation study in one form or another, and ongoing natural history studies with patient registries. Other requirements may also include, among other things, restrictions governing promotion of an approved product, submissions of safety and other post-marketing information and reports, registration and listing requirements, cGMP requirements relating to manufacturing, quality control, quality assurance and corresponding maintenance of records and documents, and requirements regarding the distribution of samples to physicians and recordkeeping. The FDA and other federal and state agencies, including the Department of Justice and other equivalent competent authorities in foreign jurisdictions, closely regulate compliance with all requirements governing prescription drug products, including requirements pertaining to marketing and promotion of drugs in accordance with the provisions of the approved labeling and manufacturing of products in accordance with cGMP requirements. Violations of such requirements may lead to investigations alleging violations of the FDCA, and other statutes, including the False Claims Act and other federal and state health care fraud and abuse laws as well as state consumer protection laws.

For example, the FDA and other equivalent competent authorities in foreign jurisdictions strictly regulate the promotional claims that may be made about prescription products, such as setmelanotide, if approved. In particular, a product may not be promoted for uses that are not approved by the FDA or such other regulatory agencies as reflected in the product's approved labeling. If we receive marketing approval for setmelanotide as a treatment for obesity caused by certain genetic deficiencies affecting the MC4 pathway, physicians may nevertheless prescribe setmelanotide to their patients in a manner that is inconsistent with the approved labeling. If we are found to have promoted such off-label uses, we may become subject to significant liability. The federal government has levied large civil and criminal fines against companies for alleged improper promotion and has enjoined several companies from engaging in off-label promotion. The FDA has also requested that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed. Oversight and management of promotional practices may require operational changes and additions, if setmelanotide is approved and commercialized. If we cannot successfully manage the promotion of setmelanotide, if approved, we could become subject to significant liability, which would materially adversely affect our business and financial condition.

In the European Union, the advertising and promotion of our products are subject to EU laws governing promotion of medicinal products, interactions with physicians, misleading and comparative advertising and unfair commercial practices. In addition, other legislation adopted by individual EU member states may apply to the advertising and promotion of medicinal products. These laws require that promotional materials and advertising in relation to medicinal products comply with the product's Summary of Product Characteristics, or SmPC, as approved by the competent authorities. The SmPC is the document that provides information to physicians concerning the safe and effective use of the medicinal product. It forms an intrinsic and integral part of the marketing authorization granted for the medicinal

product. Promotion of a medicinal product that does not comply with the SmPC is considered to constitute off-label promotion. The off-label promotion of medicinal products is prohibited in the European Union. The applicable laws at European Union level and in the individual EU member states also prohibit the direct-to-consumer advertising of prescription-only medicinal products. Violations of the rules governing the promotion of medicinal products in the European Union could be penalized by administrative measures, fines and imprisonment. These laws may further limit or restrict the advertising and promotion of our products to the general public and may also impose limitations on our promotional activities with health care professionals.

We may be subject to federal and state healthcare laws and regulations. If we are unable to comply or have not fully complied with such laws and regulations, we could face criminal sanctions, damages, civil penalties, reputational harm and diminished profits and future earnings.

Healthcare providers, physicians and others will play a primary role in the recommendation and prescription of setmelanotide, if approved. Our arrangements and interactions with healthcare professionals, third-party payors, patients and others will expose us to broadly applicable fraud and abuse, anti-kickback, false claims and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute setmelanotide, if we obtain marketing approval. The U.S. federal and state healthcare laws and regulations that may affect our ability to operate include, but are not limited to:

- The United States federal Anti-Kickback Statute, which prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, paying, or receiving remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, lease order or arranging for or recommending of the purchase, lease or order of any good or service for which payment may be made, in whole or in part, by federal healthcare programs such as Medicare and Medicaid. This statute has been interpreted to apply to arrangements between pharmaceutical companies on one hand and prescribers, purchasers and formulary managers on the other. Liability under the Anti-Kickback Statute may be established without proving actual knowledge of the statute or specific intent to violate it. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal civil False Claims Act. Although there are a number of statutory exemptions and regulatory safe harbors to the federal Anti-Kickback Statute protecting certain common business arrangements and activities from prosecution or regulatory sanctions, the exemptions and safe harbors are drawn narrowly. Practices that involve remuneration to those who prescribe, purchase, or recommend pharmaceutical and biological products, including certain discounts, or engaging such individuals as consultants, advisors, or speakers, may be subject to scrutiny if they do not fit squarely within an exemption or safe harbor. Our practices may not in all cases meet all of the criteria for safe harbor protection from anti-kickback liability. Moreover, there are no safe harbors for many common practices, such as educational and research grants, charitable donations, product support and patient assistance programs.

- The federal civil False Claims Act prohibits individuals or entities from, among other things, knowingly presenting, or causing to be presented a false or fraudulent claim for payment of government funds, or knowingly making, using or causing to made or used a false record or statement material to an obligation to pay money to the government or knowingly concealing or knowingly and improperly avoiding, decreasing or concealing an obligation to pay money to the federal government. Actions under the False Claims Act may be brought by the Attorney General or as a qui tam action by a private individual in the name of the government. Many pharmaceutical manufacturers have been investigated and have reached substantial financial settlements with the federal government under the civil False Claims Act for a variety of alleged improper activities including causing false claims to be submitted as a result of the marketing of their products for

unapproved and thus non-reimbursable uses, inflating prices reported to private price publication services which are used to set drug payment rates under government healthcare programs, and other interactions with prescribers and other customers including those that may have affected their billing or coding practices and submission to the federal government. The government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal civil False Claims Act. Pharmaceutical and other healthcare companies also are subject to other federal false claims laws, including, among others, federal criminal healthcare fraud and false statement statutes that extend to non-government health benefit programs.

- The federal Health Insurance Portability and Accountability Act of 1996, as amended by the Health Information Technology for Economic and Clinical Health Act, or HIPAA, imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program and also imposes obligations, with respect to safeguarding the privacy, security and transmission of individually identifiable health information.

- HIPAA and the federal false statements statute prohibits knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement or representation, or making or using any false writing or document knowing the same to contain any materially false, fictitious or fraudulent statement or entry in connection with the delivery of or payment for healthcare benefits, items or services.

- Numerous federal and state laws and regulations that address privacy and data security, including state data breach notification laws, state health information privacy laws, and federal and state consumer protection laws (e.g., Section 5 of the FTC Act), govern the collection, use, disclosure and protection of health-related and other personal information.

- The federal transparency requirement known as the federal Physician Payments Sunshine Act, being implemented as the Open Payments Program, requires certain manufacturers of drugs, devices, biologics and medical supplies to report payments and other transfers of value to physicians and teaching hospitals, as well as ownership and investments interests held by physicians and their immediate family members. Pharmaceutical and biological manufacturers with products for which payment is available under Medicare, Medicaid or the State Children's Health Insurance Program are required to submit a report to the Centers for Medicare and Medicaid Services within the U.S. Department of Health and Human Services on or before the 90th day of each calendar year disclosing reportable payments made in the previous calendar year.

- Analogous state laws and regulations, such as state anti-kickback and false claims laws, which may apply to items or services reimbursed under Medicaid and other state programs or, in several states, regardless of the payer. Some state laws also require pharmaceutical companies to report expenses relating to the marketing and promotion of pharmaceutical products and to report gifts and payments to certain health care providers in those states. Some of these states also prohibit certain marketing-related activities including the provision of gifts, meals, or other items to certain health care providers. In addition, California, Connecticut, Nevada, and Massachusetts require pharmaceutical companies to implement compliance programs or marketing codes of conduct.

Ensuring that our business arrangements and interactions with healthcare professionals, third-party payors, patients and others comply with applicable healthcare laws and regulations will require substantial resources. It is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations, including anticipated activities to be conducted by our sales and marketing team, were found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines and exclusion from government funded healthcare programs, such as Medicare

and Medicaid, the curtailment or restructuring of our operation, any of which could substantially disrupt our operations. Although compliance programs can mitigate the risk of investigation and prosecution for violations of these laws, the risks cannot be entirely eliminated. Any action against us for violation of these laws or regulations, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business.

Our employees may engage in misconduct or other improper activities, including violating applicable regulatory standards and requirements or engaging in insider trading, which could significantly harm our business.

We are exposed to the risk of employee fraud or other misconduct. Misconduct by employees could include intentional failures to comply with the regulations of the FDA and applicable non-U.S. regulators, provide accurate information to the FDA and applicable non-U.S. regulators, comply with healthcare fraud and abuse laws and regulations in the United States and abroad, report financial information or data accurately or disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Employee misconduct could also involve the improper use of, including trading on, information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. It is not always possible to identify and deter employee misconduct, and any precautions we take to detect and prevent this activity may be ineffective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant fines or other sanctions.

Our failure to comply with data protection laws and regulations could lead to government enforcement actions and significant penalties against us, and adversely impact our operating results.

We are subject to U.S. data protection laws and regulations (i.e., laws and regulations that address privacy and data security) at both the federal and state levels. The legislative and regulatory landscape for data protection continues to evolve, and in recent years there has been an increasing focus on privacy and data security issues. Numerous federal and state laws, including state data breach notification laws, state health information privacy laws, and federal and state consumer protection laws (e.g., Section 5 of the FTC Act), govern the collection, use, and disclosure and protection of health-related and other personal information. Failure to comply with data protection laws and regulations could result in government enforcement actions and create liability for us, which could include civil and/or criminal penalties, private litigation and/or adverse publicity that could negatively affect our operating results and business. In addition, we may obtain health information from third parties, such as research institutions with which we collaborate, that are subject to privacy and security requirements under HIPAA. Although we are not directly subject to HIPAA, other than potentially with respect to providing certain employee benefits, we could be subject to criminal penalties if we knowingly obtain or disclose individually identifiable health information maintained by a HIPAA covered entity in a manner that is not authorized or permitted by HIPAA.

EU member states, Switzerland and other countries have also adopted data protection laws and regulations, which impose significant compliance obligations. In the European Union, the collection and use of personal health data is governed by the provisions of the EU Data Protection Directive. The European Union Data Protection Directive and the national implementing legislation of the EU member states impose strict obligations and restrictions on the ability to collect, analyze and transfer personal data, including health data from clinical trials and adverse event reporting. In particular, these obligations and restrictions concern the consent of the individuals to whom the personal data relates, the information

provided to the individuals, notification of data processing obligations to the competent national data protection authorities and the security and confidentiality of the personal data. Data protection authorities from the different EU member states may interpret the EU Data Protection Directive and national laws differently and impose additional requirements, which add to the complexity of processing personal data in the European Union.

Guidance on implementation and compliance practices are often updated or otherwise revised. For example, the EU Data Protection Directive prohibits the transfer of personal data to countries outside of the European Union, including the United States, that are not considered by the European Commission to provide an adequate level of data protection.

The judgment by the Court of Justice of the European Union in Case C-362/14 Maximillian Schrems v. Data Protection Commissioner, or the Schrems case, held that the Safe Harbor Framework, which was relied upon by many United States entities as a basis for transfer of personal data from the European Union to the United States, was invalid. United States entities therefore, had only the possibility to rely on the alternate procedures for such data transfer provided in the EU Data Protection Directive.

On February 29, 2016, however, the European Commission announced an agreement with the United States Department of Commerce, or the DOC, to replace the invalidated Safe Harbor framework with a new "Privacy Shield". On July 12, 2016, the European Commission adopted a decision on the adequacy of the protection provided by the Privacy Shield. The Privacy Shield is intended to address the requirements set out by the Court of Justice of the European Union in the Schrems case. The Privacy Shield imposes more stringent obligations on companies, provides stronger monitoring and enforcement by the DOC and the Federal Trade Commission, and makes commitments on the part of public authorities regarding access to information. United States entities have been able to certify to the DOC their compliance with the privacy principles of the Privacy Shield since August 1, 2016 and rely on the Privacy Shield certification to transfer of personal data from the European Union to the United States.

In September 2016, the Irish privacy advocacy group Digital Rights Ireland brought an action for annulment of the European Commission decision on the adequacy of the Privacy Shield before the Court of Justice of the EU, Case T-670/16. In October 2016, a further action for annulment was brought by three French digital rights advocacy group, La Quadrature du Net, French Data Network and the Fédération FDN, Case T-738/16. Both cases are currently pending before the European Court of Justice. If the Court of Justice of the European Union invalidates the Privacy Shield, it will no longer be possible to rely on the Privacy Shield certification to transfer personal data from the European Union to entities in the United States. Adherence to the Privacy Shield is not, however, mandatory. Entities based in the United States are permitted to rely either on their adherence to the Privacy Shield or on the other authorized means and procedures to transfer personal data provided by the EU Data Protection Directive.

In addition, the EU Data Protection Regulation entered into force on May 24, 2016 and will apply from May 25, 2018. The EU Data Protection Regulation will introduce new data protection requirements in the European Union and substantial fines for breaches of the data protection rules. The EU Data Protection Regulation will increase our responsibility and liability in relation to personal data that we process, and we may be required to put in place additional mechanisms to ensure compliance with the new data protection rules.

Our failure to comply with these laws, or changes in the way in which these laws are implemented, could lead to government enforcement actions and significant penalties against us, and adversely impact our operating results.

Our future growth depends, in part, on our ability to penetrate foreign markets, where we will be subject to additional regulatory burdens and other risks and uncertainties.

Our future profitability will depend, in part, on our ability to commercialize setmelanotide in foreign markets for which we intend to rely on collaborations with third parties. If we commercialize setmelanotide in foreign markets, we will be subject to additional risks and uncertainties, including:

- our customers' ability to obtain reimbursement for setmelanotide in foreign markets;
- our inability to directly control commercial activities because we are relying on third parties;
- the burden of complying with complex and changing foreign regulatory, tax, accounting and legal requirements;
- different medical practices and customs in foreign countries affecting acceptance in the marketplace;
- import or export licensing requirements;
- longer accounts receivable collection times;
- longer lead times for shipping;
- language barriers for technical training;
- reduced protection of intellectual property rights in some foreign countries;
- foreign currency exchange rate fluctuations; and
- the interpretation of contractual provisions governed by foreign laws in the event of a contract dispute.

Foreign sales of setmelanotide could also be adversely affected by the imposition of governmental controls, political and economic instability, trade restrictions and changes in tariffs.

Laws and regulations governing any international operations we may have in the future may preclude us from developing, manufacturing and selling setmelanotide outside of the United States and require us to develop and implement costly compliance programs.

If we expand our operations outside of the United States, we must dedicate additional resources to comply with numerous laws and regulations in each jurisdiction in which we plan to operate. The Foreign Corrupt Practices Act of 1977, or the FCPA, prohibits any U.S. individual or business from paying, offering, authorizing payment or offering anything of value, directly or indirectly, to any foreign official, political party or candidate for the purpose of influencing any act or decision of such third party in order to assist the individual or business in obtaining or retaining business. The FCPA also obligates companies whose securities are listed in the United States to comply with certain accounting provisions requiring the company to maintain books and records that accurately and fairly reflect all transactions of the company, including international subsidiaries, and to devise and maintain an adequate system of internal accounting controls for international operations.

Compliance with the FCPA is expensive and difficult, particularly in countries in which corruption is a recognized problem. In addition, the FCPA presents particular challenges in the pharmaceutical industry, because, in many countries, hospitals are operated by the government, and doctors and other hospital employees are considered foreign officials. Certain payments to hospitals in connection with clinical trials and other work have been deemed to be improper payments to government officials and have led to FCPA enforcement actions.

Various laws, regulations and executive orders also restrict the use and dissemination outside of the United States, or the sharing with certain non-U.S. nationals, of information classified for national security

purposes, as well as certain products and technical data relating to those products. If we expand our presence outside of the United States, it will require us to dedicate additional resources to comply with these laws, and these laws may preclude us from developing, manufacturing or selling certain product candidates and products outside of the United States, which could limit our growth potential and increase our development costs.

The failure to comply with laws governing international business practices may result in substantial civil and criminal penalties and suspension or debarment from government contracting. The Securities and Exchange Commission, or SEC, also may suspend or bar issuers from trading securities on U.S. exchanges for violations of the FCPA's accounting provisions.

The results of the United Kingdom's referendum on withdrawal from the European Union may have a negative effect on global economic conditions, financial markets and our business.

On March 29, 2017, the Government of the United Kingdom initiated the formal procedure of withdrawal from the European Union. The procedure involves a two-year negotiation period in which the United Kingdom and the European Union must conclude an agreement setting out the terms of the United Kingdom's withdrawal and the arrangements for the United Kingdom's future relationship with the European Union. This negotiation period could be extended by a unanimous decision of the European Council, in agreement with the United Kingdom.

The referendum has created significant uncertainty concerning the future relationship between the United Kingdom and the European Union. This includes the laws and regulations that will apply as the United Kingdom determines which European Union laws to replace or replicate in the event of a withdrawal. From a regulatory perspective, the United Kingdom's withdrawal could result in significant complexity and risks. A basic requirement related to the grant of a marketing authorization for a medicinal product in the European Union is the requirement that the applicant is established in the European Union. Following withdrawal of the United Kingdom from the European Union, marketing authorizations previously granted to applicants established in the United Kingdom may no longer be valid. Moreover, depending upon the exact terms of the United Kingdom's withdrawal, there is an arguable risk that the scope of a marketing authorization for a medicinal product granted by the European Commission pursuant to the centralized procedure would not, in the future, include the United Kingdom. In these circumstances, an authorization granted by the United Kingdom's competent authorities would always be required to place medicinal products on the United Kingdom market.

In addition, the laws and regulations that will apply after the United Kingdom withdraws from the European Union may have implications for manufacturing sites that hold certification issued by the United Kingdom competent authorities. Our capability to rely on these manufacturing sites for products intended for the European Union market would also depend upon the exact terms of the United Kingdom's withdrawal.

The United Kingdom referendum has also given rise to calls for the governments of other EU member states to consider withdrawal from the European Union. These developments, or the perception that they could occur, have had and may continue to have a material adverse effect on global economic conditions and the stability of global financial markets. They may significantly reduce global market liquidity and restrict the ability of key market participants to operate in certain financial markets.

The efforts of the Trump administration to pursue regulatory reform may limit the FDA's ability to engage in oversight and implementation activities in the normal course, and that could negatively impact our business.

The Trump administration has taken several executive actions, including the issuance of a number of executive orders, that could impose significant burdens on, or otherwise materially delay, the FDA's ability to engage in routine regulatory and oversight activities such as implementing statutes through rulemaking, issuance of guidance, and review and approval of marketing applications. On January 30, 2017, President

Trump issued an executive order, applicable to all executive agencies, including the FDA, that requires that for each notice of proposed rulemaking or final regulation to be issued in fiscal year 2017, the agency shall identify at least two existing regulations to be repealed, unless prohibited by law. These requirements are referred to as the "two-for-one" provisions. This executive order includes a budget neutrality provision that requires the total incremental cost of all new regulations in the 2017 fiscal year, including repealed regulations, to be no greater than zero, except in limited circumstances. For fiscal years 2018 and beyond, the executive order requires agencies to identify regulations to offset any incremental cost of a new regulation. In interim guidance issued by the Office of Information and Regulatory Affairs within the Office of Management and Budget, or OMB, on February 2, 2017, the administration indicates that the "two-for-one" provisions may apply not only to agency regulations, but also to significant agency guidance documents. It is difficult to predict how these requirements will be implemented, and the extent to which they will impact the FDA's ability to exercise its regulatory authority. If these executive actions impose constraints on FDA's ability to engage in oversight and implementation activities in the normal course, our business may be negatively impacted.

Risks Related to Employee Matters and Managing Growth

Our future success depends on our ability to retain our key employees and consultants, and to attract, retain and motivate qualified personnel.

We are highly dependent on Keith M. Gottesdiener, M.D., our Chief Executive Officer and President, Hunter Smith, our Chief Financial Officer and Treasurer, Nithya Desikan, our Chief Commercial Officer, Lex H.T. Van der Ploeg, Ph.D., our Chief Scientific Officer, and Fred T. Fiedorek, M.D., our Chief Medical Officer. We have employment agreements with these individuals and will enter into new employment agreements with each of them which will become effective upon consummation of this offering, but any individual may terminate his or her employment with us at any time. The loss of their services might impede the achievement of our research, development and commercialization objectives. We also do not have any key-person life insurance on any of these key employees. We rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us and may not be subject to non-compete agreements. Recruiting and retaining qualified scientific personnel and sales and marketing personnel will also be critical to our success. We may not be able to attract and retain these personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific personnel from universities and research institutions. Failure to succeed in clinical trials may make it more challenging to recruit and retain qualified scientific personnel.

We will need to develop and expand our company, and we may encounter difficulties in managing this development and expansion, which could disrupt our operations.

In connection with becoming a public company, we expect to increase our number of employees and the scope of our operations. In particular, we will need to transition from a research and development company to a commercial company. To manage our anticipated development and expansion, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Also, our management may need to divert a disproportionate amount of its attention away from their day-to-day activities and devote a substantial amount of time to managing these development activities. Due to our limited resources, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. This may result in weaknesses in our infrastructure, and give rise to operational mistakes, loss of business and commercial opportunities, loss of employees and reduced productivity among remaining employees. The physical expansion of our operations may lead to significant costs and

may divert financial resources from other projects, such as the development of setmelanotide. If our management is unable to effectively manage our expected development and expansion, our expenses may increase more than expected, our ability to generate or increase our revenue could be reduced and we may not be able to implement our business strategy. Our future financial performance and our ability to commercialize setmelanotide, if approved, and compete effectively will depend, in part, on our ability to effectively manage the future development and expansion of our company.

In order to satisfy our obligations as a public company, we will need to hire additional qualified accounting and financial personnel with appropriate public company experience.

As a newly public company, we will need to establish and maintain effective disclosure and financial controls and make changes in our corporate governance practices. We will need to hire additional accounting and financial personnel with appropriate public company experience and technical accounting knowledge, and it may be difficult to recruit and retain such personnel. Even if we are able to hire appropriate personnel, our existing operating expenses and operations will be impacted by the direct costs of their employment and the indirect consequences related to the diversion of management resources from product development efforts.

Our internal computer systems, or those of our third-party CROs, CMOs or other contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of setmelanotide development programs.

Our internal computer systems and those of our third-party CROs, CMOs, and other contractors and consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. If such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our programs. For example, the loss of clinical trial data for setmelanotide could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach results in a loss of or damage to our data or applications or other data or applications relating to our technology or product candidate, or inappropriate disclosure of confidential or proprietary information, we could incur liabilities and the further development of setmelanotide could be delayed.

We may acquire businesses or products, form strategic alliances or create joint ventures in the future, and we may not realize their benefits.

We may acquire additional businesses or products, form strategic alliances or create joint ventures with third parties that we believe will complement or augment our existing business. If we acquire businesses with promising markets or technologies, we may not be able to realize the benefit of acquiring such businesses if we are unable to successfully integrate them with our existing operations and company culture. We may encounter numerous difficulties in developing, manufacturing and marketing any new products resulting from a strategic alliance, joint venture or acquisition that delay or prevent us from realizing their expected benefits or enhancing our business. We cannot assure you that, following any such acquisition, we will achieve the expected synergies to justify the transaction.

Risks Related to Our Common Stock and This Offering

Our executive officers, directors, principal stockholders and their affiliates will continue to exercise significant control over our company after this offering, which will limit your ability to influence corporate matters and could delay or prevent a change in corporate control.

Upon the completion of this offering, the existing holdings of our executive officers, directors, principal stockholders and their affiliates, including Pfizer Inc., investment funds affiliated with MPM Bioventures V LLC, investment funds affiliated with TRV GP, LLC, investment funds affiliated with New Enterprise Associates 13, L.P. and NEA Ventures 2009, L.P., investment funds affiliated with two public

healthcare investment funds, investment funds affiliated with Deerfield Mgmt, L.P. and J.E. Flynn Capital III, LLC, Sutrepa SAS and investment funds affiliated with OrbiMed Advisors LLC will represent beneficial ownership, in the aggregate, of approximately % of our outstanding common stock, assuming no exercise of the underwriters' option to acquire additional common stock in this offering and assuming we issue the number of shares of common stock as set forth on the cover page of this prospectus. As a result, these stockholders, if they act together, will be able to influence our management and affairs and control the outcome of matters submitted to our stockholders for approval, including the election of directors and any sale, merger, consolidation or sale of all or substantially all of our assets. These stockholders acquired their shares of common stock for substantially less than the price of the shares of common stock being acquired in this offering, and these stockholders may have interests, with respect to their common stock, that are different from those of investors in this offering and the concentration of voting power among these stockholders may have an adverse effect on the price of our common stock. In addition, this concentration of ownership might adversely affect the market price of our common stock by:

- delaying, deferring or preventing a change of control of us;
- impeding a merger, consolidation, takeover or other business combination involving us; or
- discouraging a potential acquirer from making a tender offer or otherwise attempting to obtain control of us.

See "Principal Stockholders" for more information regarding the ownership of our outstanding common stock by our executive officers, directors, principal stockholders and their affiliates.

Anti-takeover provisions in our charter documents and under Delaware law could make an acquisition of us, even one that may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management.

We are a Delaware corporation. Provisions in our amended and restated certificate of incorporation and amended and restated bylaws may delay or prevent an acquisition of us or a change in our management. In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which limits the ability of stockholders owning in excess of 15% of our outstanding voting stock to merge or combine with us. Although we believe these provisions collectively will provide for an opportunity to obtain greater value for stockholders by requiring potential acquirers to negotiate with our board of directors, they would apply even if an offer rejected by our board were considered beneficial by some stockholders. In addition, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors, which is responsible for appointing the members of our management. Any provision in our amended and restated certificate of incorporation and amended and restated bylaws or Delaware law that has the effect of delaying or deterring a change in control could limit the opportunity for our stockholders to receive a premium for their shares of our common stock, and could also affect the price that some investors are willing to pay for our common stock.

If you purchase our common stock in this offering, you will incur immediate and substantial dilution in the book value of your shares.

You will suffer immediate and substantial dilution in the net tangible book value of the common stock you purchase in this offering. Assuming an initial public offering price of $ per share, the midpoint of the price range set forth on the cover page of this prospectus, purchasers of common stock in this offering will experience immediate dilution of $ per share in net tangible book value of the common stock. In addition, investors purchasing common stock in this offering will contribute % of the total amount invested by stockholders since inception but will only own % of the shares of common stock outstanding. See "Dilution" for a more detailed description of the dilution to new investors in the offering.

An active trading market for our common stock may not develop, and you may not be able to resell your shares at or above the initial public offering price.

Prior to this offering, there has been no public market for shares of our common stock. Although we anticipate our common stock will be approved for listing on the NASDAQ Global Market, an active trading market for our shares may never develop or be sustained following this offering. The initial public offering price of our common stock will be determined through negotiations between us and the underwriters. This initial public offering price may not be indicative of the market price of our common stock after this offering. In the absence of an active trading market for our common stock, investors may not be able to sell their common stock at or above the initial public offering price or at the time that they would like to sell.

If securities or industry analysts do not publish research or reports or publish unfavorable research or reports about our business, our stock price and trading volume could decline.

The trading market for our common stock will depend in part on the research and reports that securities or industry analysts publish about us, our business, our market or our competitors. We do not control these analysts. We do not currently have and may never obtain research coverage by securities and industry analysts. If no securities or industry analysts commence coverage of our company, the trading price for our stock would be negatively impacted. In the event we obtain securities or industry analyst coverage, if one or more of the analysts who covers us downgrades our stock, our stock price would likely decline. If one or more of these analysts issues unfavorable commentary or ceases to cover us or fails to regularly publish reports on us, interest in our stock could decrease, which could cause our stock price or trading volume to decline.

Unfavorable global economic conditions could adversely affect our business, financial condition or results of operations.

Our results of operations could be adversely affected by general conditions in the global economy and in the global financial markets. The global financial crisis caused extreme volatility and disruptions in the capital and credit markets. A severe or prolonged economic downturn, such as the global financial crisis, could result in a variety of risks to our business, including weakened demand for setmelanotide and our ability to raise additional capital when needed on acceptable terms, if at all. A weak or declining economy could also strain our suppliers, possibly resulting in supply disruption, or cause our customers to delay making payments for our services. Any of the foregoing could harm our business and we cannot anticipate all of the ways in which the current economic climate and financial market conditions could adversely impact our business.

Market volatility may affect our stock price and the value of your investment.

Following this offering, the market price for our common stock is likely to be volatile, in part because our common stock has not been previously traded publicly. In addition, the market price of our common stock may fluctuate significantly in response to a number of factors, most of which we cannot control, including, among others:

- plans for, progress of, or results from preclinical studies and clinical trials of setmelanotide;
- the failure of the FDA to approve setmelanotide;
- announcements of new products, technologies, commercial relationships, acquisitions or other events by us or our competitors;
- the success or failure of other weight loss therapies and companies targeting rare diseases and orphan drug treatment;

- regulatory or legal developments in the United States and other countries;
- failure of setmelanotide, if approved, to achieve commercial success;
- fluctuations in stock market prices and trading volumes of similar companies;
- general market conditions and overall fluctuations in U.S. equity markets;
- variations in our quarterly operating results;
- changes in our financial guidance or securities analysts' estimates of our financial performance;
- changes in accounting principles;
- our ability to raise additional capital and the terms on which we can raise it;
- sales of large blocks of our common stock, including sales by our executive officers, directors and significant stockholders;
- additions or departures of key personnel;
- discussion of us or our stock price by the press and by online investor communities; and
- other risks and uncertainties described in these risk factors.

Our quarterly operating results may fluctuate significantly.

We expect our operating results to be subject to quarterly fluctuations. Our net loss and other operating results will be affected by numerous factors, including:

- variations in the level of expenses related to our development programs;
- addition or termination of clinical trials;
- any intellectual property infringement lawsuit in which we may become involved;
- regulatory developments affecting setmelanotide;
- our execution of any collaborative, licensing or similar arrangements, and the timing of payments we may make or receive under these arrangements;
- the achievement and timing of milestone payments under our existing collaboration and license agreements; and
- if setmelanotide receives regulatory approval, the level of underlying demand for that product and customers' buying patterns.

If our quarterly operating results fall below the expectations of investors or securities analysts, the price of our common stock could decline substantially. Furthermore, any quarterly fluctuations in our operating results may, in turn, cause the price of our stock to fluctuate substantially.

We will have broad discretion in how we use the proceeds of this offering. We may not use these proceeds effectively, which could affect our results of operations and cause our stock price to decline.

We will have considerable discretion in the application of the net proceeds of this offering. We intend to use the net proceeds from this offering to fund development and manufacturing of setmelanotide through completion of our Phase 3 clinical trial for the treatment of POMC deficiency obesity, the development and manufacturing of setmelanotide through completion of enrollment of our Phase 3 clinical trial for LepR deficiency obesity, the development of setmelanotide through proof of concept in our Phase 2 clinical trials for Bardet-Biedl syndrome, Alström syndrome, POMC heterozygous deficiency obesity and POMC epigenetic disorders, the preparation for commercialization of setmelanotide, including

initiatives to expand the diagnosis of genetic obesity and for working capital purposes, including general operating expenses, which may include funding for the hiring of additional personnel, capital expenditures, early commercialization activities and the costs of operating as a public company. As a result, investors will be relying upon management's judgment with only limited information about our specific intentions for the use of the net proceeds of this offering. We may use the net proceeds for purposes that do not yield a significant return or any return at all for our stockholders. In addition, pending their use, we may invest the net proceeds from this offering in a manner that does not produce income or that loses value.

Our ability to use certain net operating loss carryovers and other tax attributes may be limited.

We have incurred substantial losses during our history and we do not expect to become profitable in the near future and may never achieve profitability. Under the Internal Revenue Code of 1986, as amended, or the Code, a corporation is generally allowed a deduction for net operating losses, or NOLs, carried over from a prior taxable year. Under that provision, we can carry forward certain taxable losses of our subsidiaries to offset future taxable income, if any, until such losses are used or expire. The same is true of other unused tax attributes, such as research tax credits. As of December 31, 2016, we had approximately $46.9 and $24.4 million of unused federal and state carryforwards of NOLs, respectively, and approximately $1.0 and $0.4 million of unused federal and state carryforwards of tax credits, respectively.

If a corporation undergoes an "ownership change," generally defined as a greater than 50% change by value in its equity ownership over a three-year period, Sections 382 and 383 of the Code limit the corporation's ability to use carryovers of its pre-change NOLs, credits and certain other tax attributes to reduce its tax liability for periods after the ownership change. Our issuance of common stock pursuant to this offering may result in a limitation under Sections 382 and 383, either separately or in combination with certain prior or subsequent shifts in the ownership of our common stock. As a result, our ability to use carryovers of pre-change NOLs and credits to reduce our future U.S. federal income tax liability may be subject to limitations. This could result in increased U.S. federal income tax liability for us if we generate taxable income in a future period. Limitations on the use of NOLs and other tax attributes could also increase our state tax liability. Any such limitation could have a material adverse effect on our results of operations in future years. We have not completed a study to assess whether an ownership change for purposes of Section 382 or 383 has occurred, or whether there have been multiple ownership changes since our inception, due to the significant costs and complexities associated with such study.

The use of our tax attributes will also be limited to the extent that we do not generate positive taxable income in future tax periods. We do not expect to generate positive taxable income in the near future and we may never achieve tax profitability.

Raising additional capital may cause dilution to our existing stockholders, restrict our operations or require us to relinquish rights.

We may seek additional capital through a combination of private and public equity offerings, debt financings, collaborations and strategic and licensing arrangements. To the extent that we raise additional capital through the sale of common stock or securities convertible or exchangeable into common stock, a stockholder's ownership interest in our company will be diluted. In addition, the terms of any such securities may include liquidation or other preferences that materially adversely affect the rights of our stockholders. Debt financing, if available, would increase our fixed payment obligations and may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we raise additional funds through collaboration, strategic partnerships and licensing arrangements with third parties, we may have to relinquish valuable rights to setmelanotide, our intellectual property or future revenue streams, or grant licenses on terms that are not favorable to us.

Sales of a substantial number of shares of our common stock in the public market could cause our stock price to fall.

If those stockholders who hold shares of our common stock immediately prior to the effectiveness of the registration statement of which this prospectus forms a part sell, or indicate an intention to sell, substantial amounts of our common stock in the public market after the lock-up and other legal restrictions on resale discussed in this prospectus lapse, the market price of our common stock could decline and our ability to raise adequate capital through the sale of additional equity securities could be impaired. Upon completion of this offering, there will be shares of our common stock outstanding, assuming no exercise of the underwriters' option to purchase additional shares of common stock. Of these shares, as of the date of this prospectus, approximately shares of our common stock, plus any shares sold upon exercise of the underwriters' option to purchase additional shares of common stock, will be freely tradable, without restriction, in the public market immediately following this offering, except for shares purchased by affiliates, and the remaining shares may be sold upon expiration of the lock-up agreements pertaining to this offering 180 days after the date of this offering, subject in some cases to volume limitations. The representatives of the underwriters, however, may, in their sole discretion, permit our officers, directors and other stockholders who are subject to these lock-up agreements to sell shares prior to the expiration of the lock-up agreements.

After this offering, the holders of approximately shares of our common stock will be entitled to rights with respect to the registration of their shares under the Securities Act of 1933, as amended, or the Securities Act, subject to the lock-up agreements described above, including requiring us to file registration statements covering the shares of our common stock they hold or to include their shares in registration statements that we may file for ourselves or other stockholders. See "Description of Capital Stock—Registration Rights" in this prospectus for more information regarding these registration rights. Registration of these shares under the Securities Act would result in the shares becoming freely tradable without restriction under the Securities Act, except for shares purchased by affiliates. Any sales of securities by these stockholders could have a material adverse effect on the market price of our common stock. These registration rights have been waived in connection with this offering.

We also intend to register all the shares of common stock that we may issue under our equity incentive plans. Effective upon the effectiveness of the registration statement of which this prospectus is a part, an aggregate of shares of our common stock will be reserved for future issuance under these plans. Once we register these shares, which we plan to do shortly after the completion of this offering, they can be freely sold in the public market upon issuance, subject to the lock-up agreements referred to above. If a large number of these shares are sold in the public market, the sales could reduce the trading price of our common stock. See "Shares Eligible for Future Sale" for a more detailed description of sales that may occur in the future.

We are an "emerging growth company," and as a result of the reduced disclosure and governance requirements applicable to emerging growth companies, our common stock may be less attractive to investors.

We are an "emerging growth company" as defined in the JOBS Act, and we intend to take advantage of certain exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies including, but not limited to, not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, as amended, or Section 404, reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements, and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved. If we choose not to comply with the auditor attestation requirements of Section 404, our auditors will not be required to attest to the effectiveness of our internal control over financial reporting. As a result, investors may become less comfortable with the effectiveness of our internal controls and the risk that material weaknesses or other deficiencies in our internal controls go undetected or may increase. If we choose to provide reduced disclosures in our periodic reports and proxy statements while we are an

emerging growth company, investors would have access to less information and analysis about our executive compensation, which may make it difficult for investors to evaluate our executive compensation practices. We cannot predict if investors will find our common stock less attractive because we will rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile. We may take advantage of these reporting exemptions until we are no longer an "emerging growth company." We will remain an "emerging growth company" until the earlier of (1) the last day of the fiscal year (a) following the fifth anniversary of the completion of this offering, (b) in which we have total annual gross revenue of at least $1.07 billion, or (c) in which we are deemed to be a large accelerated filer, which means the market value of our common stock that is held by non-affiliates exceeds $700 million as of the prior June 30th, and (2) the date on which we have issued more than $1.0 billion in non-convertible debt during the prior three-year period.

We will incur increased costs as a result of operating as a public company, and our management will be required to devote substantial time to new compliance initiatives and corporation governance policies.

As a public company, and particularly after we are no longer an emerging growth company, we will incur significant legal, accounting and other expenses that we did not incur as a private company. The Sarbanes-Oxley Act of 2002, or Sarbanes-Oxley, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of the NASDAQ Global Market and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel will need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations will increase our legal and financial compliance costs and will make some activities more time-consuming and costly. For example, we expect that these rules and regulations may make it more difficult and more expensive for us to obtain director and officer liability insurance, which in turn could make it more difficult for us to attract and retain qualified members of our board of directors.

We are evaluating these rules and regulations, and cannot predict or estimate the amount of additional costs we may incur or the timing of such costs. These rules and regulations are often subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices.

For as long as we remain an emerging growth company, we may take advantage of certain exemptions from various reporting requirements that are applicable to other public companies that are not applicable to emerging growth companies as described in the preceding risk factor.

Pursuant to Section 404 of Sarbanes-Oxley, we will be required to furnish a report by our management on our internal control over financial reporting. However, while we remain an emerging growth company, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with Section 404 within the prescribed period, we will be engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, potentially engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that we will not be able to conclude, within the prescribed timeframe or at all, that our internal control over financial reporting is effective as required by Section 404. If we identify one or more material weaknesses in our internal control over financial reporting, it could result in an

adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

We may be at an increased risk of securities class action litigation.

Historically, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because biotechnology and pharmaceutical companies have experienced significant stock price volatility in recent years. If we were to be sued, it could result in substantial costs and a diversion of management's attention and resources, which could harm our business.

We do not intend to pay dividends on our common stock and, consequently, your ability to achieve a return on your investment will depend on appreciation in the price of our common stock.

We have never declared or paid any cash dividends on our common stock and do not currently intend to do so in the foreseeable future. We currently anticipate that we will retain future earnings for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends in the foreseeable future. Therefore, the success of an investment in shares of our common stock will depend upon any future appreciation in their value. There is no guarantee that shares of our common stock will appreciate in value or even maintain the price at which you purchased them.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus contains forward-looking statements, which reflect our current views with respect to, among other things, our operations and financial performance. You can identify these forward-looking statements by the use of words such as "outlook," "believes," "expects," "potential," "continues," "may," "will," "should," "seeks," "approximately," "predicts," "intends," "plans," "estimates," "anticipates" or the negative version of these words or other comparable words. Such forward-looking statements are subject to various risks and uncertainties. Accordingly, there are or will be important factors that could cause actual outcomes or results to differ materially from those indicated in these statements. We believe these factors include but are not limited to those described under "Risk Factors" and include, among other things:

- the success, cost and timing of our product development activities and clinical trials;
- our ability to obtain and maintain regulatory approval for setmelanotide and our future product candidates, if any, and any related restrictions, limitations, and/or warnings in the label of an approved product candidate;
- our ability to obtain funding for our operations;
- the commercialization of setmelanotide, if approved;
- the number of people in our target patient population;
- our plans to research, develop and commercialize setmelanotide;
- our ability to operate, and the implementation of our business strategy, as an independent company;
- our ability to attract collaborators with development, regulatory and commercialization expertise;
- our expectations regarding our ability to obtain and maintain intellectual property protection for setmelanotide;
- future agreements with third parties in connection with the commercialization of setmelanotide or our future product candidates, if any;
- the size and growth potential of the markets for setmelanotide, and our ability to serve those markets;
- our expectations for the pricing of setmelanotide;
- the rate and degree of market acceptance of setmelanotide, as well as the reimbursement coverage for setmelanotide;
- regulatory developments in the United States, the European Union and other jurisdictions;
- the performance of our third-party suppliers and manufacturers;
- the extent and success of competing therapies that are or may become available;
- our ability to attract and retain key scientific or management personnel;
- the accuracy of our estimates regarding our target patient populations, expenses, future revenues, capital requirements and needs for additional financing;
- our expectations regarding the period during which we qualify as an emerging growth company under the JOBS Act; and
- our use of the proceeds from this offering.

These factors should not be construed as exhaustive and should be read in conjunction with the other cautionary statements that are included in this prospectus. We undertake no obligation to publicly update or review any forward-looking statement, whether as a result of new information, future developments or otherwise.

MARKET, INDUSTRY AND OTHER DATA

This prospectus includes market, industry and other data and forecasts that we have derived from independent consultant reports, publicly available information, various industry publications, other published industry sources and our internal data and estimates. Independent consultant reports, industry publications and other published industry sources generally indicate that the information contained therein was obtained from sources believed to be reliable.

Due to the rarity of our target indications, there is no available comprehensive patient registry or other method of establishing with precision the actual number of patients with MC4 pathway genetic defects. As a result, we have had to rely on other available sources to derive prevalence estimates for our target indications. Since the published epidemiology studies for these disorders are based on relatively small population samples, and are not amenable to robust statistical analyses, it is possible that these projections may exceed the addressable population, particularly given the need to genotype patients to definitively confirm a diagnosis.

We have estimated the potential addressable patient populations with these disorders based on the following sources and assumptions:

- *POMC Deficiency Obesity.* There are approximately 50 patients with POMC deficiency obesity noted in a series of published case reports, each mostly reporting a single or small number of patients. However, we believe our addressable patient population for this deficiency may be approximately 100 to 500 patients in the United States, and a comparable addressable patient population in Europe, as most of the reported cases are from a small number of academic research centers, and because genetic testing for POMC deficiency is often unavailable and currently is rarely performed. Based on discussions with experts in rare diseases, we also believe the number of diagnosed cases could increase several-fold with increased awareness of this deficiency and the availability of new treatments.

- *LepR Deficiency Obesity and POMC Heterozygous Deficiency Obesity.* Our addressable patient population estimate for LepR deficiency obesity is approximately 500 to 2,000 patients in the United States, and for POMC heterozygous deficiency obesity is approximately 4,000 patients in the United States, with a comparable addressable patient population for both indications in Europe. Our estimates are based on:

  - epidemiology studies on LepR deficiency and POMC heterozygous deficiency in small cohorts of patients comprised of children with severe obesity and adults with severe obesity who have a history of early onset obesity;

  - U.S. Census Bureau figures for adults and children, and Centers for Disease Control and Prevention, or CDC, prevalence numbers for severe adult obese patients (BMI greater than 40 kg/ m^2) and for severe early onset obese children (99th percentile at ages two to 17 years old); and

  - with wider availability of genetic testing expected for LepR deficiency and POMC heterozygous deficiency and increased awareness of new treatments, our belief that up to 40% of patients with these disorders may eventually be diagnosed.

  Using these sources and assumptions, we calculated our estimates for addressable populations by multiplying (x) our estimate of the number of patients comprised of children with severe obesity and our estimate of a projected number of adults with severe obesity who have a history of early onset obesity, (y) the estimated prevalence from epidemiology studies of approximately 1% for LepR deficiency and 2% for POMC heterozygous, and (z) our estimated diagnosis rate of up to 40%.

- *Bardet-Biedl Syndrome.* Our addressable patient population estimate for Bardet-Biedl syndrome is approximately 1,500 to 2,500 patients in the United States based on:

  - Published prevalence estimates of one in 100,000 in North America, which projects to approximately 3,250 people in the United States. We believe the majority of these patients are addressable patients; and
  - We believe that with wider availability of genetic testing expected for Bardet-Biedl syndrome and increased awareness of new treatments, the number of patients diagnosed with this disorder will increase.

- *Alström Syndrome.* Our addressable patient population estimate for Alström syndrome is approximately 500 to 1,000 patients worldwide. This estimate is based on:

  - Published prevalence estimates of one in 1,000,000 in North America, which projects to approximately 325 people in the United States. We believe the majority of these patients are addressable patients; and
  - We believe that with wider availability of genetic testing expected for Alström syndrome and increased awareness of new treatments, the number of patients diagnosed with this disorder will increase.

- *POMC Epigenetic Disorders.* There is currently no epidemiology data that defines the prevalence of POMC epigenetic disorders.

We believe that the patient populations in the European Union are at least as large as those in the United States. However, we do not have comparable epidemiological data from the European Union and these estimates are therefore based solely on applying relative population percentages to the Company derived estimates described above.

We are conducting additional epidemiology studies to strengthen these prevalence projections. In parallel, we are also developing a patient registry for diagnosed patients with POMC deficiency and LepR deficiency which will further inform prevalence projections for these rare genetic orders. See "*Business—Other Clinical Initiatives in Genetic Obesity—Genotyping Study.*" for additional information.

See "Risk Factors—*Risks Related to the Development of Setmelanotide—The number of patients suffering from each of the MC4 pathway deficiencies we are targeting is small and has not been established with precision. If the actual number of patients is smaller than we estimate, our revenue and ability to achieve profitability may be materially adversely affected."* for additional information.

USE OF PROCEEDS

We estimate that the net proceeds to us from the sale of the shares of our common stock offered by us will be approximately $ million, based on an assumed initial public offering price of $ per share, the midpoint of the price range set forth on the cover page of this prospectus, and after deducting underwriting discounts and commissions. If the underwriters' option to purchase additional shares in this offering is exercised in full, we estimate that our net proceeds will be approximately $ million, after deducting underwriting discounts and commissions.

A $1.00 increase (decrease) in the assumed initial public offering price of $ per share would increase (decrease) the net proceeds to us from this offering by approximately $ million, assuming the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting underwriting discounts and commissions. Similarly, each increase (decrease) of one million shares in the number of shares of common stock offered by us would increase (decrease) the net proceeds to us from this offering by approximately $ million, assuming the assumed initial public offering price remains the same and after deducting underwriting discounts and commissions.

As of June 30, 2017, we had cash and cash equivalents and short-term investments of approximately $17.7 million and after giving effect, on a pro forma basis, to the aggregate gross proceeds of $20.5 million from the sale of our series A preferred stock in August 2017, $38.2 million. We intend to use the net proceeds from this offering, together with our existing cash resources, as follows:

- approximately $ million to fund the development and manufacturing of setmelanotide through completion of our Phase 3 clinical trial for the treatment of POMC deficiency obesity;
- approximately $ million for the development and manufacturing of setmelanotide through completion of enrollment of our Phase 3 clinical trial for the treatment of LepR deficiency obesity;
- approximately $ million for the development of setmelanotide through proof of concept in our Phase 2 clinical trials for Bardet-Biedl syndrome, Alström syndrome, POMC heterozygous deficiency obesity and POMC epigenetic disorders;
- preparation for commercialization of setmelanotide, including initiatives to expand the diagnosis of genetic obesity; and
- the remainder for working capital purposes and other general corporate purposes.

Our expected use of net proceeds from this offering represents our current intentions based upon our present plans and business condition. As of the date of this prospectus, we cannot predict with certainty all of the particular uses for the net proceeds to be received upon the closing of this offering, or the amounts that we will actually spend on the uses set forth above. The amounts and timing of our actual use of the net proceeds will vary depending on numerous factors, including the progress of our clinical trials and other development efforts for setmelanotide and other factors described in "Risk Factors" beginning on page 16, as well as the amount of cash we use in our operations. As a result, our management will have broad discretion in the application of the net proceeds, and investors will be relying on our judgment regarding the application of the net proceeds of this offering. In addition, we might decide to postpone or not pursue clinical trials or preclinical activities if the net proceeds from this offering and the other sources of cash are less than expected.

Pending application of the net proceeds, we intend to invest the net proceeds from this offering in short- and intermediate-term, interest-bearing obligations, investment-grade instruments, certificates of deposit or direct or guaranteed obligations of the U.S. government. We may still require significant additional capital to fund the continued development of setmelanotide and our operating needs thereafter. We expect to finance our additional cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances and licensing arrangements.

DIVIDEND POLICY

We currently intend to retain all available funds and any future earnings for use in the operation of our business and do not anticipate paying any dividends on our common stock in the foreseeable future. Any future determination to declare dividends will be made at the discretion of our board of directors and will depend on our financial condition, operating results, capital requirements, general business conditions and other factors that our board of directors may deem relevant.

CAPITALIZATION

The following table sets forth our cash and cash equivalents and short-term investments and capitalization as of June 30, 2017, as follows:

- on an actual basis;
- on a pro forma basis to reflect the issuance of 78,666,209 shares of our series A-1 junior preferred stock in exchange for an equal number of shares of our common stock in connection with the Distribution, the issuance of additional shares of series A preferred stock in August 2017 for gross proceeds of $20.5 million (see Note 12 within the notes to our financial statements appearing elsewhere in this prospectus) and the conversion of all of our outstanding preferred stock into 159,616,208 shares of common stock upon the closing of this offering and;
- on a pro forma as adjusted basis to give further effect to the issuance and sale of shares of our common stock in this offering at an assumed initial public offering price of $ per share, which is the midpoint of the price range listed on the cover page of this prospectus, after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us.

Our capitalization following the closing of this offering will be adjusted based on the actual initial public offering price and other terms of the offering determined at pricing. You should read this information in conjunction with our financial statements and the related notes appearing at the end of this prospectus, the "Management's Discussion and Analysis of Financial Condition and Results of Operations" section and other financial information contained in this prospectus. You should also read this table together with the information contained in this prospectus, including "Use of Proceeds," and the historical financial statements and related notes included elsewhere in this prospectus.

	As of June 30, 2017		
	Actual	Pro Forma	Pro Forma As Adjusted
		(unaudited) (in thousands)	
Cash and cash equivalents and short-term investments	$ 17,740	$ 38,215	$
Convertible preferred stock:			
Series A preferred stock; 80,950,000 shares authorized; 60,475,001 shares issued and outstanding actual; no shares issued and outstanding pro forma and pro forma as adjusted	60,147	—	
Stockholders' equity (deficit):			
Common stock, $0.001 par value; 195,700,000 shares authorized, 93,500,000 shares issued and outstanding actual; 174,449,999 shares issued and outstanding pro forma; and shares issued and outstanding pro forma as adjusted	93	174	
Additional paid-in capital	44,346	125,297	
Accumulated deficit	(89,705)	(89,705)	
Total stockholders' equity (deficit)	(45,266)	35,766	
Total capitalization	$ (27,526)	$ 73,981	$

The information above is illustrative only and our capitalization following the completion of this offering will be adjusted based on the actual initial public offering price and other terms of this offering determined at pricing.

A $1.00 increase (decrease) in the assumed initial public offering price of $ per share, the midpoint of the estimated price range shown on the cover page of this prospectus, would increase (decrease) the amount of cash and cash equivalents, additional paid-in capital, total stockholders' equity (deficit) and total capitalization on a pro forma as adjusted basis by approximately $ million, assuming the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. Similarly, each increase (decrease) of one million shares offered by us would increase (decrease) cash and cash equivalents, total stockholders' equity (deficit) and total capitalization on a pro forma as adjusted basis by approximately $ million, assuming the assumed initial public offering price remains the same, and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. A one million share increase in the number of shares offered by us together with a concomitant $1.00 increase in the assumed initial public offering price of $ per share, the midpoint of the price range set forth on the cover page of this prospectus, would increase each of cash and cash equivalents and total stockholders' (deficit) equity by approximately $ million after deducting underwriting discounts and commissions and estimated offering expenses payable by us. Conversely, a one million share decrease in the number of shares offered by us together with a concomitant $1.00 decrease in the assumed initial public offering price of $ per share, the midpoint of the price range set forth on the cover page of this prospectus, would decrease each of cash and cash equivalents and total stockholders' (deficit) equity by approximately $ million after deducting underwriting discounts and commissions and estimated offering expenses payable by us. The pro forma as adjusted information discussed above is illustrative only and will be adjusted based on the actual public offering price and other terms of this offering determined at pricing.

DILUTION

If you invest in our common stock in this offering, your ownership interest will be immediately diluted to the extent of the difference between the initial public offering price per share and the pro forma as adjusted net tangible book value per share of our common stock after this offering.

Our historical net tangible book value as of June 30, 2017 was approximately $(45.3) million, or $(0.48) per share of our common share. Our historical net tangible book value represents our total tangible assets less our total liabilities. Net historical tangible book value per common share is our historical net tangible book value divided by the number of common shares outstanding as of June 30, 2017.

Our pro forma net tangible book value as of June 30, 2017 was approximately $35.8 million, or $0.21 per share of our common stock. Pro forma net tangible book value represents our total tangible assets less our total liabilities, after giving effect to (1) to reflect the issuance of 78,666,209 shares of our series A-1 junior preferred stock in exchange for an equal number of shares of our common stock in connection with the Distribution, (2) our sale of 20,474,998 shares of series A preferred stock in August 2017 for gross proceeds of $20.5 million and (3) the conversion of all outstanding shares of our preferred stock into 159,616,208 shares of common stock upon the closing of this offering. Pro forma net tangible book value per share represents pro forma net tangible book value divided by the total number of common shares outstanding as of June 30, 2017 after giving effect to the pro forma adjustments described above.

Our pro forma as adjusted net tangible book value represents our pro forma net tangible book value, plus the effect of the issuance and sale of shares of our common stock in this offering at an assumed initial public offering of $ per share (the midpoint of the price range set forth on the cover page of this prospectus), after deducting underwriting discounts and commissions and estimating offering expenses payable by us. Pro forma as adjusted net tangible book value per share represents pro forma as adjusted net tangible book value divided by the total number of common shares outstanding as of June 30, 2017, after giving effect to the pro forma adjustments and the offering described above. Our pro forma as adjusted net tangible book value as of June 30, 2017 was approximately $ million, or $ per share of our common stock. This amount represents an immediate increase in the pro forma adjusted net tangible book value of $ per share to existing shareholders and an immediate dilution of $ per share to new investors purchasing shares at an assumed initial public offering price of $ per share (the midpoint of the price range set forth on the cover page of this prospectus).

The following table illustrates this dilution on a per share basis:

Assumed initial public offering price per share		$
Historical net tangible book value per share as of June 30, 2017	$ (0.48)	
Increase per share attributable to pro forma adjustments described above		
Pro forma net tangible book value per share at June 30, 2017	$ 0.21	
Increase per share attributable to new investors		
Pro forma as adjusted net tangible book value per share at June 30, 2017 after giving effect to the offering		
Dilution per share to new investors		$

A $1.00 increase (decrease) in the assumed initial public offering price of $ per share, which is the midpoint of the price range set forth on the cover page of this prospectus, would increase (decrease) the pro forma as adjusted net tangible book value per share after this offering by approximately $ per share and the dilution per share to investors participating in this offering by approximately $ per share, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting the estimated underwriting discounts and commissions and estimated offering costs payable by us.

The following table summarizes, on a pro forma basis as of June 30, 2017, the total number of shares purchased from us, the total consideration paid, or to be paid, and the average price per share paid, or to be paid, by existing stockholders and by new investors in this offering at an assumed initial public offering price of $ per share, which is the midpoint of the price range set forth on the cover page of this prospectus, before deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. As the table below shows, new investors purchasing shares in this offering will pay an average price per share substantially higher than our existing stockholders paid.

	Shares Purchased		Total Consideration		Average Price Per Share
	Number	Percentage	Amount (in thousands)	Percentage	
Existing stockholders		%	$	%	$
New investors		%		%	
Total		100%	$	100%	$

Except as otherwise indicated, the discussion and tables above assume no exercise of the underwriters' option to purchase additional shares of our common stock in this offering. If the underwriters' option to purchase additional shares is exercised in full:

- the percentage of outstanding common stock held by existing stockholders will be reduced to % of the total number of shares of common stock to be outstanding upon completion of this offering; and
- the number of shares of common stock held by investors participating in this offering will be increased to shares, or % of the total number of shares of common stock to be outstanding upon completion of this offering.

Effective immediately upon closing of this offering, an aggregate of shares of our common stock will be reserved for issuance under our amended and restated 2015 equity incentive plan, or the Plan, and an aggregate of shares of our common stock will be reserved for issuance under our 2017 employee stock purchase plan. Furthermore, we may choose to raise additional capital through the sale of equity or convertible debt securities due to market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. To the extent that any new options are issued under our equity incentive plans or we issue additional shares of common stock or other equity or convertible debt securities in the future, there will be further dilution to investors participating in this offering.

SELECTED FINANCIAL DATA

The following selected statements of operations data for the years ended December 31, 2015 and 2016 and the balance sheet data as of December 31, 2015 and 2016 are derived from our audited financial statements appearing elsewhere in this prospectus. The selected statements of operations data for the six months ended June 30, 2016 and 2017 and the balance sheet data as of June 30, 2017 have been derived from our unaudited financial statements included elsewhere in this prospectus. In our opinion, these unaudited financial statements have been prepared on a basis consistent with our audited financial statements and contain all adjustments, consisting only of normal and recurring adjustments, necessary for a fair presentation of such financial data. In our opinion, you should read this data together with our audited financial statements and related notes appearing elsewhere in this prospectus and the information under the caption "Management's Discussion and Analysis of Financial Condition and Results of Operations."

Our financial statements for the periods presented include allocations of costs from certain shared functions provided to us by the Relamorelin Company. These allocations were made based on either a specific identification basis or, when specific identification is not practicable, a proportional cost allocation method which allocates expenses based on the percentage of employee time and research and development effort expended on our business as compared to total employee time and research and development effort, and have been included in our financial statements for the periods presented.

The financial statements included in this prospectus may not necessarily reflect our financial position, results of operations and cash flows as if we had operated as an independent company during all of the periods presented. See "Summary—Corporate Reorganization."

Our historical results are not necessarily indicative of our future results, and our operating results for the six-month period ended June 30, 2017 are not necessarily indicative of the results that may be expected for the fiscal year ending December 31, 2017 or any other interim periods or any future year or period.

	Year Ended December 31, 2015	Year Ended December 31, 2016	Six Months Ended June 30, 2016	Six Months Ended June 30, 2017
	(in thousands, except share and per share data)		(unaudited)	
Operating expenses:				
Research and development	$ 7,148	$ 19,594	$ 8,544	$ 10,270
General and administrative	3,425	6,311	2,585	2,873
Total operating expenses	10,573	25,905	11,129	13,143
Loss from operations	(10,573)	(25,905)	(11,129)	(13,143)
Other income (expense):				
Revaluation of Series A Investor Right/Obligation and Series A Investor Instrument	(500)	—	—	(82)
Interest income, net	—	33	14	63
Total other income (expense):	(500)	33	14	(19)
Net loss and comprehensive loss	$ (11,073)	$ (25,872)	$ (11,115)	$ (13,162)
Net loss attributable to common stockholders	$ (12,000)	$ (29,074)	$ (12,711)	$ (15,534)
Net loss attributable to common stockholders per common share, basic and diluted(1)	$ (0.13)	$ (0.31)	$ (0.14)	$ (0.17)
Weighted average common shares outstanding, basic and diluted	93,500,000	93,500,000	93,500,000	93,500,000
Pro forma net loss attributable to common stockholders per common share, basic and diluted (unaudited)(1)(2)		$ (0.19)		$ (0.09)
Pro forma weighted average common shares outstanding, basic and diluted (unaudited)(1)(2)		133,500,000		153,409,393

	December 31, 2015	December 31, 2016	June 30, 2017
Balance Sheet Data:			
Cash, cash equivalents and short-term investments	$ 34,869	$ 10,537	$ 17,740
Working capital (deficit)	30,218	6,444	13,619
Total assets	37,275	12,339	20,404
Convertible preferred stock	40,000	40,000	60,147
Accumulated deficit	(50,671)	(76,543)	(89,705)
Total stockholders' equity (deficit)	$ (7,999)	$ (32,703)	$ (45,266)

(1) See Note 2 within the notes to our financial statements appearing elsewhere in this prospectus for a description of the methods used to calculate basic and diluted net loss per share and pro forma basic and diluted net loss per share.

(2) Pro forma to reflect the issuance of 78,666,209 shares of our series A-1 junior preferred stock in exchange for an equal number of shares of our common stock in connection with the Distribution, the issuance of additional shares of series A preferred stock in August 2017 (see Note 12 within the notes to our financial statements appearing elsewhere in this prospectus) and the conversion of all of our outstanding preferred stock into 159,616,208 shares of common stock upon the closing of this offering.

MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

You should read the following discussion and analysis of our financial condition and results of operations together with our financial statements and the related notes and other financial information included elsewhere in this prospectus. Some of the information contained in this discussion and analysis or set forth elsewhere in this prospectus, including information with respect to our plans and strategy for our business and related financing, includes forward-looking statements that involve risks and uncertainties. As a result of many factors, including those set forth in the "Risk Factors" section of this prospectus, our actual results could differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.

Overview

We are a biopharmaceutical company focused on the development and commercialization of peptide therapeutics for the treatment of rare genetic deficiencies that result in life-threatening metabolic disorders. Our lead peptide product candidate is setmelanotide, a potent, first-in-class MC4R agonist for the treatment of rare genetic disorders of obesity. We believe setmelanotide, for which we have exclusive worldwide rights, has the potential to serve as replacement therapy for the treatment of MC4 pathway deficiencies. Our development efforts are initially focused on obesity related to six monogenic MC4 pathway deficiencies, POMC, LepR, Bardet-Biedl syndrome, Alström syndrome POMC heterozygous and POMC epigenetic disorders, for which there are currently no effective or approved treatments. We believe that the MC4 pathway is a compelling target for treating these genetic disorders because of its critical role in regulating appetite and weight by promoting satiety and weight control, and that peptide therapeutics are uniquely suited for activating this target. We have demonstrated proof of concept in Phase 2 clinical trials in POMC deficiency obesity, LepR deficiency obesity and Bardet-Biedl syndrome, three of these genetic disorders of extreme and unrelenting appetite and obesity, in which setmelanotide dramatically reduced both weight and hunger. We are currently enrolling patients in a Phase 3 clinical trial for POMC deficiency obesity and expect to enroll the first patient in a Phase 3 clinical trial for LepR deficiency obesity in the second half of 2017. We recently demonstrated preliminary proof of concept in our Phase 2 clinical trial in Bardet-Biedl syndrome, indicating that this is also a setmelanotide-responsive, upstream MC4 pathway disorder. We are continuing to enroll patients in this trial and expect to report preliminary Phase 2 results in the fourth quarter of 2017. We expect to initiate a Phase 3 clinical trial in Bardet-Biedl syndrome in 2018. We have also initiated Phase 2 clinical trials in Alström syndrome, POMC heterozygous deficiency obesity, and POMC epigenetic disorders.

We have leveraged skilled experts, consultants, Contract Research Organizations, or CROs, and contractors to manage our clinical operations under the leadership and direction of our management. We expect to expand our infrastructure to manage our clinical, finance and commercial operations with a higher proportion of full-time employees. We have fifteen employees, four of whom hold Ph.D. or M.D. degrees. Of these employees, ten are engaged in development and commercialization activities and five are engaged in support administration, including business development and finance. In the near-term, we expect to significantly expand our clinical and finance personnel, in particular, and will incur increased expenses as a result.

Our operations to date have been limited primarily to conducting research and development activities for setmelanotide. To date, we have not generated any product revenue and have financed our operations primarily through capital contributions from the Predecessor Company, the Relamorelin Company and the LLC entity and, more recently, the private placement of equity securities to outside investors. We will not generate revenue from product sales until we successfully complete development and obtain regulatory approval for setmelanotide, which we expect will take a number of years and is subject to significant uncertainty. We expect to continue to fund our operations through the sale of equity, debt financings or other sources. We intend to build our own marketing and commercial sales infrastructure and we may

enter into collaborations with other parties for certain markets outside the United States. However, we may be unable to raise additional funds or enter into such other arrangements when needed on favorable terms, or at all. If we fail to raise capital or enter into such other arrangements as, and when, needed, we may have to significantly delay, scale back or discontinue the development or commercialization of setmelanotide. See "Risk Factors—*Risks Related to Our Financial Position and Need for Capital*" beginning on page 16 of this prospectus for additional information.

As of June 30, 2017, we had an accumulated deficit of $89.7 million. Our net losses were $11.1 million and $25.9 million for the year ended December 31, 2015 and 2016, respectively, and $11.1 million and $13.2 million for the six months ended June 30, 2016 and 2017, respectivley. We expect to continue to incur significant expenses and increasing operating losses over the foreseeable future. We expect our expenses will increase substantially in connection with our ongoing activities, as we:

- continue to conduct clinical trials for setmelanotide;
- engage CMOs for the manufacture of setmelanotide for clinical trials;
- seek regulatory approval for setmelanotide;
- expand our clinical and financial operations and build a marketing and commercialization infrastructure; and
- operate as a public company.

As of June 30, 2017, our existing cash and cash equivalents and short-term investments were approximately $17.7 million and after giving effect, on a pro forma basis, to the aggregate gross proceeds from the sale of our series A preferred stock in August 2017, $38.2 million. We expect that the net proceeds of this offering will enable us to fund our operating expenses into the first half of 2019.

Corporate Background and Distribution

We are a Delaware corporation organized in February 2013 under the name Rhythm Metabolic, Inc., and as of October 2015, under the name Rhythm Pharmaceuticals, Inc. Prior to our organization and the Corporate Reorganization, we were part of the Predecessor Company which commenced active operations in 2010. As a result of the Corporate Reorganization, we became a wholly-owned subsidiary of the LLC entity. In August 2015, December 2015, January 2017 and August 2017, we sold shares of our series A preferred stock to investors pursuant to an equity financing.

In August 2017, the LLC entity exchanged 78,666,209 of its shares of our common stock for an equal number of newly-issued shares of our series A-1 junior preferred stock, which will be converted into our common stock on one-to-one basis upon the closing of this offering, and the LLC entity distributed all of its shares of our series A-1 junior preferred stock and common stock to its members.

We shared certain costs with the Relamorelin Company and effective December 2016 in connection with the sale of the Relamorelin Company, we no longer share these costs.

Financial Operations Overview

Revenue

To date, we have not generated any revenue from product sales and do not expect to generate any revenue from the sale of setmelanotide for at least several years. We cannot predict if, when, or to what extent we will generate revenues from the commercialization and sale of setmelanotide. Setmelanotide is currently our only product candidate, and we may never succeed in achieving regulatory approval for setmelanotide or any other product candidate that we decide to pursue in the future.

Research and development expenses

Research and development expenses consist primarily of costs incurred for our research activities, including our drug discovery efforts, and the development of setmelanotide, which include:

- expenses incurred under agreements with third parties, including CROs that conduct research and development and preclinical activities on our behalf, and the cost of consultants and CMOs that manufacture drug products for use in our preclinical studies and clinical trials;
- employee-related expenses including salaries, benefits, and stock-based compensation expense;
- the cost of lab supplies and acquiring, developing, and manufacturing preclinical study materials; and
- facilities, depreciation, and other expenses, which include rent and maintenance of facilities, insurance and other operating costs.

We expense research and development costs to operations as incurred. Nonrefundable advance payments for goods or services to be received in the future for use in research and development activities are recorded as prepaid expenses. The capitalized amounts are expensed as the related goods are delivered or the services are performed.

The following table summarizes our current research and development program for setmelanotide.

	Year Ended December 31,		Six Months Ended June 30,	
Research and Development Summary	**2015**	**2016**	**2016**	**2017**
		(in thousands)		
Setmelanotide Program	$ 7,148	$ 19,594	$ 8,544	$ 10,270

We are unable to predict the duration and costs of the current or future clinical trials of setmelanotide. The duration, costs, and timing of clinical trials and development of setmelanotide will depend on a variety of factors, including:

- the scope, rate of progress, and expense of our ongoing, as well as any additional, clinical trials and other research and development activities;
- the rate of enrollment in clinical trials;
- the safety and efficacy demonstrated by setmelanotide in future clinical trials;
- changes in regulatory requirements;
- changes in clinical trial design; and
- the timing and receipt of any regulatory approvals.

A change in the outcome of any of these variables with respect to the development of setmelanotide would significantly change the costs and timing associated with its development and potential commercialization.

Research and development activities are central to our business model. Product candidates in later stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials. We expect research and development costs to increase significantly for the foreseeable future as our setmelanotide development program progresses. However, we do not believe that it is possible at this time to accurately project total program-specific expenses to commercialization and there can be no guarantee that we can meet the funding needs associated with these expenses.

General and administrative expenses

General and administrative expenses consist primarily of salaries and other related costs, including stock-based compensation, relating to our full-time employees and until December 2016, for personnel which have been allocated from the Relamorelin Company. Other significant costs include rent which previously had been allocated from the Relamorelin Company, legal fees relating to patent and corporate matters and fees for accounting and consulting services.

The following table summarizes our current general and administrative expenses.

	Year Ended December 31,		Six Months Ended June 30,	
	2015	2016	2016	2017
	(in thousands)			
General and administrative expense	$ 3,425	$ 6,311	$ 2,585	$ 2,873

We anticipate that our general and administrative expenses will increase in the future to support continued and expanding development efforts, potential commercialization of setmelanotide and increased costs of operating as a public company. These increases will likely include increased costs related to the hiring of additional personnel and fees to outside consultants, lawyers and accountants, compliance with exchange listing and SEC expenses, insurance and investor relations costs, among other expenses.

Critical Accounting Policies and Estimates

Our discussion and analysis of our financial condition and results of operations are based on our financial statements, which we have prepared in accordance with United States generally accepted accounting principles. The preparation of these financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the financial statements, as well as the reported amounts of revenues and expenses during the reporting periods. On an ongoing basis, we evaluate our estimates and judgments, including those described in greater detail below. We base our estimates on historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are described in more detail in the notes to our financial statements included elsewhere in this prospectus, we believe that the following accounting policies are the most critical to aid in fully understanding and evaluating our financial condition and results of operations.

Basis of Presentation

Presentation

We have historically existed and functioned as part of the consolidated businesses of the Predecessor Company. Our MC4 business was contributed to us from the Predecessor Company on March 21, 2013 as part of the Corporate Reorganization. At that time, we also entered into the Payroll Services Agreement. In December 2016, the shared employees terminated their existing employment agreements and entered into new agreements with us. Until December 2016, we shared costs with the Relamorelin Company, including finance, accounting, research and development and operations. These shared costs were allocated to us from the Relamorelin Company for the purposes of preparing the financial statements based on a specific identification basis or, when specific identification is not practicable, a proportional cost allocation method which allocates expenses based upon the percentage of employee time and research and development effort expended on our business as compared to total employee time and research and development effort. The proportional use basis adopted to allocate shared costs is in accordance with the

guidance of Staff Accounting Bulletin Topic 1B. Our management has determined that the proportional use method of allocating costs to us from the Relamorelin Company is reasonable.

Accrued research and development expenses

As part of the process of preparing our financial statements, we are required to estimate the value associated with goods and services received in the period in connection with research and development activities. This process involves reviewing quotations and contracts, identifying services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of the actual cost, or alternatively, the deferral of amounts paid for goods or services to be incurred in the future. The majority of our service providers invoice us monthly in arrears for services performed or when contractual milestones are met. We make estimates of our accrued expenses or prepaid expenses as of each balance sheet date in our financial statements based on facts and circumstances known to us at the time those financial statements are prepared. We periodically confirm the accuracy of our estimates with the service providers and make adjustments if necessary. The significant estimates in our accrued research and development expenses include fees paid to CROs and CMOs in connection with research and development activities.

We accrue our expenses related to CROs and CMOs based on our estimates of the services received and efforts expended pursuant to quotes and contracts with CROs and CMOs that conduct research and development and manufacturing on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. The allocation of CRO upfront expenses for both clinical trials and preclinical studies generally tracks actual work activity. However, there may be instances in which payments made to our vendors will exceed the level of services provided and result in a prepayment of the research and development expense. In accruing service fees delivered over a period of time, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from our estimate, we adjust accrued or prepaid expense accordingly. Although we do not expect our estimates to be materially different from amounts actually incurred, if our estimates of the status and timing of services performed differ from the actual status and timing of services performed, it could result in us reporting amounts that are too high or too low in any particular period. To date, there have been no material differences between our estimates of such expenses and the amounts actually incurred.

2015 Series A Investor Right/Obligation, 2015 Series A Investor Call Option & 2017 Series A Investor Instrument

Pursuant to the 2015 series A stock purchase agreement, by and among us and the other persons that are parties to such agreement as investors, or the series A investors, we issued 25,000,000 shares of series A preferred stock at a purchase price of $1.00 per share in August 2015 as part of an initial tranche of financing. Pursuant to the series A stock purchase agreement, the series A investors had the obligation, or the 2015 Series A Investor Right/Obligation, to purchase additional shares of series A preferred stock as part of a second tranche of financing based on the achievement of a specific milestone set forth in the series A preferred stock purchase agreement, or the 2015 Second Tranche Milestone. Additionally, subject to the terms and conditions set forth in the series A stock purchase agreement, the series A investors had the option, or the 2015 Series A Investor Call Option, to purchase 15,000,000 additional shares of series A preferred stock in the event that the 2015 Second Tranche Milestone was not achieved. The 2015 Series A Investor Right/Obligation was exercised and the 2015 Series A Investor Call Option expired on December 1, 2015 upon the 2015 Series A Second Tranche Closing. As a result of these two tranches, we issued 40,000,000 shares of series A preferred stock resulting in aggregate gross proceeds of $40.0 million.

Pursuant to the 2017 series A preferred stock purchase agreement, by and among us and certain purchasers, and as part of an initial tranche closing, we issued 20,475,001 shares of series A preferred stock

at a purchase price of $1.00 per share in January 2017. The series A stock purchase agreement provided for the delayed issuance by us of up to an additional 20,474,998 shares of series A preferred stock as part of a second tranche closing at a purchase price of $1.00 per share. The series A investors had the obligation, upon notification by us, or the 2017 Series A Investor Right/Obligation, to purchase 20,474,998 additional shares of series A preferred stock as part of a second tranche of financing at such time as: (1) our cash, cash equivalents and short-term investments balance, net of accounts payable and accrued liabilities, falling below $5.0 million and (2) our satisfaction of contractual and customary representations and warranties, or the 2017 Second Tranche Milestone. On August 18, 2017, the series A investors waived the $5.0 million cash balance requirement of the 2017 second tranche milestone and such second tranche financing was consummated. As a result of these two tranches, we issued 40.95 million shares of our series A preferred stock, resulting in aggregate gross proceeds of $40.95 million.

We have classified our 2015 Series A Investor Right/Obligation, our 2015 Series A Investor Call Option and our 2017 Series A Investor Instrument as liabilities as they are free-standing financial instruments. The 2015 Series A Investor Right/Obligation, the 2015 Series A Investor Call Option and the 2017 Series A Investor Instrument were recorded at fair value upon the issuance of our series A preferred stock in August 2015 and January 2017, respectively, and subsequently remeasured to fair value at each reporting period. Changes in fair value of these financial instruments are recognized as a component of other income (expense), net in the statement of operations and comprehensive loss. We estimated the fair value of the Series A Investor Right/Obligations as the probability-weighted present value of the expected benefit of the investment.

We used the Black-Scholes option-pricing model, which incorporates assumptions and estimates, to value the Series A Investor Call Options and assessed these assumptions and estimates on a quarterly basis as additional information impacting the assumptions was obtained. Estimates and assumptions impacting the fair value measurement include the fair value per share of the underlying series A preferred stock, the expected term of the Series A Investor Call Options, risk-free interest rate, expected dividend yield and expected volatility of the price of the underlying preferred stock. We determined the fair value per share of the underlying preferred stock by taking into consideration the most recent sale of our convertible preferred stock and the investors' right to invest in a subsequent tranche. As we are a private company and lack company-specific historical and implied volatility information of our stock, we estimated our expected stock volatility based on the historical volatility of publicly traded peer companies for a term comparable to the estimated term of the Series A Investor Call Options. The risk-free interest rate was determined by reference to the U.S. Treasury yield curve for time periods approximately equal to the estimated term of the Series A Investor Call Options. A dividend yield of zero was assumed. The fair value of the Series A Investor Instrument is determined to be the sum of the fair values of the 2017 Series A Investor Right/Obligation and the 2017 Investor Call Option.

Upon the closing of an initial public offering with a minimum price per share and gross proceeds of at least $1.00, as adjusted for any splits or similar changes, and $50.0 million, respectively, our series A preferred stock will automatically convert into shares of our common stock on a 1-for-1 basis.

Income taxes

Income taxes have been calculated on a separate tax return basis. Certain of our activities and costs have been included in the tax returns filed by the Relamorelin Company and the LLC entity. Prior to the Corporate Reorganization, our operations were included in the tax returns filed by the Predecessor Company. We have filed tax returns on our own behalf since the Corporate Reorganization.

We account for uncertain tax positions in accordance with the provisions of Accounting Standards Codification, or ASC, Topic 740, *Accounting for Income Taxes*, or ASC 740. When uncertain tax positions exist, we recognize the tax benefit of tax positions to the extent that the benefit will more likely than not be realized. The determination as to whether the tax benefit will more likely than not be realized is based

upon the technical merits of the tax position as well as consideration of the available facts and circumstances. As of December 31, 2016, we do not have any uncertain tax positions.

Income taxes are recorded in accordance with ASC 740, which provides for deferred taxes using an asset and liability approach. We recognize deferred tax assets and liabilities for the expected future tax consequences of events that have been included in the financial statements or tax returns. We determine our deferred tax assets and liabilities based on differences between financial reporting and tax bases of assets and liabilities, which are measured using the enacted tax rates and laws that will be in effect when the differences are expected to reverse. Valuation allowances are provided, if based upon the weight of available evidence, it is more likely than not that some or all of the deferred tax assets will not be realized.

Interest and penalties on uncertain tax positions are recorded in the provision (benefit) for income taxes in the statements of operations. During the years ended December 31, 2015 and 2016 and the six months ended June 30, 2016 and 2017, we had no amounts accrued for interest and penalties related to uncertain tax positions.

As of December 31, 2016, we had net operating loss carryforwards to reduce federal and state incomes taxes of approximately $46,934 and $24,432, respectively. If not utilized, these carryforwards begin to expire in 2033. At December 31, 2016, we also had available research and development tax credits for federal and state income tax purposes of approximately $971 and $369, respectively. The federal and state credits begin to expire in 2033 and 2028, respectively.

Utilization of the net operating loss and tax credit carryforwards may be subject to a substantial annual limitation due to ownership change limitations that have occurred previously or that could occur in the future, as provided by Section 382 of the Code, or Section 382, as well as similar state provisions and other provisions of the Code. Ownership changes may limit the amount of net operating losses and tax credit carryforwards that can be utilized annually to offset future taxable income and tax, respectively. In general, an ownership change, as defined by Section 382, results from transactions that increase the ownership of 5.0% stockholders in the stock of a corporation by more than 50% in the aggregate over a three-year period.

Stock-based compensation

Prior to August 2015, we did not have our own equity compensation plan. In August 2015, our Board of Directors and our stockholders approved and we adopted the 2015 equity incentive plan, as amended and restated and in effect prior to the closing of this offering, the Plan, which we expect to amend and restate prior to consummation of this offering. The Plan provides for the grant of incentive and non-qualified stock options and restricted stock grants to employees, consultants, advisors and directors, as determined by the Board of Directors. We have reserved 21,250,000 shares of common stock under the Plan. The first option grants issued by us under the Plan were issued in the fourth quarter of 2015. Shares of common stock issued upon exercise of stock options are generally issued from authorized but unissued shares. The Plan provides that the exercise price of incentive stock options cannot be less than 100% of the fair market value of the common stock on the date of the award for participants who own less than 10% of the total combined voting power of stock, and not less than 110% for participants who own more than 10% of the voting power. Options and restricted stock granted under the Plan will vest over periods as determined by our Compensation Committee and approved by our Board of Directors.

We estimate the fair value of our stock-based awards to employees and non-employees using the Black-Scholes option-pricing model, which requires the input of highly subjective assumptions, including (a) the expected volatility of our stock, (b) the expected term of the award, (c) the risk-free interest rate, and (d) expected dividends. Due to the lack of a public market for the trading of our common stock and a lack of company-specific historical and implied volatility data, we have based our estimate of expected volatility on the historical volatility of a group of companies in the pharmaceutical and biotechnology industries in a similar stage of development as us and that are publicly traded. For these analyses, we have

selected companies with comparable characteristics to ours including enterprise value, risk profiles and with historical share price information sufficient to meet the expected life of the stock-based awards. We compute the historical volatility data using the daily closing prices for the selected companies' shares during the equivalent period of the calculated expected term of our stock-based awards. We will continue to apply this process until a sufficient amount of historical information regarding the volatility of our own stock price becomes available. We have estimated the expected life of our employee stock options using the "simplified" method, whereby, the expected life equals the average of the vesting term and the original contractual term of the option. The risk-free interest rates for periods within the expected life of the option are based on the U.S. Treasury yield curve in effect during the period the options were granted.

We are also required to estimate forfeitures at the time of grant, and revise those estimates in subsequent periods if actual forfeitures differ from estimates. We use historical data to estimate pre-vesting option forfeitures and record stock-based compensation expense only for those awards that are expected to vest. To the extent that actual forfeitures differ from our estimates, the difference is recorded as a cumulative adjustment in the period the estimates were revised. Stock-based compensation expense recognized in the financial statements is based on awards that are ultimately expected to vest. Upon adopting ASU 2016-09 on January 1, 2017, we have elected to account for forfeitures as they occur.

Stock compensation expense incurred under the Plan was $192 and $993 during the year ended December 31, 2015 and 2016, respectively, consisting of stock-based compensation expense for awards granted to employees and our directors of $39 and $277 and non-employees and employees of the Relamorelin Company that are allocated to us of $153 and $716, respectively.

Stock compensation expense incurred under the Plan was $473 and $627 during the six months ended June 30, 2016 and 2017, respectively, consisting of stock-based compensation expense for awards granted to employees and our directors of $100 and $581, respectively, and non-employees and, for the six months ended June 30, 2016, employees of the Relamorelin Company that are allocated to us of $373 and $46, respectively. At June 30, 2017, we have unrecognized compensation expense related to these awards of $3,622 and we expect to recognize our portion over a weighted-average period of approximately 2.65 years.

The following table summarizes the classification of our stock-based compensation expenses related to the Plan recognized in our statements of operations and comprehensive loss.

	Year Ended December 31,		Six Months Ended June 30,	
	2015	2016	2016	2017
	(in thousands)			
Research and development	$ 68	$ 343	$ 152	$ 190
General and administrative	124	650	321	437
Total	$ 192	$ 993	$ 473	$ 627

The LLC entity applies the fair value recognition provisions of Financial Accounting Standards Board, or FASB, ASC Topic 718, *Compensation—Stock Compensation*, or ASC 718, to account for stock-based compensation. The LLC entity recognizes stock-based compensation expense based on the estimated fair value of each stock option or restricted common unit on the date of grant, net of estimated forfeitures. The grant date fair value of awards subject to service-based vesting, net of estimated forfeitures, is recognized on a straight-line basis over the requisite service period, which is generally the vesting period of the respective awards. In accordance with ASC 718, stock-based compensation expense related to restricted common units that are subject to both performance and service-based vesting conditions is recognized using an accelerated recognition model.

The fair value of a restricted common unit is estimated based on its fair value on the measurement date as if the restricted common unit was fully vested at that date, which is equivalent to the fair value of a common unit. Refer to our later discussion on the determination of the fair value of a common unit.

In addition to the assumptions used in the estimate of fair value of the LLC entity's restricted common units, the amount of compensation expense we and the LLC entity recognize in our statements of operations includes an estimate of restricted common unit forfeitures. Under ASC 718, we and the LLC entity are required to estimate the level of forfeitures expected to occur and record compensation expense only for those awards that we and the LLC entity ultimately expect will vest. Due to the lack of historical forfeiture activity, we and the LLC entity estimate our forfeiture rate based on data from a representative group of companies. Changes in the estimated forfeiture rate can have a significant impact on our stock-based compensation expense as the cumulative effect of adjusting the rate is recognized in the period the forfeiture estimate is changed. For example, if a revised forfeiture rate is higher than the previously estimated forfeiture rate, an adjustment is made that will result in a decrease to the stock-based compensation expense recognized in the financial statements. If a revised forfeiture rate is lower than the previously estimated forfeiture rate, an adjustment is made that will result in an increase to the stock-based compensation expense recognized in the financial statements. To date actual forfeitures have not been material.

The stock compensation expense allocated to us from the LLC entity was $106 and $175 for the years ended December 31, 2015 and 2016, respectively, and $86 and $71 for the six months ended June 30, 2016 and 2017, respectively. At June 30, 2017, we have unrecognized compensation expense related to the unvested portion of these awards of $242 and we expect to recognize this amount over a weighted-average period of approximately 1.31 years.

The following table summarizes the classification of the LLC stock-based compensation expense recognized in our statements of operations and comprehensive loss.

	Year Ended December 31,		Six Months Ended June 30,	
	2015	2016	2016	2017
	(in thousands)			
Research and development	$ 76	$ 163	$ 78	$ 71
General and administrative	30	12	8	—
Total	$ 106	$ 175	$ 86	$ 71

Determination of the fair value of LLC common units and Rhythm Pharmaceuticals, Inc. common stock

We and the LLC entity operate as private companies with no active public market for our common stock and the LLC entity's common and preferred units. Therefore, the boards of directors estimated the fair value of our common stock and the LLC entity's common units at various dates, with input from management, considering our and the LLC entity's most recently available third-party valuations of common stock and common units, respectively, and the assessment of additional objective and subjective factors that were believed to be relevant and which may have changed from the date of the most recent valuation through the date of the applicable grant or award.

We and the LLC entity determined the estimated per share fair value of our common stock and the LLC entity's common units at various dates using contemporaneous valuations performed in accordance with the guidance outlined in the American Institute of Certified Public Accountants Practice Aid, *Valuation of Privately-Held Company Equity Securities Issued as Compensation*, or the Practice Aid, for financial reporting purposes.

In conducting the contemporaneous valuations, we and the LLC entity considered all objective and subjective factors that we and the LLC entity believed to be relevant for each valuation conducted, including each respective entity's best estimate of its business condition, prospects and operating

performance at each valuation date. Within the contemporaneous valuations performed, a range of factors, assumptions and methodologies were used.

The significant factors included:

- the lack of an active public market for our common stock and the LLC entity's common and preferred units;
- the prices at which we and the LLC entity sold our and its preferred shares and units, respectively, to outside investors in arm's length transactions, and the rights, preferences and privileges of those preferred shares and units, respectively, relative to common shares and units;
- our and LLC entity's results of operations, financial position and the status of each entity's research, and preclinical development efforts;
- the material risks related to each entity's business;
- the market performance of publicly traded companies in the life sciences and biotechnology sectors, and recently completed mergers and acquisitions of companies comparable to each entity;
- the likelihood of achieving a liquidity event for the holders of our common stock and the LLC entity's units, such as an initial public offering or sale of the company given prevailing market conditions; and
- any recent contemporaneous valuations of our common stock and the LLC entity's common units prepared in accordance with methodologies outlined in the Practice Aid.

Valuation methodologies

Our and the LLC entity's valuations of common stock and common units, respectively, were prepared utilizing the discounted cash flow, or DCF, method, the guideline public company, or GPC, method, the option-pricing method, or OPM, the probability-weighted expected return method, or PWERM, and a hybrid of the PWERM and OPM, which we refer to as the hybrid method:

- *Discounted Cash Flow Method.* Under the DCF method, projected cash flows are converted to present value by applying a discount rate based on an estimated cost of equity or an estimated cost of debt. The cost of equity is estimated based on rates of return required by outside investors. An estimated cost of debt is applied when future cash flows are adjusted for the probability of success in clinical trials.
- *Guideline Public Company Method.* Under the GPC method, our future value in an initial public offering is estimated based on a comparison to clinical-stage companies which have completed initial public offerings.
- *Option Pricing Method.* Under the OPM, common and preferred stock and common and preferred units are valued by creating a series of call options with exercise prices based on the liquidation preferences and conversion terms of each equity class. Under this method, common stock and common units only have value if the funds available for distribution to common stock or common unit holders exceed the value of the liquidation preferences at the time of a liquidity event, such as a strategic sale or merger. Under the OPM, the value of one security, such as preferred stock or preferred units, is used to determine the value of the equity and the corresponding value of the common stock or common units.
- *Probability-Weighted Expected Return Method.* The PWERM is a scenario-based analysis that estimates the value per share based on the probability-weighted present value of expected future investment returns, considering each of the possible outcomes available to each entity, as well as the economic and control rights of each equity class.

- *Hybrid Method.* The hybrid method is a PWERM where the equity value in one of the scenarios is calculated using the OPM. In the hybrid method used by each entity, three types of future-event scenarios were considered: an initial public offering, a sale and dissolution. Each entity used the OPM to allocate equity value for the unspecified liquidity event.

    - The enterprise value for the initial public offering and sale scenarios was determined using a market approach. Under the market approach, each entity estimated enterprise value using the guideline public company method. The guideline public company method includes comparisons to publicly traded companies in the relevant industry that recently completed initial public offerings. For the sale scenarios, each entity estimated a premium to the initial public offering value. The enterprise values are discounted back to the valuation date at an appropriate risk-adjusted discount rate.

    - The enterprise value for the unspecified liquidity event was determined using the OPM.

Contemporaneous valuation of the LLC entity common units as of May 1, 2015.

The LLC entity performed a contemporaneous valuation of its common units on May 1, 2015 to coincide with its planned issuance of certain equity grants. The LLC entity estimated the value of its equity using the DCF method under the income approach. The LLC entity allocated equity value among its preferred and common units using the hybrid method. The hybrid method is a form of PWERM which uses the OPM for at least one scenario. The LLC entity considered two scenarios: the OPM and a second scenario in which Actavis plc exercises its option to acquire the Relamorelin Company.

Retrospective valuation of the LLC entity common units as of July 15, 2015.

The LLC entity performed a retrospective valuation of its common units as of July 15, 2015 to coincide with the amendment of the Ipsen warrant. The LLC entity estimated the value of the equity of the Relamorelin Company using the DCF method under the income approach. For Rhythm Pharmaceuticals, Inc., the LLC entity estimated the value of the equity using the OPM. The LLC entity allocated equity value on its preferred and common units using a hybrid method. The hybrid method for the LLC entity considered two scenarios: the OPM and a second scenario in which Actavis plc exercises its option to acquire the Relamorelin Company.

Contemporaneous valuation of the Rhythm Pharmaceuticals, Inc. common stock as of August 3, 2015.

We performed a contemporaneous valuation of our common stock as of August 3, 2015 to coincide with the first tranche closing of our series A preferred stock financing. We valued our equity and allocated equity value using a hybrid backsolve method. The backsolve calculation reconciled to the price of our series A preferred stock. The hybrid method considered initial public offering and OPM scenarios. We relied on the GPC method to estimate equity value in the initial public offering scenario. This valuation also included a contemporaneous valuation of the 2015 Series A Investor Right/Obligation and 2015 Series A Investor Option to invest in the second tranche of our series A preferred stock financing. We valued the Series A Investor Right/Obligation as the probability-weighted present value of the future benefit associated with the second tranche investment. We valued the Series A Investor Option using the Black-Scholes option model.

Contemporaneous valuation of LLC entity common units as of September 30, 2015.

The LLC entity performed a contemporaneous valuation of its common units as of September 30, 2015 to coincide with the quarterly revaluation of non-employee stock grants. The LLC entity estimated the value of the equity of the Relamorelin Company using the DCF method under the income approach. For Rhythm Pharmaceuticals, Inc., the LLC entity estimated the value of the equity using the hybrid method. Two scenarios were considered: an initial public offering and an OPM. The LLC entity allocated

equity value on its preferred and common units using the hybrid method. The LLC entity considered three scenarios in its hybrid method: a distribution of Rhythm Pharmaceuticals, Inc. common shares based on an initial public offering equity value for Rhythm Pharmaceuticals, Inc., a distribution of common shares based on an OPM equity value for Rhythm Pharmaceuticals, Inc., and a scenario in which Actavis plc exercises its option to acquire the Relamorelin Company. This valuation also included a contemporaneous valuation of the 2015 Series A Investor Right/Obligation and 2015 Series A Investor Option to invest in the second tranche of our series A preferred stock financing. We valued the forward contract as the probability-weighted present value of the future benefit associated with the second tranche investment. We valued the option to invest in the second tranche using the Black-Scholes option model.

Contemporaneous valuation of LLC entity common units as of October 31, 2015.

The LLC entity performed a contemporaneous valuation of its common units as of October 31, 2015 to coincide with its planned issuance of certain equity grants. The LLC entity estimated the value of the equity of the Relamorelin Company using the DCF method under the income approach. For Rhythm Pharmaceuticals, Inc., the LLC entity estimated the value of the equity using the hybrid method. Two scenarios were considered: an initial public offering and an OPM. The LLC entity allocated equity value on its preferred and common units assuming separate distributions for Rhythm Pharmaceuticals, Inc. and the Relamorelin Company. For Rhythm Pharmaceuticals, Inc., the LLC entity considered a hybrid method with two scenarios: a distribution of Rhythm Pharmaceuticals, Inc. common shares based on an initial public offering and a distribution of common shares based on an OPM equity value. For the Relamorelin Company, the LLC entity allocated equity value based on the probability-weighted present value of an exercise by Actavis plc of its option to acquire the Relamorelin Company.

Contemporaneous valuation of the Rhythm Pharmaceuticals, Inc. common stock as of October 31, 2015.

We performed a contemporaneous valuation of our common stock as of October 31, 2015 to coincide with the planned issuance of certain equity grants. We valued our equity and allocated equity value using a hybrid backsolve method. The backsolve calculation reconciled to the price of our series A preferred stock. The hybrid method considered initial public offering and OPM scenarios. We relied on the GPC method to estimate equity value in the initial public offering scenario.

Contemporaneous valuation of the Rhythm Pharmaceuticals, Inc. Series A Investor Right/Obligation as of December 1, 2015.

We performed a contemporaneous valuation of the 2015 Series A Investor Right/Obligation to invest in the second tranche of our series A preferred stock financing. This valuation coincided with our 2015 Series A Second Tranche Closing on December 1, 2015. We valued the Series A Investor Right/Obligation as the benefit associated with the second tranche investment. The benefit is a function of the difference between the fair value of the Series A shares and the Series A Investor Right/Obligation exercise price on the date of closing and the number of shares acquired. We estimated the fair value of the Series A Investor Right/Obligation as the probability weighted average of two scenarios: an IPO and a remain-private scenario.

Contemporaneous valuation of LLC entity common units as of December 31, 2015.

The LLC entity performed a contemporaneous valuation of its common units as of December 31, 2015 to coincide with the quarterly revaluation of non-employee stock grants. The LLC entity estimated the value of the equity of the Relamorelin Company using the DCF method under the income approach. For Rhythm Pharmaceuticals, Inc., the LLC entity estimated the value of the equity using the hybrid method. Two scenarios were considered: an initial public offering and an OPM. The LLC entity allocated equity value on its preferred and common units using the hybrid method. The LLC entity allocated equity value on its preferred and common units assuming separate distributions for Rhythm Pharmaceuticals, Inc.

and the Relamorelin Company. For Rhythm Pharmaceuticals, Inc., the LLC entity considered a hybrid method with two scenarios: a distribution of Rhythm Pharmaceuticals, Inc. common shares based on an initial public offering and a distribution of common shares based on an OPM equity value. For the Relamorelin Company, the LLC entity allocated equity value based on the probability-weighted present value of an exercise by Actavis plc of its option to acquire the Relamorelin Company.

Contemporaneous valuation of the Rhythm Pharmaceuticals, Inc. common stock as of December 31, 2015.

We performed a contemporaneous valuation of our common stock as of December 31, 2015 to coincide with the issuance of certain equity grants. We valued our equity and allocated equity value using a hybrid backsolve method. The backsolve calculation reconciled to the price of our series A preferred stock. The hybrid method considered initial public offering and OPM scenarios. We relied on the GPC method to estimate equity value in the initial public offering scenario.

Contemporaneous valuation of the Rhythm Pharmaceuticals, Inc. common stock as of March 31, 2016.

We performed a contemporaneous valuation of our common stock as of March 31, 2016 to coincide with the issuance of certain equity grants. We valued our equity and allocated equity value using a hybrid backsolve method. The backsolve calculation reconciled to the price of our series A preferred stock. The hybrid method considered initial public offering and OPM scenarios. We relied on the GPC method to estimate equity value in the initial public offering scenario.

Contemporaneous valuation of the Rhythm Pharmaceuticals, Inc. common stock as of June 30, 2016.

We performed a contemporaneous valuation of our common stock as of June 30, 2016 to coincide with the issuance of certain equity grants. We valued our equity and allocated equity value using a hybrid backsolve method. The backsolve calculation reconciled to the price of our series A preferred stock. The hybrid method considered initial public offering and OPM scenarios. We relied on the GPC method to estimate equity value in the initial public offering scenario.

Contemporaneous valuation of the Rhythm Pharmaceuticals, Inc. common stock as of September 30, 2016.

We performed a contemporaneous valuation of our common stock as of September 30, 2016 to coincide with the issuance of certain equity grants. We valued our equity and allocated equity value using a hybrid backsolve method. The backsolve calculation reconciled to the price of our series A preferred stock. The hybrid method considered initial public offering and OPM scenarios. We relied on the GPC method to estimate equity value in the initial public offering scenario.

Contemporaneous valuation of the Rhythm Pharmaceuticals, Inc. common stock as of November 16, 2016.

We performed a contemporaneous valuation of our common stock as of November 16, 2016 to coincide with the revaluation of non-employee stock grants. As of November 16, 2016, the employees of the Relamorelin Company terminated their employment contracts with the Relamorelin Company and entered into new employment agreements with the Company. A new fair value of the remaining unvested awards for these employees was determined as of November 16, 2016 and will be expensed in accordance with ASC 718, Compensation—Stock Compensation over their remaining vesting period. We valued our equity and allocated equity value using a hybrid backsolve method. The backsolve calculation reconciled to the price of our series A preferred stock. The hybrid method considered initial public offering and OPM scenarios. We relied on the GPC method to estimate equity value in the initial public offering scenario.

Contemporaneous valuation of the Rhythm Pharmaceuticals, Inc. common stock as of December 31, 2016.

We performed a contemporaneous valuation of our common stock as of December 31, 2016 to coincide with the issuance of certain equity grants. We valued our equity and allocated equity value using a hybrid backsolve method. The backsolve calculation reconciled to the price of our series A preferred stock. The hybrid method considered initial public offering and OPM scenarios. We relied on the GPC method to estimate equity value in the initial public offering scenario. This valuation also included a contemporaneous valuation of the 2017 Series A Investor Instrument. The fair value of the 2017 Series A Investor Instrument is determined to be the sum of the fair values of the 2017 Series A Investor Right/Obligation and 2017 Series A Call Option. We valued the 2017 Series A Investor Right/Obligation as the probability-weighted present value of the future benefit associated with the second tranche investment. We valued the 2017 Investor Call Option using the Black-Scholes option model.

Contemporaneous valuation of the Rhythm Pharmaceuticals, Inc. common stock as of March 31, 2017.

We performed a contemporaneous valuation of our common stock as of March 31, 2017 to coincide with the issuance of certain equity grants. We valued our equity and allocated equity value using a hybrid backsolve method. The backsolve calculation reconciled to the price of our series A preferred stock. The hybrid method considered initial public offering and OPM scenarios. We relied on the GPC method to estimate equity value in the initial public offering scenario. This valuation also included a contemporaneous valuation of the 2017 Series A Investor Instrument. The fair value of the 2017 Series A Investor Instrument is determined to be the sum of the fair values of the 2017 Series A Investor Right/Obligation and 2017 Series A Call Option. We valued the 2017 Series A Investor Right/Obligation as the probability-weighted present value of the future benefit associated with the second tranche investment. We valued the 2017 Investor Call Option using the Black-Scholes option model.

Contemporaneous valuation of the Rhythm Pharmaceuticals, Inc. common stock as of June 30, 2017.

We performed a contemporaneous valuation of our common stock as of June 30, 2017 to coincide with the issuance of certain equity grants. We valued our equity and allocated equity value using a hybrid method. The hybrid method considered an initial public offering and a remain-private scenario in which value is allocated using the OPM. We relied on the GPC method to estimate equity value in the initial public offering scenario. In the remain-private scenario, equity value was estimated using an OPM backsolve calculation. This valuation also included a contemporaneous valuation of the 2017 Series A Investor Instrument. The fair value of the 2017 Series A Investor Instrument is determined to be the sum of the fair values of the 2017 Series A Investor Right/Obligation and 2017 Series A Call Option. We valued the 2017 Series A Investor Right/Obligation as the probability-weighted present value of the future benefit associated with the second tranche investment. We valued the 2017 Investor Call Option using the Black-Scholes option model.

Results of Operations

Comparison of six months ended June 30, 2016 and June 30, 2017.

The following table summarizes our results of operations for the six months ended June 30, 2016 and 2017, together with the changes in those items in dollars and as a percentage:

	Six Months Ended June 30,		Change	
	2016	2017	$	%
	(in thousands)			
Statement of Operations Data:				
Operating Expenses:				
Research and development	$ 8,544	$ 10,270	$ 1,726	20%
General and administrative	2,585	2,873	288	11%
Total operating expenses	11,129	13,143	2,014	18%
Loss from operations	(11,129)	(13,143)	(2,014)	(18)%
Other (expense) income, net	14	(19)	(33)	(236)%
Net loss and comprehensive loss	$ (11,115)	$ (13,162)	$ (2,047)	(18)%

Research and development expense. Research and development expense increased by $1.7 million to $10.3 million in 2017 from $8.5 million in 2016, an increase of 20%. The increase was primarily due to the initiation of additional new clinical trials in 2017 and an increase in other development activities associated with setmelanotide. We hired additional personnel in the clinical operations department at the end of 2016 and early 2017.

General and administrative expense. General and administrative expense increased by $0.3 million to $2.9 million in 2017 from $2.6 million in 2016, an increase of 11%. The increase was primarily due to stock compensation expense related to new option grants in 2017 and general office expenses due to the increase in headcount at end of 2016 and early 2017.

Comparison of years ended December 31, 2015 and December 31, 2016.

The following table summarizes our results of operations for the years ended December 31, 2015 and 2016, together with the changes in those items in dollars and as a percentage:

	Year Ended December 31,		Change	
	2015	2016	$	%
	(in thousands)			
Statement of Operations Data:				
Operating Expenses:				
Research and development	$ 7,148	$ 19,594	$ 12,446	174%
General and administrative	3,425	6,311	2,886	84%
Total operating expenses	10,573	25,905	15,332	145%
Loss from operations	(10,573)	(25,905)	(15,332)	(145)%
Other income (loss)	(500)	33	533	(107)%
Net loss and comprehensive loss	$ (11,073)	$ (25,872)	$ (14,799)	(134)%

Research and development expense. Research and development expense increased by $12.4 million to $19.6 million in 2016 from $7.1 million in 2015, an increase of 174%. The increase was primarily due to non-cash expenses in 2016 of $0.5 million in stock compensation. Our research and development costs increased subsequent to the initial series A financing at the end of fiscal year 2015 due to the initiation of additional new clinical trials and additional development activities for setmelanotide and the hiring of additional personnel in the clinical operations department in the fourth quarter of 2015 and 2016, as well as an increase in the overall proportion of research and development expenses allocated to us in 2016.

General and administrative expense. General and administrative expense increased by $2.9 million to $6.3 million in 2016 from $3.4 million in 2015, an increase of 84%. The increase in general and administrative expense was primarily attributable to the write down of capitalized deferred issuance cost of $1.8 million in 2016. As well as an increase in the overall proportion of general and administrative expenses allocated to us in 2016.

Liquidity and Capital Resources

Through August 2015, we received capital contributions from the Predecessor Company, the Relamorelin Company and the LLC entity from time to time as needed. In August 2015, December 2015, January 2017 and August 2017, we received aggregate gross proceeds of $81.0 million from the sale of our series A preferred stock. As of June 30, 2017, our existing cash and cash equivalents and short-term investments were approximately $17.7 million. After giving effect, on a pro forma basis, to the aggregate proceeds of the sale of our series A preferred stock in August 2017 of $20.5 million, our cash and cash equivalents and short-term investments are $38.2 million as of June 30, 2017.

Cash flows

The following table provides information regarding our cash flows for the years ended December 31, 2015 and 2016, and the six months ended June 30, 2016 and 2017:

	Year Ended December 31,			Six Months Ended June 30,		
	2015	2016	Change	2016	2017	Change
		(in thousands)				
Net cash provided by (used in):						
Operating activities	$ (6,977)	$ (23,219)	$ (16,242)	$ (12,597)	$ (13,158)	$ (561)
Investing activities	(17)	(5,110)	(5,093)	(6,286)	(5,036)	1,250
Financing activities	41,711	—	(41,711)	—	20,377	20,377
Net increase (decrease) in cash and cash equivalents	$ 34,717	$ (28,329)	$ (63,046)	$ (18,883)	2,183	21,066

Net cash used in operating activities

The use of cash in all periods resulted primarily from our net losses adjusted for non-cash charges and changes in components of working capital.

Net cash used in operating activities was $7.0 million for the year ended December 31, 2015, and consisted primarily of a net loss of $9.4 million adjusted for non-cash items, which were comprised of stock-based compensation, warrant amendment expense and mark to market revaluation of the 2015 Series A Investor Right/Obligation. The significant items in the change in operating assets and liabilities include an increase in accounts payable, accrued expenses and other current liabilities of $4.7 million offset by an increase of approximately $2.1 million in deferred issuance costs and prepaid expenses and other current assets.

Net cash used in operating activities was $23.2 million for the year ended December 31, 2016, and consisted primarily of a net loss of $24.5 million adjusted for non-cash items, which consisted of stock-based compensation, depreciation and amortization and deferred rent expense. The significant items in the change in operating assets and liabilities include a decrease in intercompany payable, accrued expense and deferred income of $1.0 million, offset by an increase in accounts payables of approximately $0.5 million and decreases in deferred issuance costs of approximately $1.5 million.

Net cash used in operating activities was $12.6 million for the six months ended June 30, 2016, and consisted primarily of a net loss of $10.5 million adjusted for non-cash items, which consisted of stock-based compensation, depreciation and amortization and deferred rent expense. The significant items in the change in operating assets and liabilities include a decrease in accrued expenses of $1.8 million and an increase in deferred issuance costs of approximately $0.3 million.

Net cash used in operating activities was $13.2 million for the six months ended June 30, 2017, and consisted primarily of a net loss of $12.3 million adjusted for non-cash items, which consisted of stock-based compensation, depreciation and amortization and deferred rent expense and the mark to market revaluation of the Series A Investor Instrument. The change in operating assets and liabilities reflected a total use of cash of approximately $0.8 million mainly with deferred issuance costs and accounts payables.

Net cash used in investing activities

Net cash used in investing activities for the year ended December 31, 2015 represent our design costs incurred related to our new facility lease.

Net cash used in investing activities for the year ended December 31, 2016 relates to the net purchases of short-term investments of $4.1 million and the buildout of our new headquarters facility and furniture and equipment of $1.1 million.

Net cash used in investing activities for the six months ended June 30, 2016 relates to the net purchases of short-term investments of $5.3 million and the buildout of our new headquarters facility and furniture and equipment of $1.0 million.

Net cash used in investing activities for the six months ended June 30, 2017 relates to the net purchases of short-term investments of $5.0 million.

Net cash provided by financing activities

Net cash provided by financing activities in prior periods consisted primarily of capital contributions from the LLC entity in the form of cash transfers, and shared costs incurred by the Relamorelin Company and the Predecessor Company or paid by the Relamorelin Company or the Predecessor Company on our behalf.

Net cash provided by financing activities was $41.7 million for the year ended December 31, 2015, consisting of $39.6 million of net proceeds from the issuance of series A preferred stock and an equity contribution of $2.1 million.

Net cash provided by financing activities was $20.4 million for the six months ended June 30, 2017, and represents the net proceeds from the first tranche of our January 2017 issuance of series A preferred stock.

Funding requirements

We expect our expenses to increase in connection with our ongoing activities, particularly as we continue the clinical development of and seek marketing approval for setmelanotide. In addition, if we obtain marketing approval for setmelanotide, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution to the extent that such sales, marketing and distribution are not the responsibility of potential collaborators. We expect to incur additional costs

associated with operating as an independent company, and upon the closing of this offering, operating as a public company.

We expect that the net proceeds from this offering, together with our existing cash and cash equivalents, will enable us to fund our operating expenses into the first half of 2019. We may need to obtain substantial additional funding in connection with our research and development activities and any continuing operations thereafter. If we are unable to raise capital when needed or on favorable terms, we would be forced to delay, reduce or eliminate our research and development programs or future commercialization efforts.

Our future capital requirements will depend on many factors, including:

- the scope, progress, results and costs of clinical trials for our setmelanotide program;
- the costs, timing and outcome of regulatory review of our setmelanotide program;
- the obligations owed to Ipsen pursuant to our license agreement;
- the extent to which we acquire or in-license other product candidates and technologies;
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims; and
- our ability to establish and maintain additional collaborations on favorable terms, if at all.

Developing our setmelanotide program is a time-consuming, expensive and uncertain process that may take years to complete, and we may never generate the necessary data or results required to obtain marketing approval and achieve product sales. In addition, setmelanotide, if approved, may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of setmelanotide that we do not expect to be commercially available for several years, if at all. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives. Adequate additional financing may not be available to us on acceptable terms, or at all.

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances and licensing arrangements. In August 2015, December 2015, January 2017 and August 2017, respectively, we issued 25,000,000, 15,000,000, 20,475,001 and 20,474,998, shares of series A preferred stock, respectively, at a price of $1.00 per share, resulting in gross proceeds of $81.0 million.

To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interest of our stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our common stockholders. Debt financing, if available, involves agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends.

If we raise funds through additional collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish valuable rights to our setmelanotide program on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market our setmelanotide program that we would otherwise prefer to develop and market ourselves.

Our independent auditors have indicated in their report on our December 31, 2016 financial statements that there is substantial doubt about our ability to continue as a going concern. A "going concern" opinion indicates that the financial statements have been prepared assuming we will continue as a going concern and do not include adjustments to reflect the possible future effects on the recoverability

and the classification of assets or the amounts and classification of liabilities that may result if we do not continue as a going concern.

Contractual obligations

We enter into agreements in the normal course of business with CROs and CMOs for clinical trials and clinical supply manufacturing and with vendors for clinical research studies and other services and products for operating purposes. We do not classify these as contractual obligations where the contracts are cancelable at any time by us, generally upon 30 days' prior written notice to the vendor.

Milestone and royalty payments associated with our license agreements with Ipsen and Camurus have not been included as contractual obligations as we cannot reasonably estimate if or when they will occur. Under the terms of the Ipsen license agreement, assuming that setmelanotide is successfully developed, receives regulatory approval and is commercialized, Ipsen may receive aggregate payments of up to $40.0 million upon the achievement of certain development and commercial milestones under the license agreement and royalties on future product sales. The majority of the aggregate payments under the Ipsen license agreement are for milestones that may be achieved no earlier than first commercial sale of setmelanotide. In the event that we enter into a sublicense agreement, we will make payments to Ipsen, depending on the date of the sublicense agreement, ranging from 10% to 20% of all revenues actually received under the sublicense agreement. Under the terms of the Camurus license agreement, assuming that setmelanotide is successfully developed, receives regulatory approval and is commercialized, Camurus may receive aggregate payments of up to $64.75 million upon the achievement of certain development and commercial milestones under the license agreement and royalties on future product sales. The majority of the aggregate payments under the Camurus license agreement are for milestones that may be achieved no earlier than first commercial sale of setmelanotide.

In November 2015, we entered into a Lease Agreement for an office facility at 500 Boylston Street, Boston, Massachusetts. The lease term commenced in May 2016 and has a term of five years with a five year renewal option to extend the lease.

Future minimum payments under the operating lease agreements as of December 31, 2016, are as follows:

	Operating Lease
2017	$ 291
2018	298
2019	305
2020	311
2021	131
Total	1,336

Off-balance Sheet Arrangements

We did not have, during the periods presented, and we do not currently have, any off-balance sheet arrangements, as defined under applicable SEC rules.

Quantitative and Qualitative Disclosures about Market Risk

We are not exposed to market risk related to changes in interest rates or foreign currency exchange rates.

JOBS Act

In April 2012, the JOBS Act was enacted. Section 107 of the JOBS Act provides that an "emerging growth company," or EGC, can take advantage of the extended transition period provided in Section 7(a)(2)(B) of the Securities Act for complying with new or revised accounting standards. Thus, an EGC can delay the adoption of certain newly implemented accounting standards until those standards would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of this extended transition period and, as a result, we will adopt new or revised accounting standards on the relevant dates on which adoption of such standards is required for other public companies.

We are in the process of evaluating the benefits of relying on other exemptions and reduced reporting requirements under the JOBS Act. Subject to certain conditions, as an EGC, we intend to rely on certain of these exemptions, including without limitation, (i) providing an auditor's attestation report on our system of internal controls over financial reporting pursuant to Section 404(b) of the Sarbanes-Oxley Act and (ii) complying with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements, known as the auditor discussion and analysis. We will remain an EGC until the earlier of (1) the last day of the fiscal year (a) following the fifth anniversary of the completion of this offering, (b) in which we have total annual gross revenue of at least $1.07 billion, or (c) in which we are deemed to be a large accelerated filer, which means the market value of our common stock that is held by non-affiliates exceeds $700 million as of the prior December 31st, and (2) the date on which we have issued more than $1.0 billion in non-convertible debt securities during the prior three-year period.

BUSINESS

Overview

We are a biopharmaceutical company focused on the development and commercialization of peptide therapeutics for the treatment of rare genetic deficiencies that result in life-threatening metabolic disorders. Our lead peptide product candidate is setmelanotide, a potent, first-in-class melanocortin-4 receptor, or MC4R, agonist for the treatment of rare genetic disorders of obesity. We believe setmelanotide, for which we have exclusive worldwide rights, has the potential to serve as replacement therapy for the treatment of melanocortin-4, or MC4, pathway deficiencies. MC4 pathway deficiencies result in the disruption of satiety signals and energy homeostasis in the body, which, in turn, leads to intense feelings of hunger and to obesity. Our development efforts are initially focused on obesity related to six single gene-related, or monogenic, MC4 pathway deficiencies—pro-opiomelanocortin, or POMC, leptin receptor, or LepR, Bardet-Biedl syndrome, Alström syndrome, POMC heterozygous, and POMC epigenetic disorders—for which there are currently no effective or approved treatments. We believe that the MC4 pathway is a compelling target for treating these genetic disorders because of its critical role in regulating appetite and weight by promoting satiety and weight control, and that peptide therapeutics are uniquely suited for activating this target.

We have demonstrated proof of concept in Phase 2 clinical trials in POMC deficiency obesity, LepR deficiency obesity, and Bardet-Biedl syndrome, three genetic disorders of extreme and unrelenting appetite and obesity, in which setmelanotide dramatically reduced both weight and hunger. The U.S. Food and Drug Administration, or FDA, has acknowledged the importance of these results by giving setmelanotide breakthrough therapy designation for the treatment of obesity associated with genetic defects upstream of the MC4 receptor in the leptin-melanocortin pathway, which includes both POMC deficiency obesity and LepR deficiency obesity. Setmelanotide is currently in Phase 3 development for POMC deficiency obesity and LepR deficiency obesity. We are currently enrolling patients in our POMC deficiency obesity Phase 3 clinical trial. We expect to complete enrollment by the end of 2017 and to report Phase 3 data in the first half of 2019. We expect to enroll the first patient in our LepR deficiency obesity Phase 3 clinical trial in the second half of 2017, and to complete enrollment in 2018. We recently demonstrated preliminary proof of concept in our Phase 2 clinical trial in Bardet-Biedl syndrome, indicating that this is also a setmelanotide-responsive, upstream MC4 pathway disorder. We are continuing to enroll patients in this trial and expect to report preliminary Phase 2 results in the fourth quarter of 2017. We expect to initiate a Phase 3 clinical trial in Bardet-Biedl syndrome in 2018. We have also initiated Phase 2 clinical trials in Alström syndrome, POMC heterozygous deficiency obesity and POMC epigenetic disorders, and expect to enroll patients in these trials in the second half of 2017. We anticipate reporting preliminary results in these additional Phase 2 indications in the first half of 2018. Approximately 275 obese subjects and patients have been treated with setmelanotide in previous and ongoing clinical trials in which setmelanotide demonstrated statistically significant weight loss with good tolerability.

Obesity is epidemic in the United States and current treatment approaches have demonstrated limited long-term success for most obese patients. We are taking a different approach to obesity drug development by leveraging new understanding of the genetic causes of severe obesity to develop innovative therapies that we believe have the potential for compelling efficacy. Setmelanotide's unique mechanism of action at MC4R enables a targeted approach to treating very severe obesity in patients with specific, monogenic defects in the MC4 signaling pathway. By restoring impaired function in this pathway, setmelanotide can serve as replacement therapy for genetic deficiencies, with the potential for dramatic improvements in weight and appetite. We believe we are at the forefront of improving treatment outcomes in subtypes of severe obesity that are caused by genetically-defined defects in the MC4 pathway.

Setmelanotide activates MC4R, which is part of the key pathway that can independently regulate energy homeostasis, which refers to the body's energy balance, and appetite. The critical role of the MC4 pathway in weight regulation was validated with the discovery that single genetic defects along this pathway

result in early onset and severe obesity. An expanding set of severe obesity genetic defects are now identified that involve genes in the pathway which are either upstream of MC4R—for example POMC deficiency obesity and LepR deficiency obesity—or genes that are downstream of MC4R or affect MC4R itself. We are focusing setmelanotide clinical development on patients with monogenic upstream genetic defects in which obesity is life-threatening but the downstream MC4 pathway is fully functional. We believe setmelanotide has the potential to restore lost activity in the MC4 pathway by bypassing the defects upstream of MC4R, and activating the MC4 pathway below such defects. In this way, setmelanotide may serve as replacement therapy to reestablish weight and appetite control in patients with these genetic disorders.

The first generation of MC4R agonists were predominantly small molecules that failed in clinical trials due to safety issues, particularly increases in blood pressure, in addition to having limited efficacy. In contrast, setmelanotide, a novel eight amino acid peptide, retains the specificity and functionality of the naturally occurring hormone that activates MC4R, and has exhibited preliminary evidence of efficacy without adversely affecting blood pressure in our Phase 1 and ongoing Phase 2 clinical trials. We are currently evaluating setmelanotide, which is administered by subcutaneous, or SC, injection, for the treatment of six genetic disorders of obesity: POMC deficiency obesity, LepR deficiency obesity, Bardet-Biedl syndrome, Alström syndrome, POMC heterozygous deficiency obesity, and POMC epigenetic disorders. We have positive Phase 2, proof of concept results for two of these indications thus far—POMC deficiency obesity and LepR deficiency obesity—and both indications are currently in Phase 3 development.

POMC deficiency obesity is a life-threatening, ultra-rare orphan disease, with approximately 50 patients reported to date. Ultra-rare orphan diseases are generally categorized as those that affect fewer than 20 patients per million. We estimate that our addressable patient population for this disorder is approximately 100 to 500 patients in the United States. Patients with POMC deficiency have unrelenting hunger, or hyperphagia, that begins in infancy and they develop severe, early onset obesity. POMC deficiency obesity results from two different homozygous genetic defects, both upstream of MC4R, that result in loss of function in the MC4 pathway. Currently, there is no approved treatment for the obesity and hyperphagia associated with this genetic disorder. We have initiated a Phase 3 open label, single arm, multinational trial to evaluate the safety and efficacy of setmelanotide for POMC deficiency obesity, with setmelanotide administered once daily by subcutaneous, or SC, injection for 12 months. We are currently enrolling patients in this POMC deficiency obesity Phase 3 clinical trial. We expect to complete enrollment by the end of 2017 and to report Phase 3 data in the first half of 2019. Previously, we completed a positive Phase 2 clinical trial in which two patients were enrolled and received treatment. The first patient in this trial lost 146.6 lbs over 118 weeks, from a baseline weight of 341.7 lbs, and the second patient lost 89.3 lbs over 64 weeks, from a baseline weight of 336.9 lbs. Both patients experienced substantial reductions in hunger, with hunger scores falling to one to two from baseline scores of nine to 10. Hunger scores were measured using a Likert score of zero to 10, where zero represents no hunger and 10 represents extreme hunger. Setmelanotide was generally well tolerated in this Phase 2 trial.

LepR deficiency obesity is an ultra-rare orphan disease that results in hyperphagia and severe early-onset obesity, with an estimated prevalence of 1% of subjects with severe, early-onset obesity. We estimate that our addressable patient population for this disorder is approximately 500 to 2,000 patients in the United States. Like other deficiencies upstream in the MC4 pathway, LepR deficiency results in loss of function in the MC4 pathway. Therefore, patients with this indication also manifest hyperphagia and severe obesity from early childhood. Currently, there is no approved treatment for the obesity and hyperphagia associated with LepR deficiency obesity. We have initiated a Phase 3 open label, single arm, multinational trial to evaluate the safety and efficacy of setmelanotide for LepR deficiency obesity, with setmelanotide administered once daily by SC injection for 12 months. We expect to enroll the first patient in our LepR deficiency obesity Phase 3 clinical trial in the second half of 2017, and to complete enrollment in 2018. Previously, we completed a positive Phase 2 clinical trial in which three patients were enrolled and

received treatment in this trial each experiencing significant weight loss and substantial reductions in hunger. Setmelanotide was generally well tolerated in this Phase 2 trial.

Based on our POMC deficiency obesity and LepR deficiency obesity Phase 2 results, the FDA granted setmelanotide breakthrough therapy designation for the treatment of obesity associated with genetic defects upstream of the MC4 receptor in the leptin-melanocortin pathway, which includes both POMC deficiency obesity and LepR deficiency obesity, enabling an expedited path to approval of setmelanotide for these two indications. In April 2016, the FDA granted our orphan drug designation request for setmelanotide for the treatment of POMC deficiency obesity.

Bardet-Biedl syndrome is a life-threatening, ultra-rare orphan disease with a prevalence of approximately one in 100,000 in North America. We estimate that our addressable patient population for Bardet-Biedl syndrome obesity is approximately 1,500 to 2,500 patients in the United States. Bardet-Biedl syndrome is a monogenic disorder that causes severe obesity and hyperphagia as well as vision loss, polydactyly, kidney abnormalities, and other signs and symptoms. Currently there are no approved or effective therapies for Bardet-Biedl syndrome. We recently demonstrated preliminary proof of concept based on data from five patients in our Phase 2 clinical trial in Bardet-Biedl syndrome, indicating that this is also a setmelanotide-responsive, upstream MC4 pathway disorder. Four of these five patients showed early, but significant weight loss and all five patients showed clear improvements in every hunger assessment. We are continuing to enroll patients in this trial and expect to report preliminary Phase 2 results in the fourth quarter of 2017. Setmelanotide has so far been generally well tolerated in this trial. We expect to initiate a Phase 3 clinical trial in Bardet-Biedl syndrome in 2018.

We are also focusing on additional monogenic, upstream MC4 pathway deficiencies for which setmelanotide can function as replacement therapy and provide activation of the pathway downstream of the defect, promoting satiety and weight control. We have initiated a Phase 2 proof of concept trial for the treatment of Bardet-Biedl syndrome, which is a rare monogenic disorder that we believe has an addressable patient population of approximately 1,500 to 2,500 patients in the United States. Bardet-Biedl syndrome causes severe obesity and hyperphagia as well as vision loss, polydactyly, kidney abnormalities, and other signs and symptoms. For these patients, hyperphagia and obesity can have significant health consequences for which there is currently no approved treatment. We have initiated Phase 2 trials for Alström syndrome, a life-threatening, ultra-rare orphan disease, for which we estimate our addressable population is approximately 500 to 1,000 patients worldwide, for POMC heterozygous deficiency obesity, for which we estimate our addressable population is approximately 4,000 patients in the United States, and for POMC epigenetic disorders. For these patients, hyperphagia and obesity can have significant health consequences for which there is currently no approved treatment. We expect to enroll patients with Alström syndrome, POMC heterozygous deficiency obesity, and POMC epigenetic disorders in the second half of 2017 and to report preliminary results from these trials in the first half of 2018.

Our company was founded in November 2008 by former biopharmaceutical executives who have successfully developed, commercialized and in-licensed innovative pharmaceutical products, and we have subsequently expanded our senior management team to further broaden our team's experience in developing, registering and commercializing new drugs. In addition, our scientific advisory board, or SAB, members have extensive clinical expertise in obesity, endocrinology and metabolic diseases. We intend to leverage the experience of our senior management team and SAB to develop and commercialize setmelanotide. Through our senior management team's network of industry contacts, we will continue to evaluate additional product candidate licensing and acquisition opportunities. We are backed by strong and dedicated investors that include both private equity venture capital funds and public healthcare investment funds. Our investors include MPM Capital, New Enterprise Associates, Third Rock Ventures, Ipsen, Pfizer Venture Investments, OrbiMed, Deerfield Management and two public healthcare investment funds.

Our patent portfolio includes composition of matter patents for setmelanotide that expire in the United States in 2027, with possible patent term extension to 2032 under the Hatch-Waxman Act.

Our Strategy

Our goal is to be a leader in developing and commercializing targeted therapies for genetic deficiencies that result in life-threatening metabolic disorders. The key components of our strategy are:

- **Rapidly develop setmelanotide for rare genetic disorders of obesity caused by MC4 pathway deficiencies.** We are aiming to dramatically improve patient outcomes in severe obesity by targeting setmelanotide's mechanism of action to the treatment of patients with genetically-defined defects in the MC4 pathway. We are focusing setmelanotide clinical development on monogenic upstream genetic defects in which obesity is life-threatening but where the downstream MC4 pathway is fully functional. We intend to pursue faster paths to approval for setmelanotide in these orphan disorders. We believe that focusing on these rare life-threatening conditions enables us to rapidly develop and commercialize setmelanotide using relatively small clinical trials.

- **Advance setmelanotide for POMC deficiency obesity and LepR deficiency obesity as our first indications in upstream MC4 pathway deficiencies.** We are currently evaluating setmelanotide for the treatment of six genetic disorders of obesity: POMC deficiency obesity, LepR deficiency obesity, Bardet-Biedl syndrome, Alström syndrome, POMC heterozygous deficiency obesity, and POMC epigenetic disorders. We currently have a Phase 3 trial underway for POMC deficiency obesity and expect to report Phase 3 data in the first half of 2019. We have also initiated a Phase 3 trial for LepR deficiency obesity. We expect to enroll the first patient in our LepR deficiency obesity Phase 3 clinical trial in the second half of 2017, and to complete enrollment in 2018. We are working with the FDA, based on our breakthrough therapy designation, to prepare NDA filings with an expedited path to approval for POMC deficiency obesity and LepR deficiency obesity.

- **Expand setmelanotide development to additional upstream MC4 pathway deficiencies, including Bardet-Biedl syndrome, Alström syndrome, POMC heterozygous deficiency obesity, and POMC epigenetic disorders.** We believe we can leverage our mechanistic understanding of and experience with both POMC deficiency obesity and LepR deficiency obesity to advance development of setmelanotide for other upstream MC4 pathway deficiencies. Accordingly, we have initiated Phase 2 clinical trials in these rare genetic disorders. We have obtained preliminary proof of concept in Bardet-Biedl syndrome, demonstrating that this is also a setmelanotide-responsive, upstream MC4 pathway disorder. We expect to report preliminary Phase 2 results in Bardet-Biedl syndrome in the fourth quarter of 2017 and preliminary results for the other Phase 2 indications in the first half of 2018.

- **Commercialize setmelanotide for rare disease indications in core strategic markets.** We intend to establish our own commercial sales and marketing organization in the United States and other core strategic markets. We expect this sales organization will target physicians treating these rare genetic disorders of obesity, including pediatric and adult endocrinologists. We believe that building our own commercial operations will deliver a greater return on our product investment than if we license the rights to commercialize these products to third parties. We may also selectively establish partnerships in markets outside the United States for sales, marketing and distribution.

- **Leverage the broad experience of our team in clinical and commercial drug development, and product acquisitions.** We will apply our team's extensive experience in developing and commercializing innovative medicines to the development and launch of setmelanotide. In addition, we intend to identify and acquire new pipeline programs in related diseases. Our team is complemented by highly experienced external consultants and collaborators in the areas of drug discovery, development, manufacturing and regulatory approval.

Our Product Pipeline

The following chart depicts key information regarding the development of setmelanotide, including the indications we are pursuing within MC4 pathway deficiencies, the current state of development and our expected upcoming milestones:

Market Overview

Recent Advances in the Understanding of Obesity

Diet and lifestyle modifications remain the cornerstones of weight loss therapy, but they are limited by a lack of long-term success for most obese patients. The long-term efficacy of these interventions and for existing drug therapies is often limited by the counter-regulatory mechanisms of the human body. For example, with diet induced weight loss, typically there is a large decrease in energy expenditure that offsets that weight loss. Accordingly, the discovery that the MC4 pathway can regulate both appetite and energy homeostasis separately—helping maintain the balance between food intake and energy burn—has defined an important target for therapeutics. In addition to POMC deficiency obesity and LepR deficiency obesity, recent advances in genetic studies have identified several diseases that are the result of genetic defects affecting the MC4 pathway, including Bardet-Biedl syndrome, Alström syndrome, POMC heterozygous deficiency obesity, and POMC epigenetic disorders. With a deeper understanding of this critical signaling pathway, we are taking a different approach to drug development by focusing on specific genetic deficiencies affecting the MC4 pathway. We believe that this approach has the potential to provide dramatic improvements in weight and appetite by restoring lost function in the MC4 pathway.

Obesity Caused by Rare Genetic Deficiencies Affecting the MC4 Pathway

The MC4 pathway serves a critical role in the control of food intake and energy balance. Its activity decreases appetite and caloric intake, and increases energy expenditure, with MC4R acting as the final step in the signaling pathway. This important hypothalamic, or lower brainstem, pathway has been the focus of extensive investigation for many years, and we have a deep understanding of this mechanism, which is unlike the targets of most other anti-obesity therapies. As a result, we believe we can better predict the

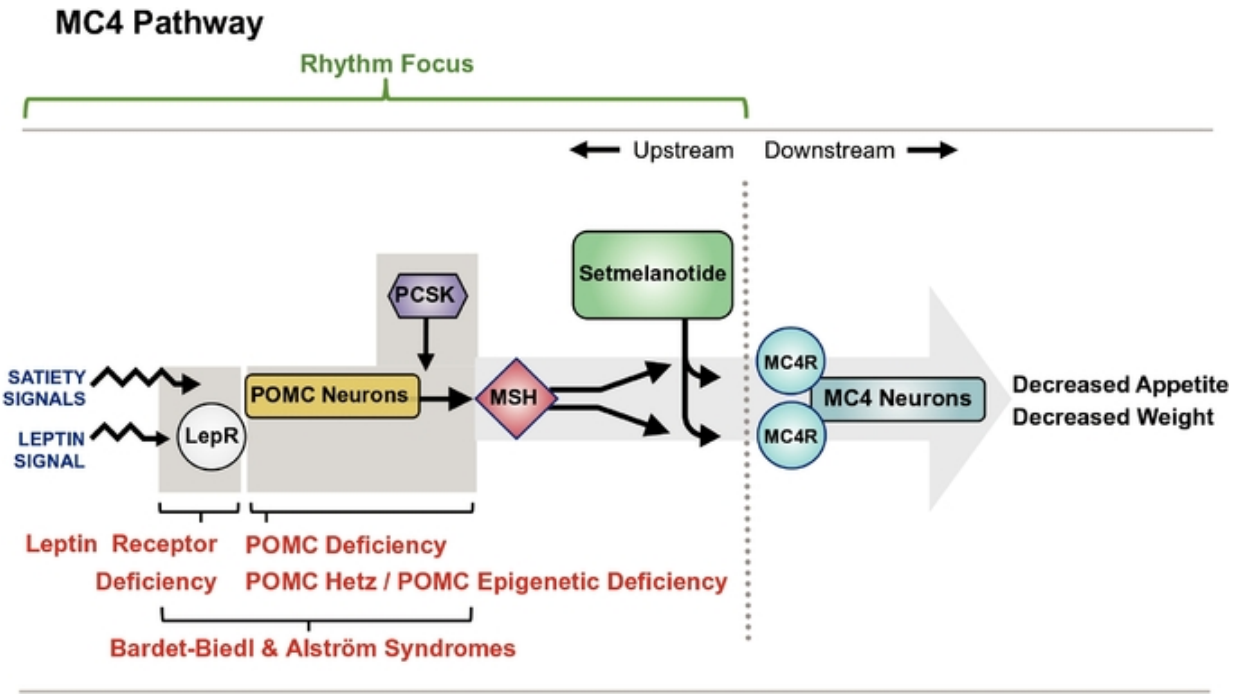
efficacy and safety profile expected from modulating this target. The critical role of the MC4 pathway in weight regulation was also validated with the discovery that single genetic defects at many points in this pathway result in early onset, severe obesity.

The MC4 pathway is illustrated in the figure below, from the activation of the pathway to the resulting decrease in appetite and weight. Under normal conditions, POMC neurons are activated by brain satiety signals, including those resulting from the hormone leptin acting through LepR. POMC neurons produce a protein, which is specifically processed by the proprotein convertase subtilisin/kexin 1, or PCSK, enzyme, into melanocyte stimulating hormone, or MSH, the natural ligand, or activator, for MC4R. When genetic mutations disrupt this pathway, the result is hyperphagia and severe obesity.

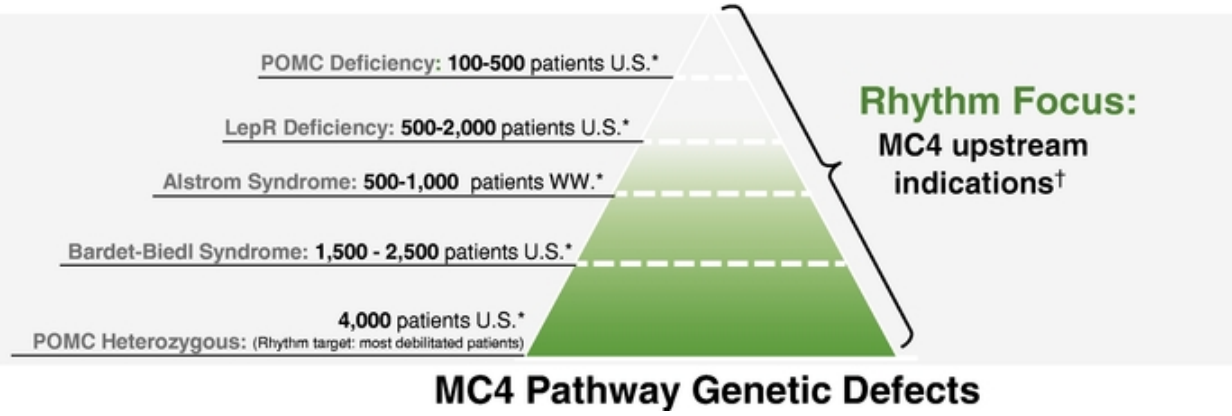
We are focused on developing setmelanotide for genetic disorders that result in defects in this pathway that are upstream of MC4R. Setmelanotide has the potential to restore lost function in this pathway by activating the intact MC4 pathway below the genetic defect. In this way, we believe setmelanotide acts as replacement therapy.

The figure below also illustrates some of the upstream MC4 pathway deficiencies that are the targets of our development activities.

Setmelanotide Development Targets: Upstream Deficiencies Affecting the MC4 Pathway



The figure below summarizes the indications on which we are focusing for the development of setmelanotide, including our estimates for the addressable patient populations within these indications.



* The patient numbers above are based on company estimates.

† Epidemiological estimates are not yet available for POMC epigenetic disorders.

We believe that the patient populations in the European Union are at least as large as those in the United States. However, we do not have comparable epidemiological data from the European Union and these estimates are therefore based solely on applying relative population percentages to the Company-derived estimates described above.

Obesity Caused by Upstream Genetic Deficiencies Affecting the MC4 Pathway

We have completed three positive Phase 2 trials of setmelanotide that provide proof of concept for three upstream MC4 pathway genetic defects in which obesity is life-threatening but the downstream MC4 pathway is fully functional: POMC deficiency obesity, LepR deficiency obesity, and Bardet-Biedl syndrome, which together we estimate have an addressable population of up to 5,000 people in the United States.

POMC Deficiency Obesity

POMC deficiency obesity is an ultra-rare genetic disorder, with severe, early onset obesity, defined here as a body mass index, or BMI, of greater than 40 kg/m^2, and hyperphagia as hallmark clinical features. Patients with POMC deficiency obesity are extremely rare. There are approximately 50 patients with POMC deficiency obesity noted in a series of published case reports, each mostly reporting a single or small number of patients. However, we estimate that our addressable patient population for this disorder is approximately 100 to 500 patients in the United States, as most of the reported cases are from a small number of academic research centers, and because genetic testing for POMC deficiency is often unavailable and rarely performed. Based on discussions with experts in rare diseases, we also believe the number of diagnosed cases will increase several-fold with increased awareness of this disorder and the availability of new treatments.

POMC deficiency obesity is caused by the loss of both genetic copies of either the gene for POMC or the gene for PCSK. This results either in loss of POMC neuropeptide synthesis, in the case of homozygous deficiency in the POMC gene, or in disruption of the required processing of the POMC neuropeptide product to MSH by the PCSK enzyme, in the case of homozygous deficiency in the PCSK gene. The end result of both of these two homozygous genetic defects is lack of MSH to bind and activate MC4R, ultimately leading to the lack of stimulation of downstream MC4 neurons and causing severe, early onset

obesity and hyperphagia. POMC homozygous deficiency may also be associated with hormonal deficiencies, such as hypoadrenalism, as well as red hair and fair skin.

POMC deficiency is characterized by voracious infant feeding, rapid weight gain and severe obesity, often in early infancy, with patients demonstrating remarkable weight increases many standard deviations from the normal weight growth curves. These patients and their caregivers have attempted to stabilize body weight with the help of psychologists, nutritionists and pediatric endocrinologists, all without significant success. We are currently enrolling patients in our POMC deficiency obesity Phase 3 clinical trial. We expect to complete enrollment by the end of 2017 and to report Phase 3 data in the first half of 2019. Currently there are no approved or effective therapies for POMC deficiency obesity.

Leptin Receptor Deficiency Obesity

LepR deficiency obesity is an ultra-rare genetic disorder that causes hyperphagia and severe, early onset obesity. LepR deficiency accounts for an estimated 1% of cases of severe, early onset obesity. Based on epidemiology studies in small cohorts of patients with severe, early onset obesity, we estimate that our addressable patient population for this disorder is approximately 500 to 2,000 patients in the United States.

Leptin's role in obesity has been elucidated by characterization of severely obese people with homozygous mutations that impair the activity of leptin, including disruption of signaling at the LepR, known as LepR deficiency obesity. Under normal conditions, leptin can activate POMC neurons and the downstream MC4, but like other deficiencies upstream in the MC4 pathway, lack of signaling at LepR results in loss of function in the MC4 pathway.

Like POMC deficiency obesity, patients with LepR deficiency obesity exhibit hyperphagia and severe obesity from early childhood. LepR deficiency is also associated with hypogonadism and reduced immune function. We expect to enroll the first patient in our LepR deficiency obesity Phase 3 clinical trial in the second half of 2017, and to complete enrollment in 2018. Currently there are no approved or effective therapies for LepR deficiency obesity.

Bardet-Biedl Syndrome

Bardet-Biedl syndrome is a life-threatening, ultra-rare orphan disease with a prevalence of approximately one in 100,000 in North America. We estimate that our addressable patient population for Bardet-Biedl syndrome obesity is approximately 1,500 to 2,500 patients in the United States. Bardet-Biedl syndrome is a monogenic disorder that causes severe obesity and hyperphagia as well as vision loss, polydactyly, kidney abnormalities, and other signs and symptoms. For Bardet-Biedl syndrome patients, hyperphagia and obesity can have significant health consequences.

Bardet-Biedl syndrome is part of a class of disorders called ciliopathies, or disorders associated with the impairment of cilia function in cells. Cilia are hair-like cellular projections that play a fundamental role in the regulation of several biological processes, including satiety signaling. Cilia dysfunction is thought to contribute to hyperphagia and obesity in Bardet-Biedl syndrome. Bardet-Biedl syndrome is a genetically heterogeneous disease that is caused by as many as 21 separate Bardet-Biedl loci defects that result in a similar syndrome, though each Bardet-Biedl syndrome patient only has one of these defects.

Recent scientific studies identify deficiencies affecting the MC4 pathway as a potential cause of the obesity and hyperphagia associated with Bardet-Biedl syndrome and demonstrate that an MC4R agonist can directly impact these symptoms. Studies in mouse models of Bardet-Biedl syndrome show that deficiencies in the MC4 pathway contribute to the obesity and hyperphagia in Bardet-Biedl syndrome, with animals developing hyperphagic tendencies as early as 10 weeks of age. Notably, these mice have decreased leptin receptor signaling, with the essential hallmarks of failure to activate POMC neurons. The potential utility of MC4 agonists is also supported by studies in Bardet-Biedl syndrome rodent models, where mice have responded to an MC4 agonist resulting in reduced food intake and body weight. We have obtained preliminary proof of concept in Bardet-Biedl syndrome demonstrating that this is also a setmelanotide-responsive, upstream MC4 pathway disorder. We anticipate reporting preliminary results for Bardet-Biedl syndrome in the fourth quarter of 2017, and initiating Phase 3 clinical trials in 2018. Currently there are no approved or effective therapies for Bardet-Biedl syndrome.

Other Upstream Genetic Defects in the MC4 Pathway

In addition to POMC deficiency obesity, LepR deficiency obesity and Bardet-Biedl syndrome, there are other upstream, MC4 pathway deficiencies for which we believe setmelanotide may function as replacement therapy, including defects that partially modulate POMC activity, such as POMC heterozygous deficiency obesity and POMC epigenetic disorders, as well as deficiencies that may indirectly impair POMC and LepR signaling, such as Alström syndrome.

Alström Syndrome

Alström syndrome is a life-threatening, ultra-rare orphan disease with a prevalence of approximately one in 1,000,000 in North America. We estimate that our addressable patient population for Alström syndrome is approximately 500 to 1,000 patients worldwide. Alström syndrome is a monogenic disorder that causes childhood obesity and hyperphagia as well as progressive vision loss, deafness, cardiomegaly, insulin resistance and other signs and symptoms. Variable features include short stature, cardiomyopathy, and progressive lung, liver, and kidney dysfunction. Symptoms of Alström syndrome first appear in infancy, and progressive development of multi-organ pathology leads to a reduced life expectancy, with survival rare beyond the age of 50.

Alström syndrome is a ciliopathy caused by mutations in the ALMS1 gene, which has been shown to be important for cilia function. Like Bardet-Biedl syndrome, recent scientific studies identify genetic deficiencies affecting the MC4 signaling pathway as a potential cause of the obesity and hyperphagia associated with Alström syndrome. Studies in a mouse model of Alström syndrome show a reduction in the number of cilia in specific neurons in the hypothalamus that are critical for MC4 pathway signaling. While Alström syndrome is less well studied than Bardet-Biedl syndrome, the similar pathophysiology of cilial dysfunction and clinical presentation support that deficiencies in the MC4 pathway are implicated in the obesity and hyperphagia observed in Alström syndrome. We expect to enroll patients with Alström syndrome in a Phase 2 clinical trial in the second half of 2017 and anticipate reporting preliminary results in the first half of 2018. Currently there are no approved or effective therapies for Alström syndrome.

POMC Heterozygous Deficiency Obesity

POMC heterozygous deficiency results in a strong predisposition to obesity, though the epidemiology and clinical characterization of these patients is less well known. POMC heterozygous deficiency obesity is caused by the loss of one of the two genetic copies of either the gene for POMC or the gene for PCSK. An estimated 2% of severe, early onset obesity patients have POMC heterozygous deficiency obesity, which is much more common than the ultra-rare POMC deficiency obesity in which both copies of either the POMC or PCSK genes are impaired. We believe that the most severe POMC heterozygous deficiency obesity patients may be suitable for treatment with setmelanotide. We estimate that our addressable patient population within severe POMC heterozygous deficiency obesity is approximately 4,000 patients in the United States, based on epidemiology studies in small cohorts of patients with severe early onset obesity and adult obesity. Animal models support that such heterozygous deficiency in the critical MC4 pathway can result in a strong predisposition to severe obesity. The effect of heterozygous deficiency was first demonstrated in MC4R heterozygous deficiency obesity.

It is thought that the obesity of patients with POMC heterozygous deficiency may have a broader spectrum of severity than POMC deficiency obesity. Therefore, our focus will be on the most severe of the POMC heterozygous deficiency obesity patients, with our estimate that only a small percentage of these patients will benefit from targeted therapy with substantial efficacy. As a result, we have initiated a Phase 2 proof of concept trial to confirm our hypothesis that the subset of patients with very severe POMC heterozygous deficiency obesity may be highly responsive to setmelanotide therapy. We expect to enroll patients with POMC heterozygous deficiency obesity in a Phase 2 clinical trial in the second half of 2017 and to report preliminary results in the first half of 2018. There are currently no approved or effective therapies for POMC heterozygous deficiency obesity.

POMC Epigenetic Disorders

Recent scientific studies have identified patients with obesity due to a partial lack of MSH that is caused by epigenetic POMC variant. Given the recent discovery of these epigenetic disorders, there is currently no epidemiology data that defines the prevalence of POMC epigenetic disorders. However, we believe this these are rare disorders. Epigenetics implies DNA modifications, which can change gene expression without altering the DNA sequence itself. The most stable epigenetic modification is called DNA methylation. Recently, our academic collaborators in Berlin have described a POMC hypermethylation variant, which correlates with increased body weight in children and adults. Therefore, the presence of the POMC epigenetic variant leads to an increased risk of obesity based on reduced POMC gene activity. We expect that these patients under-express the POMC gene product and as a result have a partial MSH deficiency. We have initiated a Phase 2 proof of concept trial to confirm our hypothesis that the subset of patients with very severe POMC epigenetic disorders may be highly responsive to setmelanotide therapy. We expect to enroll patients with POMC epigenetic disorders in a Phase 2 clinical trial in the second half of 2017 and anticipate reporting preliminary results in the first half of 2018. There are currently no approved or effective therapies for these disorders.

Obesity Caused by Downstream Genetic Deficiencies Affecting the MC4 Pathway

MC4 Heterozygous Deficiency Obesity

MC4 heterozygous deficiency is caused by the absence of one genetic copy of the gene for MC4R. Consistent with POMC heterozygous deficiency, MC4 heterozygous deficiency results in a strong predisposition to early onset and severe obesity. MC4 heterozygous deficiency is the most common genetic cause of obesity. An epidemiological study performed in Europe in 2006 reported a prevalence of 2.6% of genetic defects in the MC4 gene in the obese population with a BMI of greater than 30 kg/m^2, and studies performed in both Europe and the United States in 2000 and 2003, respectively, reported a prevalence of up to 4% of these genetic defects in more severely obese populations with a BMI of greater than 35 kg/m^2. These prevalence rates suggest that there are approximately one million people in the United States with obesity caused by a mutation of the MC4R gene.

These patients have a higher risk than the general population for early onset obesity and complications such as diabetes. Furthermore, MC4 deficiency may offset the beneficial effects of diet and exercise for sustained weight loss, limiting treatment options for these individuals. There are currently no approved or effective therapies for MC4 heterozygous deficiency obesity.

We believe that MC4 heterozygous deficient patients can respond to setmelanotide therapy by increasing activity that results from the one normal copy of the MC4 gene. However, while setmelanotide appears to show strong efficacy in a Phase 1b trial for the treatment of MC4 heterozygous deficiency obesity patients, we are focusing instead on genetic defects that are upstream of the MC4 receptor. This is because we believe that many of these upstream genetic disorders cause even more severe, often life-threatening obesity, and because setmelanotide has the potential to restore lost function in these upstream disorders, delivering more compelling efficacy.

Expanding Attention to the Diagnosis of Genetic Obesity

The Endocrine Society issued new Pediatric Obesity Guidelines in January 2017 that, for the first time, recommend genotyping patients with severe pediatric obesity and hyperphagia. These guidelines estimate that up to 7% of patients with extreme pediatric obesity have a genetic mutation, including genetic MC4 pathway deficiencies, that drives their obesity. The guidelines also suggest that this percentage of severe pediatric obesity patients will increase, with newer methods and wider awareness of the need for genetic testing.

We are supporting several initiatives to expand the diagnosis of genetic obesity, including The Genetic Obesity Project. The Genetic Obesity Project has initiated a genotyping study, or GO-ID genotyping study,

and a patient registry, or GO-ID registry, both focusing initially on identifying people with POMC deficiency obesity and LepR deficiency obesity and which we intend to expand to include other MC4 pathway deficiencies. Our preliminary results in 560 genotyped patients suggest we can successfully identify these patients. We have also conducted a genetic obesity epidemiology analysis of MC4 pathway genetic defects in a large representative sample of the U.S. population. Based on preliminary findings from this analysis, we believe the prevalence of these MC4 pathway deficiencies could be substantially larger than our current estimates. Our work in the epidemiology for these rare genetic disorders of obesity is continuing.

Limitations of Current Therapies

Although drugs approved for general obesity can potentially be used in obese patients with MC4 pathway deficiencies, all have limited efficacy and aim to treat symptoms rather than addressing the underlying biology. There are currently no treatments approved specifically for obesity and hyperphagia in POMC deficiency obesity, LepR deficiency obesity, Bardet-Biedl syndrome, Alström syndrome, POMC heterozygous deficiency obesity, or POMC epigenetic disorders. Bariatric surgery is not an option in patients with upstream defects in the MC4 pathway who have severe obesity and hyperphagia.

Setmelanotide: A First-in-Class MC4R Agonist in Two Phase 3 Programs

Setmelanotide is a potent, first-in-class, MC4R agonist peptide administered by daily subcutaneous, or SC, injection. Setmelanotide is in Phase 3 for the treatment of two rare genetic disorders of obesity caused by MC4 pathway deficiencies, and in Phase 2 for other MC4 pathway disorders. MC4R modulates a key pathway in humans that regulates energy homeostasis and food intake.

The critical role of the MC4 pathway in weight regulation was validated with the discovery that single genetic defects in this pathway result in severe, early onset obesity. The first generation MC4R agonists were small molecules that failed in clinical trials primarily due to safety issues, particularly increases in blood pressure, as well as limited efficacy. In contrast, setmelanotide is a peptide that retains the specificity and functionality of the naturally occurring hormone that activates MC4R. Approximately 275 obese subjects and patients have been treated with setmelanotide in previous and ongoing clinical trials in which setmelanotide demonstrated significant weight loss with good tolerability.

Clinical Development in Rare Genetic Disorders of Obesity Caused by MC4 Pathway Deficiencies

Setmelanotide is currently in Phase 3 development for the treatment of two ultra-rare monogenic disorders of obesity, POMC deficiency obesity and LepR deficiency obesity, each of which has had one pivotal trial. We are currently enrolling patients in our POMC deficiency obesity Phase 3 clinical trial, and expect to complete enrollment by the end of 2017 and to report Phase 3 data in the first half of 2019. We expect to enroll the first patient in our LepR deficiency obesity Phase 3 clinical trial in the second half of 2017, and to complete enrollment in 2018. In addition, setmelanotide is in Phase 2 development for the treatment of other rare monogenic disorders of obesity, including Bardet-Biedl syndrome, Alström syndrome, POMC heterozygous deficiency obesity, and POMC epigenetic disorders. We hypothesize that all of these disorders are genetically defined deficiencies upstream in the MC4 pathway. We have initiated two very similar Phase 2 protocols, each of which is designed to capture a broad range of indications under one investigational protocol. We recently demonstrated preliminary proof of concept in Bardet-Biedl syndrome, indicating that this is also a setmelanotide-responsive, upstream MC4 pathway disorder. We are continuing to enroll patients in this trial and expect to report preliminary Phase 2 results in the fourth quarter of 2017. We expect to initiate a Phase 3 clinical trial in Bardet-Biedl syndrome in 2018. We expect to enroll patients with Alström syndrome, POMC heterozygous deficiency obesity, and POMC epigenetic disorders in the second half of 2017 and to report preliminary results from these trials in the first half of 2018. We have also completed a Phase 2 trial in Prader-Willi syndrome, or PWS. Based on FDA consultations to date, and the FDA awarding breakthrough therapy designation, we believe we can seek indications for obesity caused by upstream defects in the MC4 pathway with faster paths to approval, as

compared to typical obesity drug candidates, because of the high unmet need and rare prevalence of these disorders. We expect to use the results of our Phase 3 clinical trials of setmelanotide in POMC deficiency obesity and LepR deficiency obesity as the foundation for proceeding directly to approval for those indications.

We believe our data in POMC deficiency obesity, LepR deficiency obesity, and Bardet-Biedl syndrome provide strong proof of concept that setmelanotide, when targeted for deficiencies affecting the upstream portion of the MC4 pathway, can provide compelling efficacy for weight loss and decrease in hunger. Proof of concept for substantial weight loss in patients with downstream, heterozygous mutations of the MC4R gene itself has also been achieved in a small, four week, Phase 1b clinical trial. While these downstream defects are not our current area of focus, we believe they provide evidence for substantial, though lesser, weight loss efficacy in a setting of a partially defective, downstream defect in the MC4 pathway, which impacts a significantly larger population.

Initial setmelanotide clinical trials were in patients with general obesity, which provided preliminary evidence of the safety and efficacy of the drug, and were the foundation for the Phase 2 trials in rare genetic disorders of obesity. In these trials, setmelanotide has generally achieved weight loss without adversely increasing blood pressure. These trials in the general obese population are described separately below.

The following table outlines our ongoing and planned setmelanotide trials in rare monogenic disorders of obesity.

Setmelanotide: Key Clinical Programs in Monogenic MC4 Pathway Disorders of Defined Obesity

	POMC Deficiency Pivotal	**LepR Deficiency Pivotal**	**POMC/LepR Deficiency Proof of Concept**	**Other Populations Proof of Concept Basket Protocols[6]**
Clinical trial phase	Phase 3	Phase 3	Phase 2	Phase 2
Status	Initiated 1Q2017	Initiated 2Q2017[5]	Initiated 2014, Completed 4Q 2016 for these indications	Initiated 2016[7][8]
Treatment groups[1]	Setmelanotide[2]	Setmelanotide[2]	Setmelanotide	Setmelanotide
Number of patients	10[3]	10[3]	2 POMC, 3 LepR	20[9]
Patient demographics	Adult/pediatric POMC deficient[4]	Adult/pediatric LepR deficient[4]	Adults/Adolescents	Adult/pediatric[4] Multiple indications: Bardet-Biedl syndrome; Alström syndrome; POMC heterozygous deficiency obesity; POMC epigenetic disorders
Duration of treatment	52 weeks + Extensions	52 weeks + Extensions	12 weeks + Extensions	12 weeks + Extensions
Location	United States, Germany, United Kingdom, France	United States, Germany, United Kingdom, France[10]	Germany	United States, Germany, United Kingdom, France

(1) Setmelanotide, administered as once daily SC injection.

(2) These trials include a placebo controlled, double-blind withdrawal period.

(3) Approximately 10 POMC deficiency obesity and 10 LepR deficiency obesity patients are anticipated in each pivotal trial.

(4) POMC deficiency includes homozygous deficiency in either the POMC or PCSK genes; pediatric patients ³ 12 years are currently being studied, and lower age pediatric patients will also be studied when applicable.

(5) Trial site activation activities ongoing and first enrolled patient anticipated by the second half of 2017.

(6) Basket protocols study a variety of different indications or patient populations administratively in one protocol, though each population is enrolled and analyzed separately.

(7) One of our proof of concept basket protocols was originally the Phase 2 trial for POMC deficiency obesity and LepR deficiency obesity initiated in Germany in 2016 and provided proof of concept in these indications. This trial was later amended in 2016 to

include other MC4 pathway disorders. Our second basket protocol is open, or is being opened in other geographical locations (United States 2016; United Kingdom, France in 2017).

(8) We have enrolled Bardet-Biedl syndrome patients, and we anticipate enrolling patients in the other indications, Alström syndrome, POMC heterozygous deficiency obesity and POMC epigenetic disorders, by the fourth quarter of 2017.

(9) Approximately five patients are planned for each of the four MC4 pathway indications.

(10) We have ongoing trials in the United States and trial approvals are in process in Germany, United Kingdom, and France.

Setmelanotide: Clinical Development Program in Genetically Defined Obesity

Phase 2 Clinical Development in POMC Deficiency Obesity

We have completed a Phase 2 proof of concept, open label clinical trial, Study RM-493-011, in patients with POMC deficiency obesity. With the two patients in this trial, we have provided proof of concept for the compelling effect of setmelanotide in this disorder and after discussions with the FDA, have initiated a Phase 3 trial for this indication. To validate the scientific and clinical importance of our Phase 2 findings, the results of this trial were published on July 21, 2016 in the New England Journal of Medicine, and the accompanying editorial described the trial as demonstrating impressive hunger reduction and weight loss as well as improved insulin sensitivity.

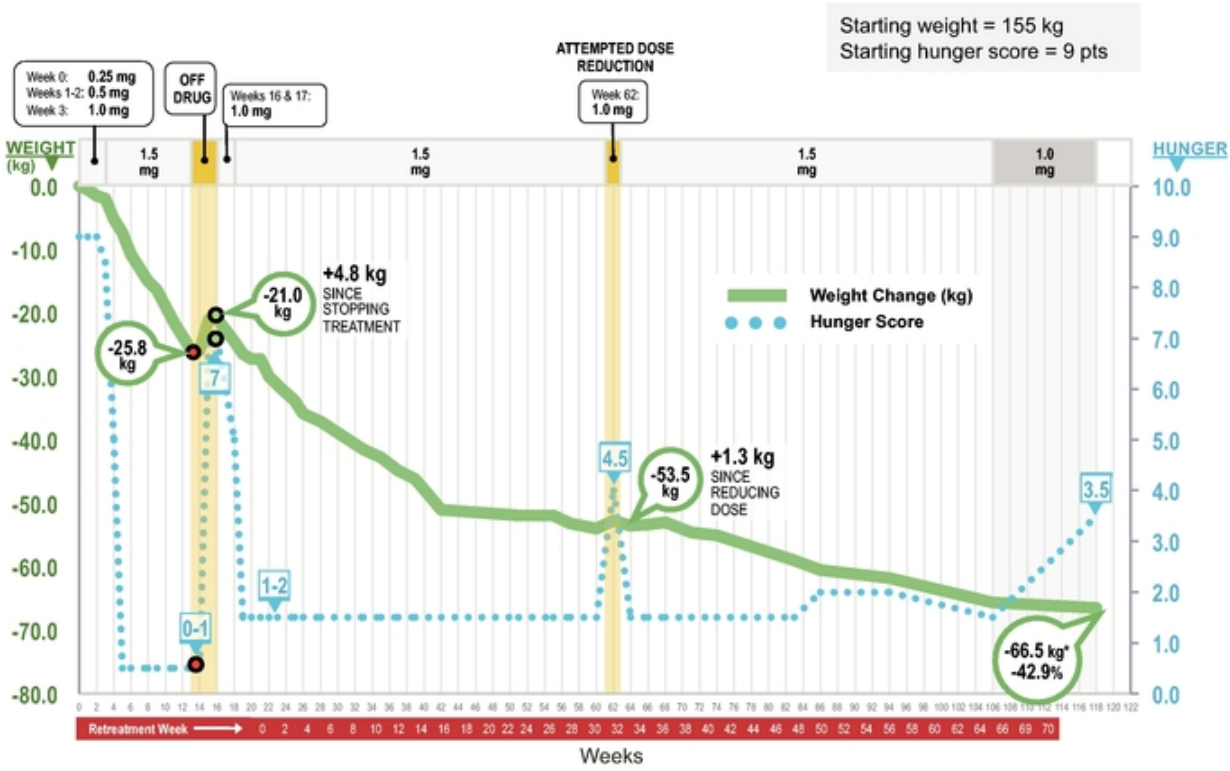
The first setmelanotide-treated patient was a 20-year old woman, who at three months of age experienced the onset of obesity and hyperphagia. In spite of enormous efforts, the patient was never able to stabilize her body weight, except for brief periods, and she has remained hyperphagic. Ahead of our trial, the patient's self-reported trial hunger score was eight to nine out of 10 points, representing extreme hunger. She was entered into the trial at adulthood because of her severe obesity, with a baseline weight of 155 kg, or 341.7 lbs., and a BMI of 49.8 kg/m^2, and significant risk of comorbidities and a reduced life expectancy.

The trial, initially a 13-week, open label, ascending dose Phase 2 trial, was approved by the German Federal Institute for Drugs and Medical Devices, with open-label one year extensions, and was planned to include approximately four to six patients with genetically confirmed POMC deficiency obesity. After efficacy-gated dose escalation, aiming for weekly weight loss of approximately two kg, or 4.4 lbs., the primary endpoint was weight loss, with other key endpoints including hunger score, body composition, insulin and glucose parameters, metabolic and cardiovascular risk factors, energy expenditure and general safety and tolerability.

After 13 weeks of therapy, with approximately the first four weeks at sub-therapeutic doses, our initial patient demonstrated weight loss of 25.8 kg, or 56.9 lbs., representing 16.7% of her initial body weight, with approximately two to three kilograms per week of weight loss demonstrated at the highest 1.5 mg/day dose. Hunger scores, measured using a Likert score of zero to 10, where zero represents no hunger and 10 represents extreme hunger, mirrored the rate of weight loss, moving from scores of eight to nine prior to our trial to zero to one, as the patient was treated with increasing doses of setmelanotide. After termination of the 13-week main trial, the patient underwent a three-week withdrawal period off drug and regained 4.8 kg, or 10.6 lbs., with a return to moderate to severe hunger. Following approval to restart setmelanotide treatment, there was an immediate reduction of hunger and subsequently a continuation of body weight loss. This patient was on continuous treatment for 106 weeks, with a total weight loss of 65.6 kg, or 144.6 lbs., representing 42.3% of her initial body weight. There was no apparent difference in the rate of weight loss during the initial extension phase versus the main trial, however over time, the rate of weight loss has slowed, though this patient has continued to lose weight. The patient's need for continued therapy was supported by a short period of withdrawal after the patient had been treated for over one year. Reducing her daily dose from 1.5 mg/day to 1.0 mg/day resulted in an increase in her hunger scores from one to two points to four to five points, resulting in the patient requesting to be returned to her 1.5 mg/day dose, after which her hunger scores returned to one to two points. This data supports the physiological prediction that pharmacological treatment for this condition to suppress hunger will be required chronically. After approximately 106 weeks of treatment, her dose was reduced to 1 mg/day, and while her weight remained stable from week 106 to week 118, her hunger scores increased to three to four points on the lower dose.

The results for this patient are shown in the figure below.

Initial Patient in the Setmelanotide POMC Deficiency Obesity Phase 2 Trial[(1)]



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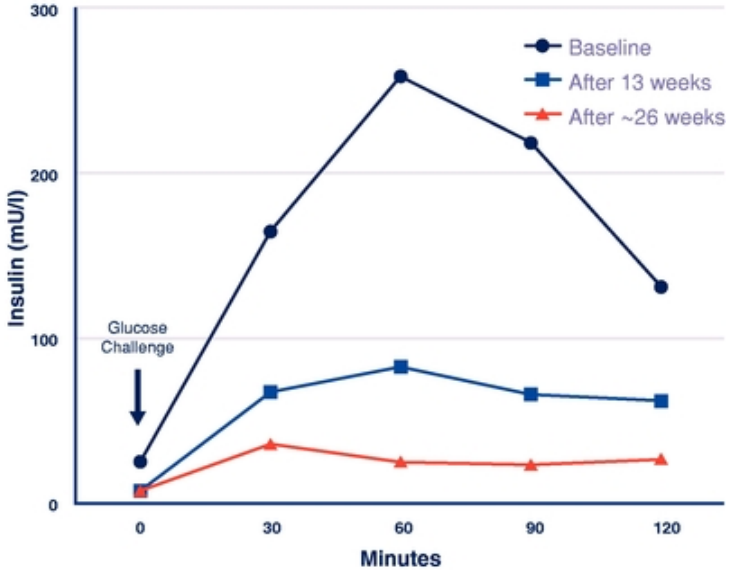
* Figures represent cumulative weight lost in kgs.

(1) Daily setmelanotide dose adjustments over time are indicated at the top of the panel.

In general, diet induced weight loss in patients with general obesity is accompanied by significant counter-regulatory effects, including reductions in energy expenditure and increases in hunger. These lead to weight regain in the majority of patients. In contrast, the initial patient in our trial did not manifest these counter-regulatory responses, even after six months of therapy and a tremendous reduction of body weight. This data supports an effect of setmelanotide on energy expenditure independent from the profound effects on hyperphagia, corroborating results from previous trials of setmelanotide in patients with general obesity. Also of note, the reduction in body weight was mainly due to a loss of body fat mass, and lean body mass was not greatly altered. In this initial patient, setmelanotide was also associated with excellent tolerability, additional favorable changes in cardiovascular risk parameters, or lipids, and improvements in blood pressure and heart rate.

MC4R activation also causes improvements in glucose and insulin parameters in animal models, independent of weight loss. As shown in the figure below, for the initial patient in our POMC deficiency proof of concept trial, setmelanotide demonstrated a marked improvement in insulin resistance during treatment. While weight loss likely played an important role in this improvement, we believe the independent effect of MC4R agonism may also have contributed.

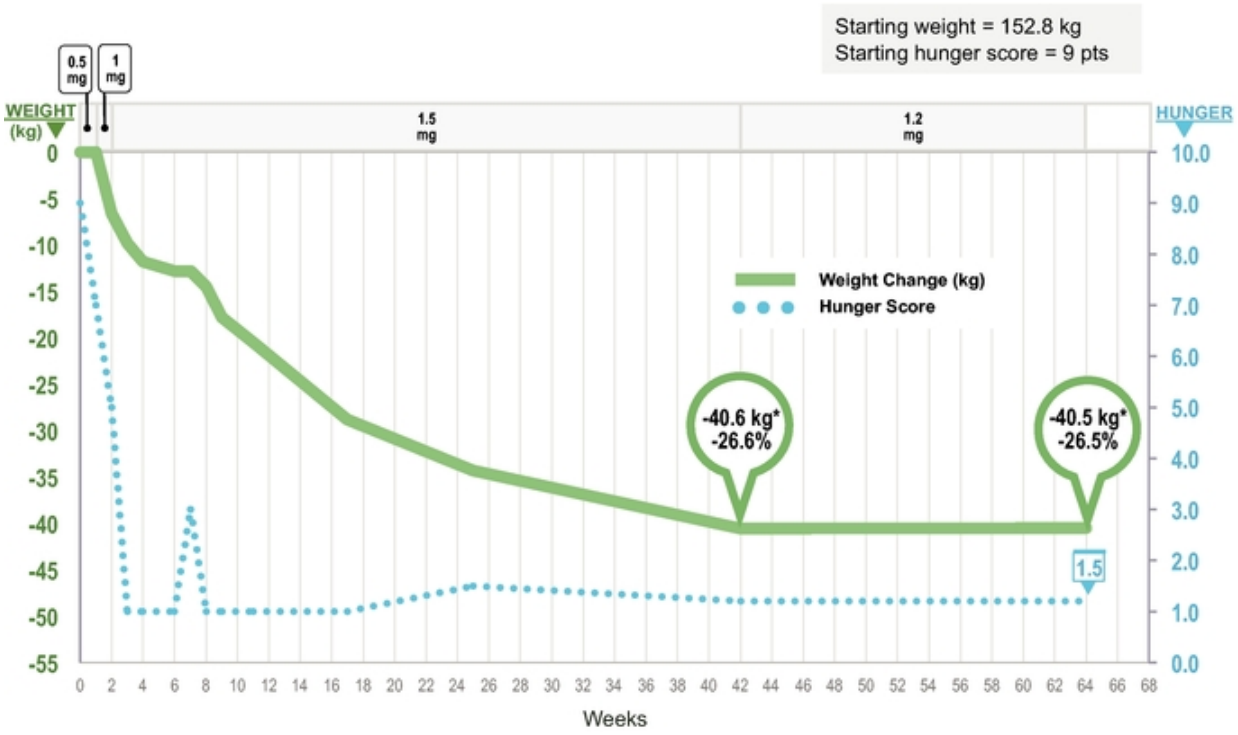
Setmelanotide Treatment Effects on Insulin Resistance (Insulin Response in Oral Glucose Tolerance Test) at Baseline, After 13 Weeks of Treatment (Phase 1), and at Approximately 26 Weeks During the Long-term Extension for our POMC Initial Patient



Results are also available for treatment with setmelanotide of a second patient with POMC deficiency obesity. The second patient is a 26-year old woman who also experienced early onset of obesity and hyperphagia. Like the first patient, in spite of significant efforts, she was never able to stabilize her body weight, and she has remained hyperphagic. Ahead of our trial, the patient's self-reported trial hunger score was nine out of 10 points, representing extreme hunger, and her weight and BMI at trial entry were 152.8 kg, or 336.9 lbs., and 54.1 kg/m^2, respectively.

After 42 weeks of therapy at the 1.5 mg/day dose, our second patient demonstrated weight loss of 40.6 kg, or 89.5 lbs., representing 26.6% of her initial body weight, with approximately two to three kilograms per week of weight loss demonstrated initially. Hunger scores, measured using a Likert score of zero to 10, where zero represents no hunger and 10 represents extreme hunger, mirrored the rate of weight loss, with scores moving from nine prior to the trial to one on most weeks during the trial, as the patient was treated with increasing doses of setmelanotide. Similar to the initial patient, setmelanotide demonstrated an improvement in insulin resistance during treatment in our second POMC deficiency obesity patient. This patient continues on active treatment, with a total of 62 weeks on therapy, although this patient is now on a reduced 1.2 mg/day dose, and her weight has stabilized at a weight loss of 40.5 kg, or 89.3 lbs.

Our Second Patient in the Setmelanotide POMC Deficiency Obesity Phase 2 Trial[(1)]



* Figures represent cumulative weight lost in kgs.

(1) Daily setmelanotide dose adjustments over time are indicated at the top of the panel.

Setmelanotide was generally well tolerated in the POMC deficiency obesity Phase 2 trial, with few adverse events, all mild and infrequent, and all previously reported in other clinical trials. These included reduced appetite and tanning of skin and nevi, or moles, intermittent and mild injection site reactions, and in rare instances tiredness, dry mouth, and gastrointestinal symptoms. The single serious adverse event was an influenza immunization reaction, which resulted in an overnight hospitalization and was considered unrelated to trial drug. A similar immunization reaction had occurred in this patient in a previous influenza immunization prior to treatment, and the patient has continued on setmelanotide since that event.

The results from the initial patients in our POMC deficiency obesity proof of concept trial are compelling, but these data have limitations due to open label treatment. However the strong treatment effect is supported by these patients' long histories of weight gain and hyperphagia prior to treatment, and a strong dose response in the dose escalation phase. More importantly, the biology of this disorder has been well studied, and the clinical responses in these patients were strongly predicted by the deep understanding of the role of the MC4 pathway in appetite and weight regulation. The interruption of treatment effectively allowed the first patient to serve as her own control, demonstrating an immediate and rapid increase in hunger and weight after a short-term treatment withdrawal, and a rapid response to re-treatment, thereby further demonstrating the strong effect of setmelanotide. The greater than two years of treatment of our first patient, and the greater than one year of treatment for our second patient also support the ability of setmelanotide to be effective for longer treatment periods. Finally, our data supports that this indication will require chronic treatment.

Most importantly, this initial proof of concept data provides support for the belief that setmelanotide will restore activity in patients with upstream defects in the MC4 pathway, by helping patients lose weight and reduce hyperphagia. This was confirmed in our second MC4 pathway rare genetic obesity, LepR deficiency obesity. Similarly, we would expect efficacy in other upstream MC4 pathway genetic disorders, many of which are under study in Phase 2 proof of concept trials.

Phase 3 Clinical Development in POMC Deficiency Obesity

After discussions with the FDA as part of our breakthrough therapy designation, we initiated our Phase 3 trial in POMC deficiency obesity in January 2017, Study RM-493-012. This is an open label, one-year trial, including a double-blind placebo-controlled withdrawal period, of setmelanotide in POMC deficiency obesity. This pivotal trial will assess long-term efficacy of setmelanotide given once daily by SC injection. The trial will begin with an initial period of dose titration lasting between two and 12 weeks where the individual patient's therapeutic dose will be established by upwards dose titration in two week intervals. Thereafter, patients will continue on active treatment at their individually titrated optimal therapeutic dose for an additional 10 weeks, for a total combined dosing duration of 12 weeks at the individual patient's therapeutic dose. Patients who demonstrate at least five kilograms weight loss at the end of the open label treatment period will continue onto the double-blind, variably-timed, placebo-controlled, withdrawal period lasting eight weeks inclusive of a four-week period of placebo treatment. Following the withdrawal period, all patients will complete an additional period of setmelanotide treatment to bring the total therapeutic dosing period to one year.

We plan to treat approximately 10 patients in this trial. We will initially enroll patients aged 12 years and older, but, subject to FDA approval, intend to amend the protocol to include patients aged six years and older before completion of the trial. The primary endpoint of the trial will be percent change in body weight over one year, with key secondary endpoints of safety and tolerability, hunger, change in body fat mass and glucose parameters, and the effect of withdrawal of setmelanotide in the double-blind, placebo controlled period. We have also obtained Scientific Advice for this protocol from the European Medicines Agency, or EMA, and the trial is currently enrolling in the United States, United Kingdom, and Germany, and has been approved in France.

We expect to complete enrollment by the end of 2017, and to report Phase 3 data in the first half of 2019.

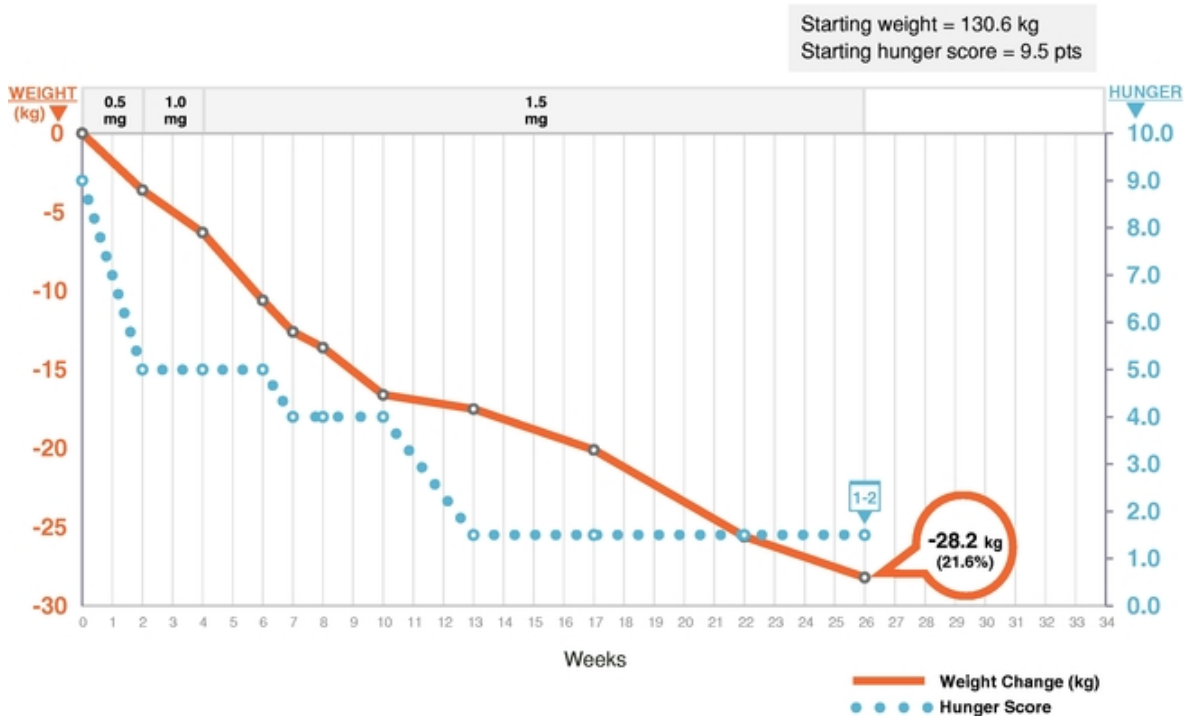
Phase 2 Clinical Development in LepR Deficiency Obesity

Leptin's role in obesity has been elucidated by characterization of severely obese people with homozygous mutations that impair the activity of leptin, including disruption of signaling at the LepR, known as LepR deficiency obesity. To study setmelanotide in this indication we initially amended our Phase 2 clinical trial in POMC deficiency obesity, Study RM-493-011, to also include this new and related genetically defined population of severely obese patients. We then completed this part of the Phase 2 proof of concept, open label clinical trial in patients with LepR deficiency obesity by treating three patients in this trial, who demonstrated weight loss and hunger reduction as outlined below.

Results from treatment with setmelanotide in these three LepR deficiency obesity patients are available. The first LepR deficiency obesity patient was a 21-year old male, who experienced early onset of obesity and hyperphagia. After little success in controlling his weight, he underwent, and failed, a gastric banding procedure, and had regained over 20 kg in the last year since his procedure. Ahead of our trial, the patient's self-reported trial hunger score was nine out of 10 points, representing extreme hunger, and his weight and BMI at trial entry were 130.6 kg, or 287.9 lbs., and 39.9 kg/m^2, respectively. After initiation and upwards dose titration over 13 weeks of setmelanotide treatment, the patient demonstrated prompt and striking reductions in appetite and body weight with a total loss of 17.5 kg body weight, representing 13.4% of his initial body weight. Hunger scores decreased from nine points at baseline to one to two points

at 13 weeks. With continued treatment, the patient lost 28.2 kg, or 62.2 lbs, representing 21.6% of his initial body weight, and continued with a hunger score of one to two for 26 weeks of total treatment. The weight loss was predominantly caused by a reduction in body fat and resting energy expenditure stayed stable during this period. This patient also had pre-trial insulin levels that were elevated as examined by an oral glucose tolerance test, as were glucose values, demonstrating insulin resistance. These values improved with setmelanotide treatment. Notably, there was also an improvement in the patient's lipid profile over 13 weeks of setmelanotide treatment. Setmelanotide was generally well tolerated in this LepR deficiency obesity trial.

Initial Patient in the Setmelanotide LepR Deficiency Obesity Phase 2 Trial[(1)]

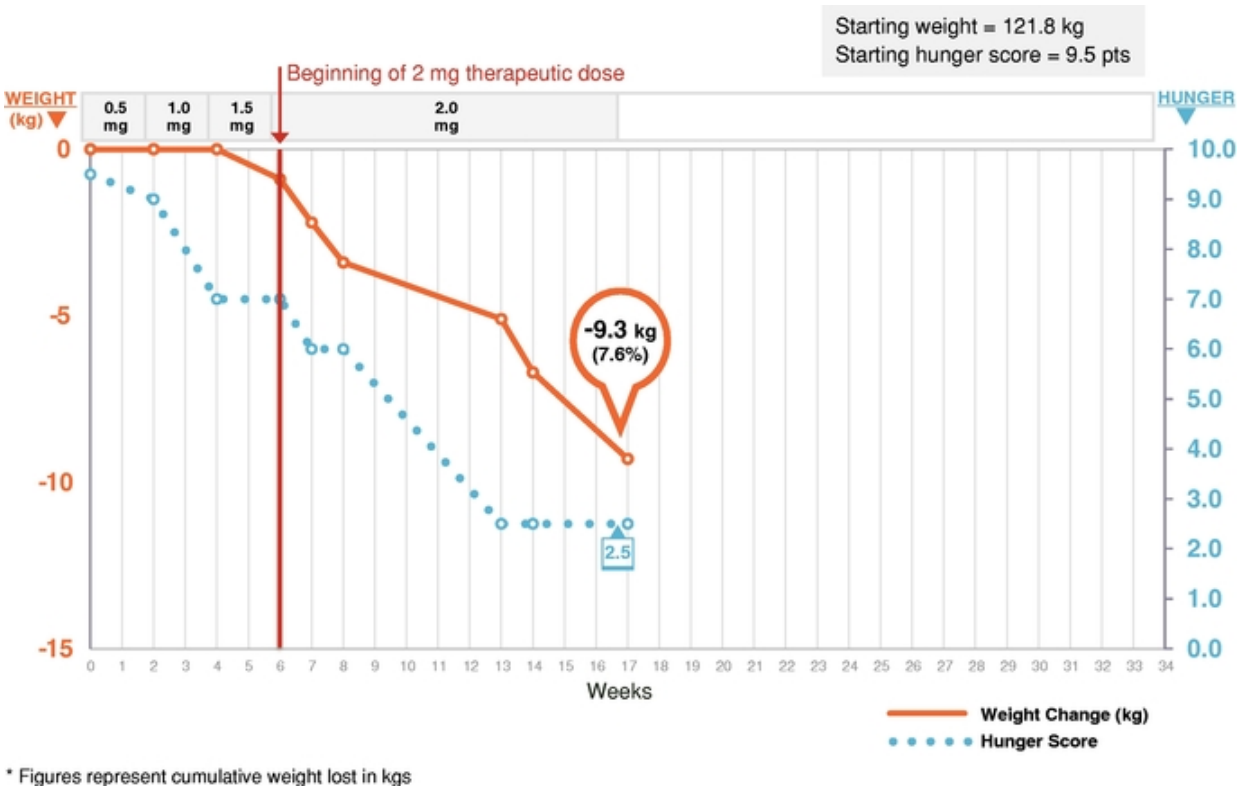


* Figures represent cumulative weight loss in kgs.

(1) Daily setmelanotide dose adjustments over time are indicated at the top of the panel.

The second LepR deficiency obesity patient is a 22-year old male who also experienced early onset of obesity and hyperphagia. His growth curve since infancy demonstrated early onset, severe obesity that had continued through his whole life, with little ability to control his weight gain. Ahead of our trial, the patient's self-reported trial hunger score was nine to 10 out of 10 points, and his weight and BMI at trial entry were 121.8 kg, or 265.8 lbs., and 40.6 kg/m^2, respectively. He was treated for 17 weeks with setmelanotide and his dose was escalated up to 1.5 mg once daily with only modest effects on weight and hunger scores. However, when he was advanced to 2 mg once daily, he demonstrated prompt and striking reductions in appetite and body weight. After 17 weeks, including 11 weeks on his therapeutic dose of 2 mg/day, he had lost 9.3 kg, or 20.5 lbs, representing 7.6% of his body weight, and his hunger score dropped to two to three points. This patient had few metabolic abnormalities at baseline, but he was hyperinsulinemic as examined by an oral glucose tolerance test. After 13 weeks of treatment, the hyperinsulinemia started to improve and the blood glucose levels during the oral glucose tolerance test normalized.

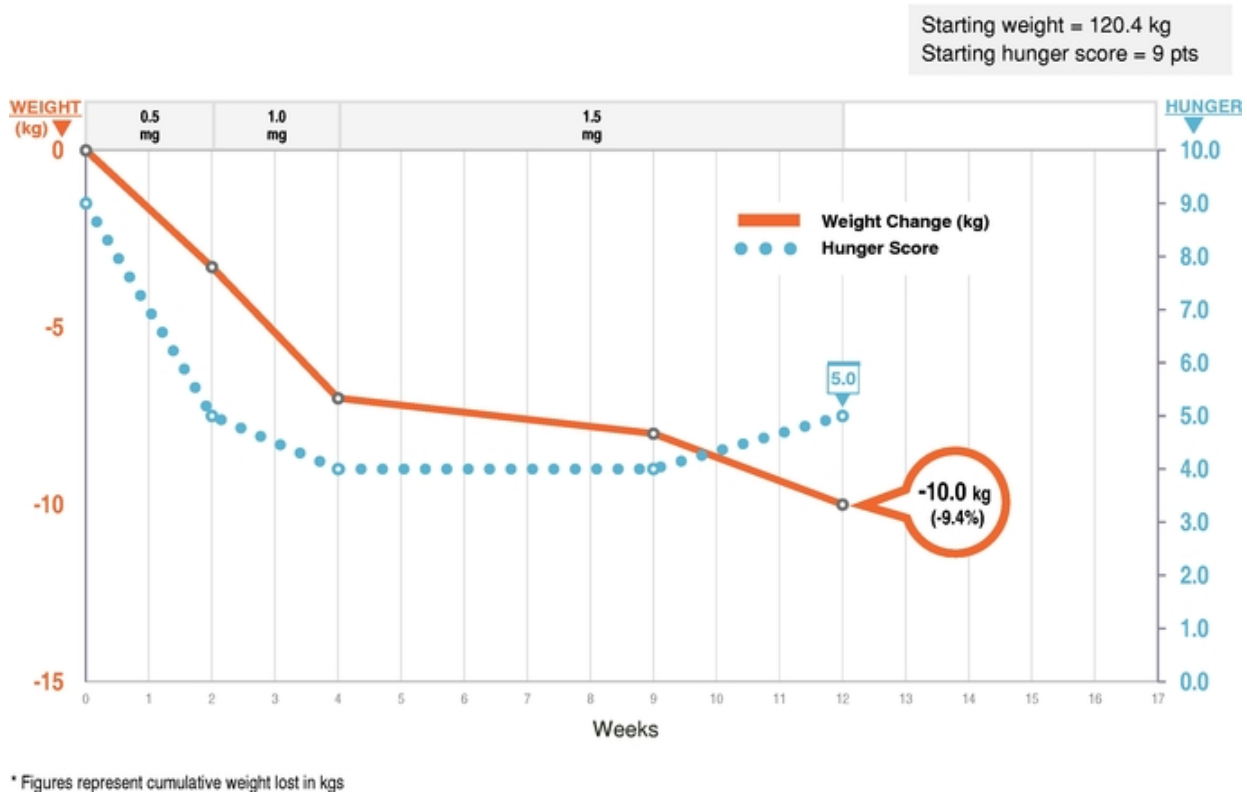
Our Second Patient in the Setmelanotide LepR Deficiency Obesity Phase 2 Trial[(1)]



(1) Daily setmelanotide dose adjustments over time are indicated at the top of the panel.

The third LepR deficiency obesity patient is a 14-year old female adolescent, and the first adolescent patient treated with setmelanotide. Her growth curve since infancy demonstrated early onset, severe obesity her whole life, with little ability to control her weight gain. Ahead of our trial, the patient's self-reported trial hunger score was nine out of 10 points, and her weight and BMI at trial entry were 120.4 kg, or 265.4 lbs., and 44.2 kg/m^2, respectively. She has now been treated with setmelanotide for 12 weeks, and showed initial prompt and striking reductions in appetite and body weight. On the 0.5 mg and 1 mg dose titration steps, she lost 10 kg, or 22 lbs, representing 6.9% of her body weight, over four weeks. She was advanced to 1.5 mg/once daily, and at 13 weeks her weight loss was 9.3 kg, or 22.0 lbs, representing 9.4% of her body weight, though her hunger score had only dropped to five points.

Our Third Patient in the Setmelanotide LepR Deficiency Obesity Phase 2 Trial[(1)]



(1) Daily setmelanotide dose adjustments over time are indicated at the top of the panel.

This trial provides the second proof of concept for the effectiveness of setmelanotide in patients with upstream defects in the MC4 pathway, showing marked weight reduction and decreases in hunger in patients with LepR deficiency obesity. Based on this proof of concept for the compelling efficacy of setmelanotide in this disorder, we have transitioned the LepR development program to Phase 3.

Phase 3 Clinical Development in LepR Deficiency Obesity

Our LepR deficiency obesity development program is now in Phase 3. We expect to enroll our first patient in our LepR deficiency obesity Phase 3 clinical trial in the second half of 2017, and to complete enrollment in 2018. This is an open label, one-year trial, including a double-blind placebo-controlled withdrawal period, of setmelanotide in LepR deficiency obesity. This pivotal trial will assess long-term efficacy of setmelanotide given once daily by SC injection in LepR deficiency obesity, and is planned to be very similar to the Phase 3 ongoing trial in POMC deficiency obesity. The trial will begin with an initial period of dose titration lasting between two and 12 weeks where the individual patient's therapeutic dose will be established by upwards dose titration in two week intervals. Thereafter, patients will continue on active treatment at their individually titrated optimal therapeutic dose for an additional 10 weeks, for a total combined dosing duration of 12 weeks at the individual patient's therapeutic dose. Patients who demonstrate at least five kilograms weight loss at the end of the open label treatment period will continue onto the double-blind, variably-timed, placebo-controlled, withdrawal period. Following the withdrawal period, all patients will complete an additional period of setmelanotide treatment to bring the total therapeutic dosing period to one year.

We plan to treat approximately 10 patients in this trial, aged 12 years and older, and subject to FDA approval, we intend to amend the protocol to include patients aged six years and older before completion of the trial. The primary endpoint of the trial will be percent change in body weight over one year, with key secondary endpoints of safety and tolerability, hunger, change in body fat mass and glucose parameters, and the effect of withdrawal of setmelanotide in the double-blind, placebo controlled period. We have submitted this trial to the FDA, and will also conduct the trial in the United Kingdom, France and Germany.

Based on the FDA awarding breakthrough therapy designation for the treatment of obesity associated with genetic defects upstream of the MC4 receptor in the leptin-melanocortin pathway, which includes the LepR deficiency obesity indication, we believe we can seek indications for this type of obesity with a faster path to approval, as compared to typical obesity drug candidates, because of the high unmet need and rare prevalence of this disorder.

Phase 2 Clinical Development in Bardet-Bield Syndrome

Bardet-Biedl syndrome is a life-threatening, orphan disease with prevalence of approximately one in 100,000 in North America. We estimate that the addressable patient population for Bardet-Biedl syndrome is approximately 1,500 to 2,500 patients in the United States. It is a rare monogenic disorder that causes severe obesity and hyperphagia as well as vision loss, polydactyly, kidney abnormalities, and other signs and symptoms. Bardet-Biedl syndrome is part of a class of disorders called ciliopathies, or disorders associated with the impairment of cilia function in cells. Cilia are hair-like cellular projections that play a fundamental role in the regulation of several biological processes, including satiety signaling. Cilia dysfunction is thought to contribute to hyperphagia and obesity in Bardet-Biedl syndrome. Bardet-Biedl syndrome is a genetically heterogeneous disease that is caused by as many as 21 separate Bardet-Biedl loci defects resulting in a similar syndrome, though each Bardet-Biedl syndrome patient only has one of these defects.

The role of abnormal cilia development and function in obesity has been elucidated in animal models, most strongly for Bardet-Biedl. Studies in mouse models of Bardet-Biedl syndrome show that deficiencies in the MC4 pathway contribute to the obesity and hyperphagia in Bardet-Biedl syndrome, with animals developing hyperphagic tendencies early in life. Notably, these mice have decreased leptin receptor signaling, with the essential hallmarks of failure to activate POMC neurons. This is supported in Bardet-Biedl syndrome rodent models, where the mice respond to an MC4 agonist resulting in reduced food intake and body weight. The relation of Bardet-Biedl syndrome gene mutations to the MC4 pathway is supported by clinical data. Patients with Bardet-Biedl syndrome have higher leptin than expected for their degree of adiposity, or leptin resistance, which is consistent with the notion that ciliopathy-induced leptin signaling dysfunction is associated with leptin resistance.

Overall, these data support that the phenotypes of these ciliopathies, while complex with additional clinically important features along with obesity and hyperphagia, may be responsive to setmelanotide treatment, and will be investigated in our proof of concept Phase 2 trial.

We are studying Bardet-Biedl syndrome patients who are severely obese, or whose BMI is equal to or greater than 40kg/m^2, to provide proof of concept that Bardet-Biedl syndrome patients will also demonstrate decreased hunger and significant weight loss, similar to that seen in patients with POMC deficiency obesity, or LepR deficiency obesity. We have enrolled the first five patients in this trial, and plan to enroll additional patients for this indication in the second half of 2017 at sites in the United States and possibly Europe. We anticipate reporting preliminary results for Bardet-Biedl syndrome in the fourth quarter of 2017, and to initiate Phase 3 clinical trials in 2018.

For this trial, additional assessments of hunger using daily hunger scores and questionnaires were also obtained. We plan to use these new assessments in our ongoing Phase 2 and Phase 3 trials and for future trails. These new assessments are as follows:

- Daily Hunger Scores. In addition to our morning assessment of hunger, as performed in the Phase 2 trials in POMC deficiency obesity and LepR deficiency obesity, we are also obtaining a daily hunger

score rating in response to the question: "In the last 24 hours, how hungry did you feel when you were the *most* hungry?" Patients are asked to give a response that is measured on a scale of 0-10, whereby 0 points signifies "not hungry at all" and 10 points indicates the patient feels his or her "hungriest possible."

- Questionnaires. For patients 16 years of age and younger, we are using two observer related questionnaires as exploratory endpoints. These questionnaires are completed by the patient's parent or other caregiver.

  - The Food Problem Diary, or FPD, is based on food-related behaviors. This questionnaire was adapted from a similar questionnaire that was used with patients with Prader-Willi syndrome. The questionnaire is rated on a 30-point scale where 30 points is strong evidence of hyperphagia and 0 points is evidence of no hyperphagia. The best possible response therefore is 0 points.

  - The Significant Event Questionnaire, or SEQ, counts events not typically seen in this population, such as a patient leaving food on his or her plate at a meal. This questionnaire consists of eight "yes" or "no" questions. The best possible response is 8 points, since this questionnaire tracks events and behavior not typically seen in patients with MC4 pathway disorders. In contrast with other score scales, a higher score in this hunger assessment category represents improvement, and thus, the results are plotted in reverse scale and downward trends indicate improvement.

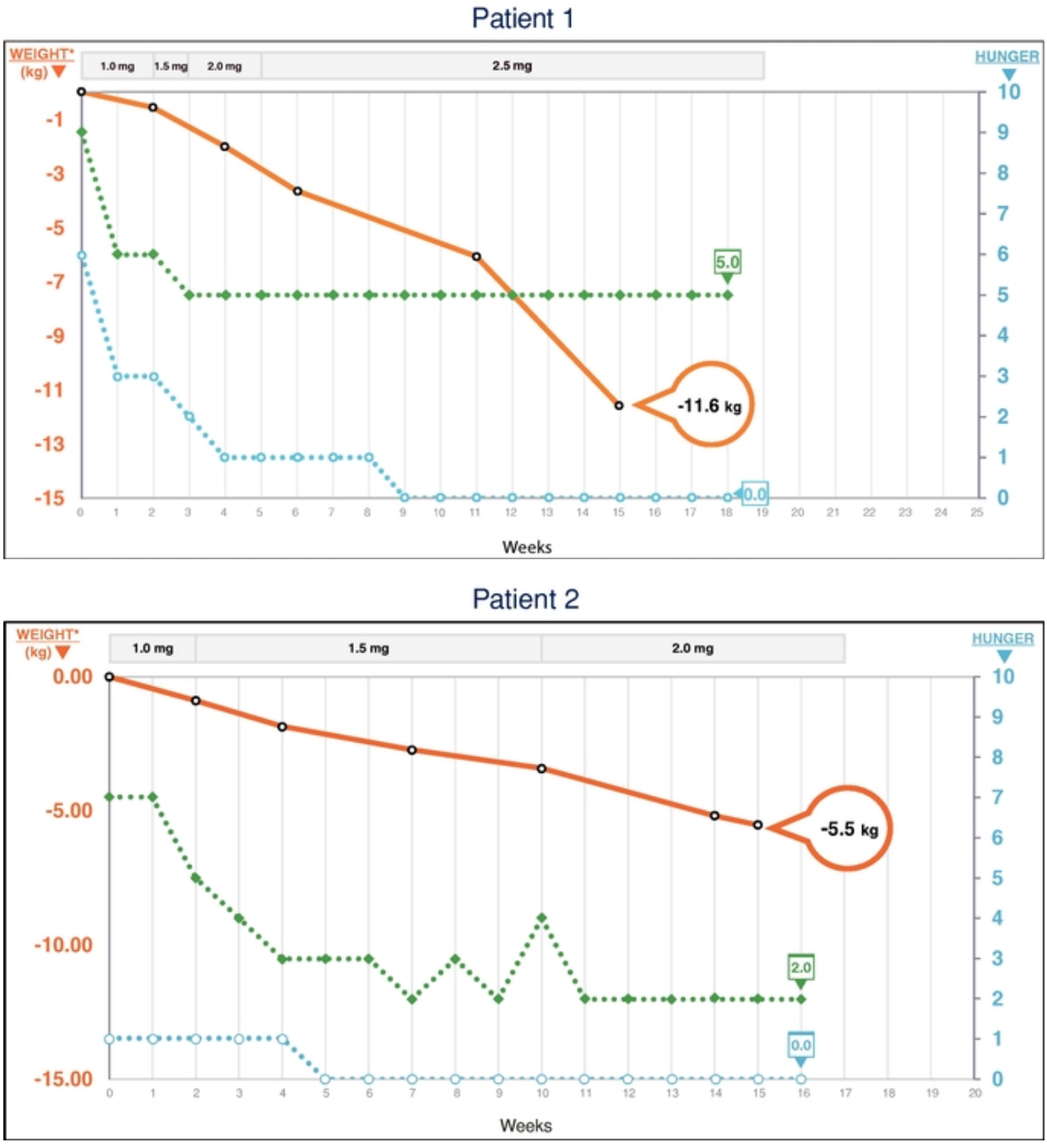
We believe that proof of concept in Bardet-Biedl syndrome has been demonstrated by improvements in hunger and weight reduction, supporting that this is a setmelanotide-responsive, MC4 pathway disorder. Four different Bardet-Biedl genotypes were studied in this trial. The age of the patients ranged from 12 to 61 years of age. The starting weights of the patients ranged from 98.3 to 147.5 kg and BMI ranged from 42 to 49. The starting hunger scores for the adult patients ranged from 6 to 9 points on the 10-point scale, with higher scores indicating more hunger and the SEQ scores for the two adolescent patients were both 1.

Description of the Five Bardet-Biedl patients in the Phase 2 Proof of Concept study

Patient Number	Age (yrs)	Bardet-Biedl Type	Starting Weight (kg)	Starting BMI	Starting Hunger Score
1	25	1	147.5	44	Most hungry score = 9
2	61	2	99.4	44.2	Most hungry score = 7
3	16	10	121.6	44	FPD = 6/ SEQ = 1
4	17	12	98.3	42	Most hungry score = 6
5	12	1	119.3	49	FDP = 15/SEQ = 1

The Bardet-Biedl syndrome patients were treated with setmelanotide for a range of six to 18 weeks. Within that period, five to 14 weeks represented time spent in the dose titration period designed to define an individualized therapeutic dose. Two of the five patients remain in the titration phase. Four of the five patients showed early, but significant weight loss of 11.6, 5.5, 9.7 and 6.6 kg lost or 25.6, 12.1, 21.4, and 14.6 lbs. All five patients showed clear improvements in every hunger assessment. The outlier patient, patient #5 had marked improvements in hunger assessments. This patient's FPD improved from a baseline of 15 points to 7 points, and her SEQ improved from a baseline of 1 point to the maximum value of 8 points. The fifth patient did not show any reduction in weight, but rather presented a gain of 2.2 kg, or 4.9 lbs. over 18 weeks. This patient was a 12-year old with Type 1 diabetes who entered the trial with extremely poor glucose control (HbA1c, or an average blood sugar level, of = 10.1%). We are investigating the reason for the disconnect between her improvement in hunger and lack of weight loss, but it was noteworthy that during treatment her diabetes was better controlled, and her HbA1c showed a large improvement to 7.6%. Setmelanotide was generally well tolerated in the Bardet-Biedl syndrome Phase 2 proof of concept study.

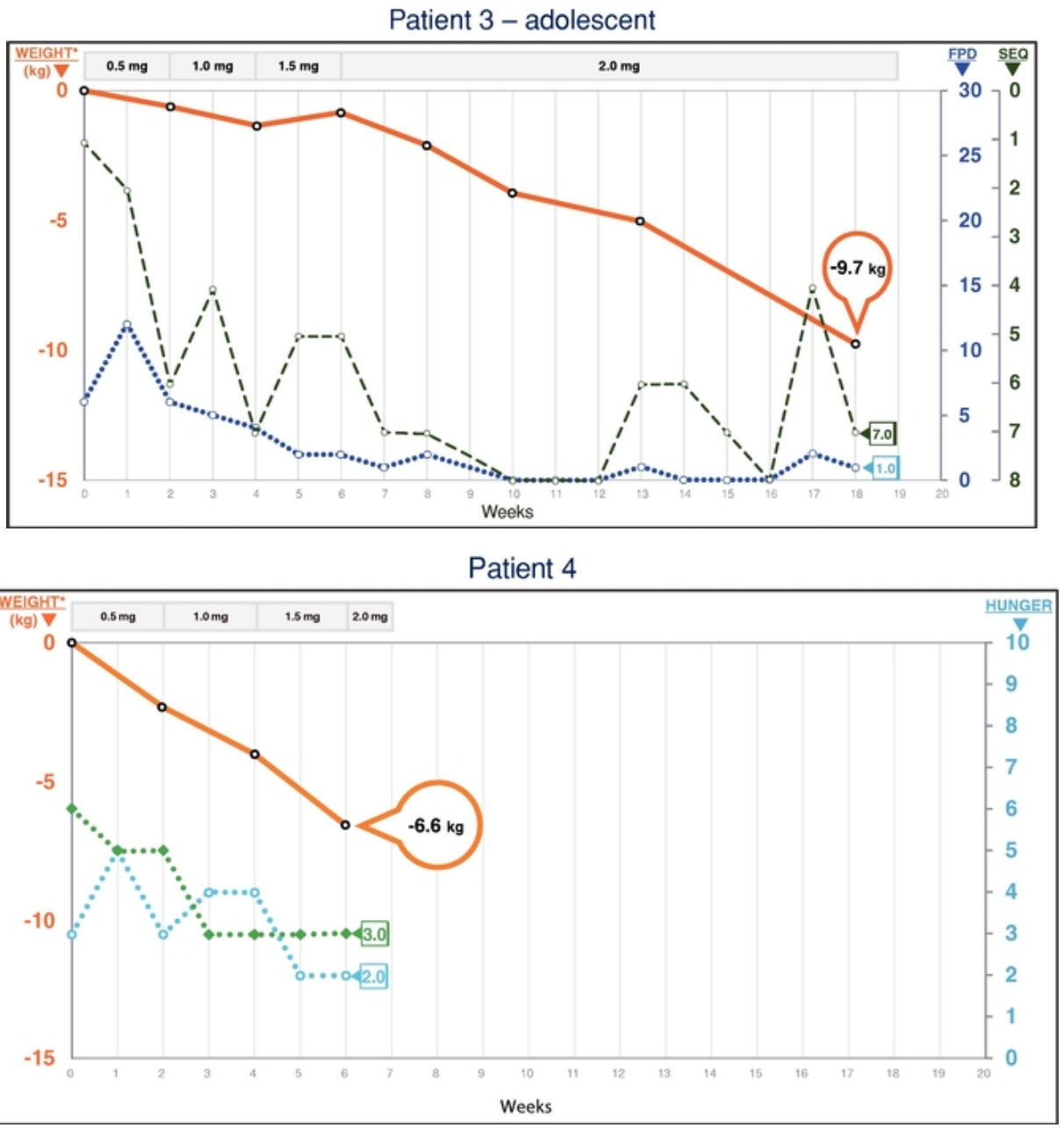
Our Four Patients in the Setmelanotide Bardet-Biedl Syndrome Phase 2 Trial who showed improvements in both weight and hunger[(1)(2)]



(1) Daily setmelanotide dose adjustments over time are indicated at the top of the panel.

(2) In some cases, dates for entry of weight and hunger assessment data may differ within a single patient.

Our Four Patients in the Setmelanotide Bardet-Biedl Syndrome Phase 2 Trial who showed improvements in both weight and hunger[(1)(2)]



(1) Daily setmelanotide dose adjustments over time are indicated at the top of the panel.

(2) In some cases, dates for entry of weight and hunger assessment data may differ within a single patient.

Phase 2 Proof of Concept Studies Focused on Patients with Monogenic Disorders of the MC4 Pathway: Alström syndrome, Heterozygous Mutations in the MC4 Pathway, and Epigenetic Disorders of the MC4 Pathway

We are conducting Phase 2, proof of concept trials in a variety of monogenic, upstream disorders of the MC4 pathway, including Alström syndrome, POMC heterozygous mutations in the MC4 pathway, and epigenetic disorders of the MC4 pathway. These trials are Phase 2 open label, single arm, proof of concept trials assessing the effect of setmelanotide on the rare genetic disorders of obesity described below. We hypothesize that all of these disorders may be genetically-defined deficiencies upstream in the MC4 pathway. Each trial includes a three month proof of concept phase at which weight loss, hunger and other metabolic parameters will be evaluated. If patients demonstrate significant weight loss and acceptable safety and tolerability, they will continue in one-year extensions for evaluation of setmelanotide's effects at one year and onwards of total therapeutic dosing. Similar to our previous trials, this trial will begin with an initial period of dose titration where the individual patient's therapeutic dose will be established by upwards dose titration in two week intervals. We plan to enroll approximately five patients for each of these rare genetic populations. We will conduct these trials, as well as the ongoing Bardet-Biedl sydrome trial described above, under basket protocols, which are designed to capture a broad range of patient populations to be treated under one investigational protocol. We believe this approach is efficient for studying many potential indications, and we intend to add additional populations to these basket protocols over the next one to two years.

The genetic disorders we are studying in our additional Phase 2 proof of concept trials are outlined below.

a. Clinical Development in Alström Syndrome Obesity

Alström syndrome is a life-threatening, ultra-rare orphan disease with a prevalence of approximately one in 1,000,000 in North America and we estimate that the addressable patient population for Alström syndrome obesity is approximately 500 to 1,000 patients worldwide. Alström syndrome shares many clinical features with Bardet-Biedl syndrome, including obesity and hyperphagia, and is also characterized by progressive vision loss, deafness, congestive heart failure, hyperinsulinemia and type 2 diabetes mellitus. Similarly, Alström syndrome is a ciliopathy caused by mutations in the ALMS1 gene, which has also been shown to be important for cilia function. Like Bardet-Biedl syndrome, recent scientific studies identify genetic deficiencies affecting the MC4 signaling pathway as a potential cause of the obesity and hyperphagia associated with Alström syndrome. Studies in a mouse model of Alström syndrome show a reduction in the number of cilia in specific neurons in the hypothalamus that are critical for MC4 pathway signaling. While Alström syndrome is less well studied than Bardet-Biedl syndrome, the similar pathophysiology of cilial dysfunction and clinical presentation support that deficiencies in the MC4 pathway are implicated in the obesity and hyperphagia observed in Alström syndrome. Therefore, we hypothesize that setmelanotide treatment can be applied to treat Alström syndrome.

We will enroll Alström syndrome patients who are severely obese, or whose BMI is equal to or greater than 40kg/m^2, to provide proof of concept that Alström syndrome patients will also demonstrate decreased hunger and significant weight loss, similar to that seen in patients with POMC deficiency obesity, or LepR deficiency obesity. We plan to enroll our first patients for this indication in the second half of 2017 at sites in the United States and Europe, and to complete enrollment in 2018. We expect to report preliminary results in the first half of 2018.

b. Clinical Development in MC4 Pathway Heterozygous Deficiency Obesity

MC4 pathway heterozygous deficiency obesity is caused by the loss of one of the two genetic copies of either the genes for POMC, PCSK, or LepR. Animal models support that such heterozygous deficiency in the critical leptin-melanocortin pathway can result in a strong predisposition to severe

obesity. The effect of genetic heterozygous deficiency obesity was first demonstrated for another gene in the MC4 pathway: MC4R heterozygous deficiency obesity. Later data also supported that POMC heterozygous deficiency obesity also results in a strong predisposition to obesity, though the epidemiology and clinical characterization of these patients is less well known. An estimated 2% of severe, early onset obesity patients have POMC heterozygous deficiency obesity, which is much more common than the ultra-rare POMC deficiency obesity in which both copies of either the POMC or PCSK genes are impaired. Our initial clinical focus will be on the most severely obese MC4 pathway heterozygous patients to test the hypothesis that severely obese heterozygous POMC patients might also respond substantially to setmelanotide treatment.

We will study patients who are severely obese, or whose BMI is equal to or greater than 40kg/m^2, and who are heterozygous deficient for POMC. These patients have a heterozygous genetic mutation of the POMC or PCSK gene resulting in full or partial loss of MC4 pathway signaling to the downstream MC4R. The purpose of studying these patients in this trial is to provide proof of concept that severely impaired MC4 pathway heterozygous deficiency obesity patients will also demonstrate significant weight loss, similar to though possibly of less magnitude, as that seen in patients with POMC deficiency obesity or LepR deficiency obesity. We plan to enroll our first patients for this indication in the second half of 2017 at sites in the United States and Europe, and to complete enrollment in 2018. We expect to report preliminary results in the first half of 2018.

Of particular interest to us are mutations to the section of the POMC gene that is translated into the protein, beta-melanocyte stimulating hormone (b-MSH). These mutations have been implicated in human and canine obesity. In 2002, researchers identified one specific heterozygote mutation of b-MSH, called the R236G mutation, in two children with extreme childhood obesity. This R236G mutation results in an abnormal b-MSH protein with a markedly reduced ability to activate the MC4R itself, and may also prevent other natural MC4R ligands from activating the MC4R. These combined effects may result in more significant obesity than other heterozygous mutations. The overall prevalence of this mutation is rare, 0.7% of the obese population is estimated to carry this mutation, but our genotyping study of 560 patients with early onset, childhood obesity has identified five heterozygote patients with the R236G mutation, all with severe obesity. Because, in both our genotyping study and in the scientific literature, this mutation is associated with severe obesity and has a relatively-high observed prevalence, this mutation will be a focus when enrolling our Phase 2 trial in POMC heterozygous obesity.

We also plan to study patients who are heterozygous deficient for LepR deficiency obesity in the near future, though we have not yet initiated study in this population. Less is known about the epidemiology and clinical impact of LepR heterozygous deficiency obesity. In addition, we have hypothesized that patients who are composite heterozygous, or who have heterozygosity in two of the genes of the MC4 pathway, both POMC and LepR, and who therefore might have some impairment at more than one location in the MC4 pathway, might also be responsive to setmelanotide. We plan to begin studying these composite heterozygous patients at a future date.

c. Clinical Development in Patients with Epigenetic Changes at the POMC receptor

In our proof of concept Phase 2 trials, we also plan to study patients suffering from obesity due to a partial lack of MSH due to an epigenetic POMC variant. Epigenetics changes are DNA modifications that can change gene expression without altering the DNA sequence itself. The most stable epigenetic modification is called DNA methylation. Recently, our academic collaborators in Berlin have described a POMC hypermethylation variant, which correlates with increased body weight in children and adults. Therefore, the presence of the POMC genetic/epigenetic variant leads to an increased risk for obesity based on reduced POMC gene activity. We expect that these patients under express the POMC gene product and as a result have a partial MSH deficiency.

There is convincing evidence that such epigenetic variants are potentially major factors for an increased individual risk to develop obesity later in life, and we hypothesize that the most obese patients in their populations may benefit from treatment with setmelanotide. However, epigenetic variation is likely not the only reason for the development of obesity in this patient group, because these variants are also observed in normal weight individuals, although to a lesser extent. At this point, no epidemiology data is available to estimate the size of the POMC epigenetic deficiency obese population.

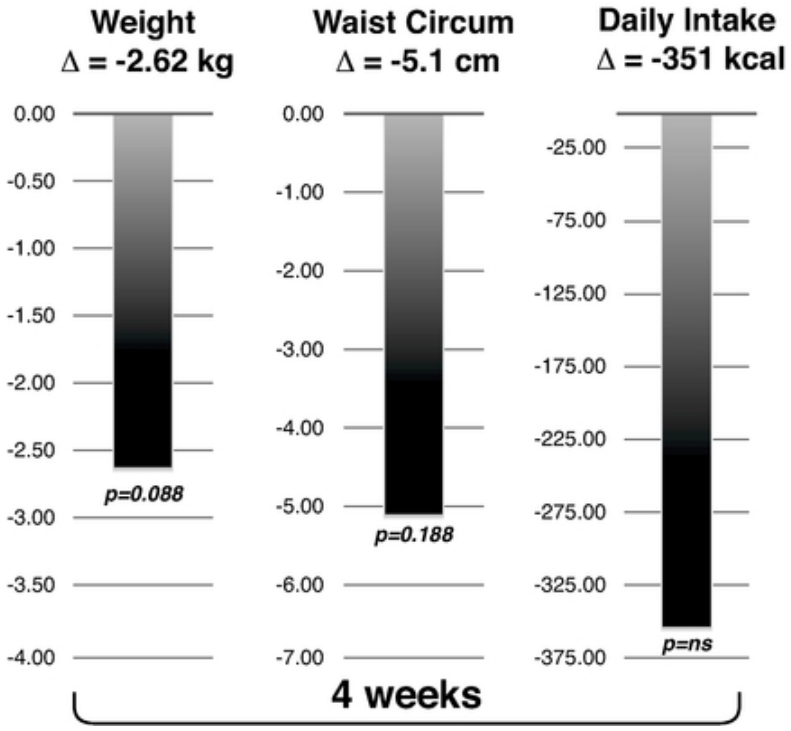
We will study patients who are severely obese, or whose BMI is equal to or greater than 40kg/m^2, and who have hypermethylation at the POMC gene. The purpose of studying these patients in this trial is to provide proof of concept that severely impaired, epigenetic POMC variant obesity patients will also demonstrate significant weight loss similar to, though possibly of less magnitude, as that seen in patients with POMC deficiency obesity or LepR deficiency obesity. We plan to enroll our first patients for this indication in the second half of 2017 at sites in the United States and Europe, and to complete enrollment in 2018. We expect to report preliminary results in the first half of 2018.

Phase 1b Clinical Development in Patients with Heterozygous MC4R Gene Mutations

Early studies in downstream MC4 pathway defects demonstrated good efficacy and tolerability, and served as a foundation for potentially greater efficacy in upstream MC4 pathway deficiencies. We established proof of concept for efficacy of setmelanotide in patients with an MC4R heterozygous genetic mutation in one cohort of patients in our Phase 1b clinical trial. This clinical trial was a double-blind, placebo-controlled, randomized Phase 1b clinical trial designed to evaluate the effect of setmelanotide on weight loss and safety in obese patients with a heterozygous mutation of the MC4R gene. The initial cohort of eight patients was treated for four weeks with setmelanotide or placebo. The setmelanotide group showed weight loss of 3.48 kg, or 7.67 lbs., approximately 2.62 kg, or 5.78 lbs., more weight loss than the placebo group, which showed weight loss of 0.85 kg, or 1.87 lbs. Other parameters supporting weight loss were also positively impacted by setmelanotide. We believe that these results support the hypothesis that setmelanotide can be effective in weight loss in MC4R deficient patients, and provide evidence of the minimum expected treatment effect of setmelanotide, approximately 0.9 kg/week, or 1.98 lbs./week, of weight loss over four weeks, even in a situation where setmelanotide's action is on a downstream MC4 pathway that is no longer fully functional due to heterozygous MC4R mutations. However, our focus is on upstream disorders of the MC4 pathway where we hypothesize that setmelanotide can serve as replacement therapy and provide more compelling efficacy.

The following figure depicts preliminary data relating to our setmelanotide Phase 1b clinical trial in MC4 heterozygous deficiency obesity patients:

Setmelanotide Phase 1b Trial MC4 Heterozygous Patients: Placebo Subtracted Differences[(1)(2)]



(1) Over four weeks of treatment with setmelanotide 0.01 mg/kg/day by continuous SC infusion.

(2) Preliminary data.

In general, we consider a p-value of 0.05 to be significant. P-values are an indication of statistical significance reflecting the probability of an observation occurring due to chance alone. However, it is not possible to determine a p-value for very small sample sizes, such as one- or two-patient trials.

Other Clinical Initiatives in Genetic Obesity

Genotyping Study

Leveraging new understanding of severe obesity caused by specific genetic defects has the potential to improve both diagnosis and treatment for specific types of life-threatening obesity. Therefore, we are sponsoring the Genetic Obesity Project, which is dedicated to improving the understanding of severe obesity that is caused by specific genetic defects—particularly rare genetic disorders that result in life-threatening obesity. As part of that initiative, we have initiated a genotyping study—the Genetic Obesity ID -- Genotyping Study—in which eligible patients are genotyped for rare genetic disorders of obesity. The goal is to develop a screening algorithm for selecting patients to be genotyped and diagnosed with POMC deficiency obesity and LepR deficiency obesity, and to guide further genotyping efforts; in addition, it is our expectation that patients who can participate in our clinical trials will be genetically identified. We are currently including other MC4 pathway deficiencies in the study. Key entry criteria for the study include a history of severe, early onset obesity, along with hyperphagia and are consistent with the recently published Pediatric Obesity guidelines published by the Endocrine Society. Study investigators, who are academic experts in childhood obesity, are located in both the United States and Europe. We plan to work with these investigators to publish the results of this study and guidance on the

use of the algorithm for screening, to enable more systematic diagnoses of these rare genetic disorders of obesity. Our preliminary results in 560 genotyped patients, described below, suggest we can successfully identify these patients using our algorithms. We intend to validate these early results in larger numbers of patients, but we believe these results provide preliminary support for our genotyping approach.

Number of Patients	Percent	Genetic Defect
2	0.36%	POMC deficiency obesity (PCSK1)
3	0.54%	LepR deficiency obesity
59	10.5%	Heterozygous deficiency
5	0.89%	R236G Heterozygous deficiency

Genetic Epidemiology Studies

We have estimated the patient population for our rare genetic disorders of obesity primarily by identifying patients or by estimating from clinical epidemiology information. Another method to estimate the size of these ultra-rare populations is by genetic epidemiology—using newly available large genomic databases, both full genome sequencing or exome sequencing, that are now becoming available. We have begun some substantial efforts with a series of such databases and/or collaborators and much of our preliminary work has been with a database of approximately 140,000 genomes, representative of the U.S. population.

While results from this effort are preliminary, they have been very supportive of our clinical epidemiological estimates, even when using conservative assumptions. They support that estimates of the number of patients in the United States who are homozygous deficient in the POMC gene, which is one of the genetic defects causing POMC deficiency obesity, and who are homozygous deficient in the LepR gene are at least as large as our assumptions provided above, if not larger. In addition, the estimates of patients who are homozygous deficient in the PCSK1 gene, which is the other genetic defect causing POMC deficiency obesity, may be substantially larger than our estimates, at more than 1,000 patients in the United States. We have already begun to expand this work into other genomic databases that contain patients with different demographics, and are actively working with a series of academic and industry collaborators. The ongoing expansion of genomic data available in other forums also has the effect of supporting this effort. An important improvement in this effort will be working with data linked to phenotypic information to better characterize the genetic information we are analyzing. However, until these data are confirmed in additional genetic epidemiology databases, we must continue to base our patient population estimates on clinical epidemiological information.

Setmelanotide: Clinical Development Program in Prader-Willi Syndrome

PWS is a life threatening, orphan multigenic disease with prevalence estimates ranging from approximately one in 8,000 to one in 52,000, with at least 8,000 diagnosed patients in the United States. A hallmark of PWS is hyperphagia, leading to severe obesity and other complications. For PWS patients, hyperphagia and obesity are the greatest threats to their health, and these patients are likely to die prematurely as a result of choking, stomach rupture, or from complications caused by morbid obesity.

The genetics of PWS are complex, involving many genes on chromosome 15 that are not properly expressed. Recent discoveries highlight that a defect in one of these, the melanoma antigen family L2, or MAGEL2, gene, in rodent models impairs the function of POMC neurons, which are key components of the MC4 pathway. Studies have suggested a link between defects in MAGEL2 in some humans with obesity, hyperphagia, autism spectrum disorders, reduced intellectual ability and most other aspects of behavior and metabolism associated with PWS. However, the connection of PWS with the MC4 pathway is complex.

We have completed a Phase 2 proof of concept, double-blind, placebo-controlled, randomized clinical trial in PWS, Study RM-493-010, which enrolled 40 patients for four weeks of active setmelanotide treatment, administered once daily by SC injection. This trial was intended to assess the effects of

setmelanotide on weight reduction, and PWS-specific hyperphagia-related behaviors, as PWS patients do not respond to hunger questionnaires, as well as determine its safety profile. Based on the data from this Phase 2 clinical trial, we do not believe we will be positioned to proceed directly into a Phase 3 clinical trial.

The trial included a two-week run-in period, a four-week double blind, randomized, placebo-controlled parallel group main trial, a two-week double-blind, randomized, placebo-controlled withdrawal period during which half of the trial patients were randomized to either continue to receive their therapy or be switched to the alternative therapy, from active to placebo, or vice versa, and a two-week active-treatment extension. There were four treatment arms in the trial: placebo (N=14); 0.5 mg of setmelanotide SC injection daily (N=4), 1.5 mg of setmelanotide SC injection daily (N=12), and 2.5 mg of setmelanotide SC injection daily (N=10). Patients were 17 to 54 years of age, with a mean BMI of 39.4 kg/m^2, and with a genetically confirmed diagnosis of PWS. Primary endpoints for the trial included safety and tolerability, weight loss and hyperphagia, with hyperphagia to be measured by a PWS hyperphagia observer reported outcome, or ORO, questionnaire. Secondary endpoints included dual-energy x-ray absorptiometry measurements, pharmacokinetics, effects during the randomized withdrawal stage, and effects on quality of life and food-related and other behaviors. Primary evaluations were assessed at the end of the four-week double blind parallel group stage, as well as after the withdrawal stage and open label extension.

The results of the trial showed modest effects on hyperphagia, which did not approach statistical significance, and no effect on weight, though there may have been some small evidence of clinically-important weight loss in the very small group of patients who were randomized to the highest dose of setmelanotide over the longest interval of treatment (N=4 patients, post-hoc evaluation, non-significant). There was good safety and tolerability, providing support for the 2.5 mg daily dose, with only injection site reactions common in both active and placebo groups. There were no serious adverse events, no significant safety issues or changes in labs or other safety parameters, and the one discontinuation was due to injection site reactions.

PWS is a complex multigenic disease, and the hypothesis that PWS is an upstream MC4 pathway disorder is supported primarily on the role of only one of those genes, MAGEL2, in animal models of obesity. Our results may support that PWS is not an upstream MC4 pathway disorder. Alternatively, other design factors may have influenced the outcome of this trial, and we will reassess in 2018 the possibility of future Phase 2 trials in PWS that address these potential factors: longer duration of treatment, younger patient population, improved setmelanotide pharmacokinetics, consideration of higher doses, and operational limitations of the completed Phase 2 trial.

Setmelanotide Clinical Development in General Obesity Patients

Initial studies in general obesity provided preliminary evidence of efficacy and of good tolerability, and served as a foundation for the clinical development of setmelanotide. The general obese population is defined as having a BMI of equal to or greater than 30 kg/m^2. In our initial clinical trials, we delivered setmelanotide with continuous SC infusion using an insulin pump. More recently, our administration has been converted to a once daily SC injectable formulation. In addition, we have an ongoing trial to assess the pharmacokinetics of a new, long-acting formulation of setmelanotide.

The table below summarizes the setmelanotide studies that we conducted in general obese patients under IND # 112595 submitted to the Division of Metabolism and Endocrinology Products, Center for Drug Evaluation and Research, FDA.

Completed and Ongoing Setmelanotide Clinical Trials in the General Obese Population

Short Study Title	Population	Route of Administration Formulation	Number of Subjects/ Patients	Status
RM-493-001 Single Ascending Dose Trial in Healthy Obese Subjects	Obesity	Continuous infusion	36 healthy obese subjects	Completed
RM-493-002 Multiple Ascending Dose Trial in Healthy Obese Subjects	Obesity	Continuous infusion SC injection	54 healthy obese subjects	Completed
RM-493-003 A Phase 2a Weight Loss Trial in Obese Patients using Continuous Infusion	Obesity	Continuous infusion	74 healthy obese subjects	Completed
RM-493-005 Pre-screening Genetic Testing of Healthy Obese Subjects	N/A Genetic Screening Study	N/A	N/A	Completed
RM-493-006 A Phase 1b 2-Period Crossover Trial on Energy Expenditure in Obese Subjects	Energy Expenditure In Obesity	Continuous infusion	12 healthy obese subjects	Completed
RM-493-008 A Phase 1 Pharmacokinetic Trial of New Once-daily Injectable Formulations	PK/Obesity	SC injection	12 healthy obese subjects	Completed
RM-493-009 A Staged, Phase 1b/Phase 2a Pharmacokinetic/Weight Loss Trial in Obese Patients using Sub-Cutaneous Injection	Obesity	SC injection	97 healthy obese subjects	Completed
RM 493 017 A Long-Acting Formulation PK Study of RM-493	Obesity	SC injection of long-acting formulation	30 healthy obese subjects	Ongoing

SC=subcutaneous.

Phase 2 Clinical Development in the General Obese Population

a. Phase 2 Clinical Trial Results with Continuous Infusion

We conducted our first Phase 2 clinical trial of setmelanotide using continuous SC infusion. This was a 12-week, Phase 2 proof of concept clinical trial in general obese patients using the SC continuous infusion formulation of setmelanotide delivered by an insulin pump. We treated approximately 74 obese patients with either placebo or setmelanotide at a dose of 1.0 mg over

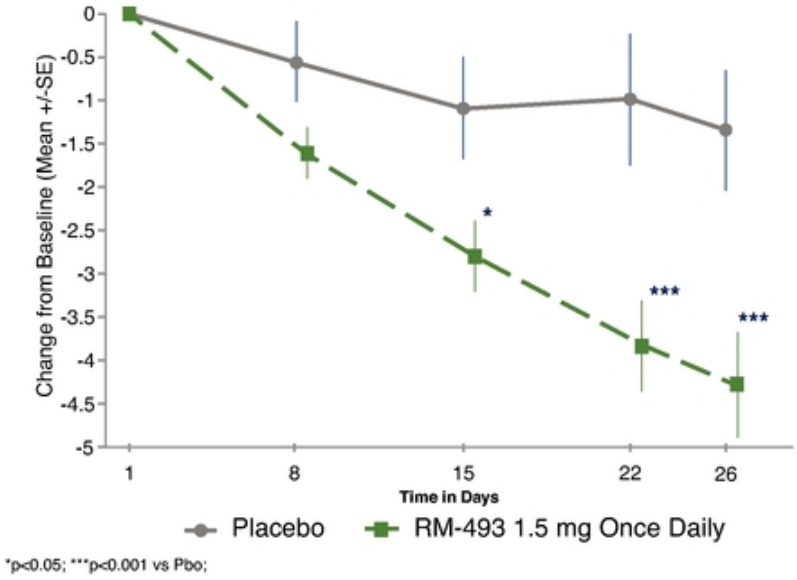
24 hours, with no serious adverse events or other safety indications from laboratory tests, electrocardiograms or vital signs noted in the setmelanotide treatment group. Evaluation of the pharmacokinetics, or blood levels, of setmelanotide from this clinical trial demonstrated that the SC continuous infusion method of drug administration was not optimal. A large number of patients did not meet the target pharmacokinetic exposures of setmelanotide that our Phase 1 clinical trials suggested would have to be achieved in order for setmelanotide to show efficacy. This clinical trial did not demonstrate statistically significant weight loss compared to the placebo. We believe patients in this clinical trial lacked adequate exposure to setmelanotide, and concluded that all future efficacy clinical trials in obese patients should be conducted using the SC injection method. This belief is based on a prior Phase 1 pharmacokinetic trial, which used the SC injection formulation and demonstrated higher pharmacokinetic exposures in obese patients.

b. Phase 2 Clinical Trial with Once Daily SC Injection

We conducted a three-stage, randomized, placebo-controlled, Phase 2 12-week general obesity trial, with approximately 100 obese patients, using our SC injection formulation, primarily with once daily dosing. We designed this Phase 2 clinical trial to bridge between the earlier clinical trials that used continuous infusion and all future clinical trials that use the formulation for once daily SC injection. Therefore, the primary purpose of the staged approach in this trial was to assess if appropriate pharmacokinetic targets could be reached with the new SC injection, first in an in-patient setting similar to the setting where robust weight loss was demonstrated in the Phase 1 general obesity trial, and then in an outpatient setting.

Overall, setmelanotide demonstrated significant weight loss over 12-weeks in all stages, with placebo subtracted weight loss, or the difference in the amount of weight gained or lost in the active treatment group as compared to the placebo treatment group, from baseline of –2.78% to –4.69% and p-values ranging from 0.005 to <0.001. However, weight loss was more pronounced and consistent in the cohort treated with an initial four-week, observed dosing, inpatient period, for which overall placebo subtracted weight loss from baseline at week 12 ranged from –3.87% to –4.69%, all with p-values of less than 0.005, with the most pronounced weight loss during the in-patient period. The once daily SC injection formulation also showed consistent and predictable pharmacokinetic measurements during the four-week inpatient interval in the first stage, validating the characteristics of the SC injection formulation. However, this trial demonstrated challenges in drug administration and compliance when administered in an outpatient setting in the general obese population.

Setmelanotide Phase 2 SC Injection Trial 4-week In-Patient Dosing Period: Percent Weight Loss for Setmelanotide 1.5 mg/day SC injection vs Placebo over 26 days of Observed Dosing



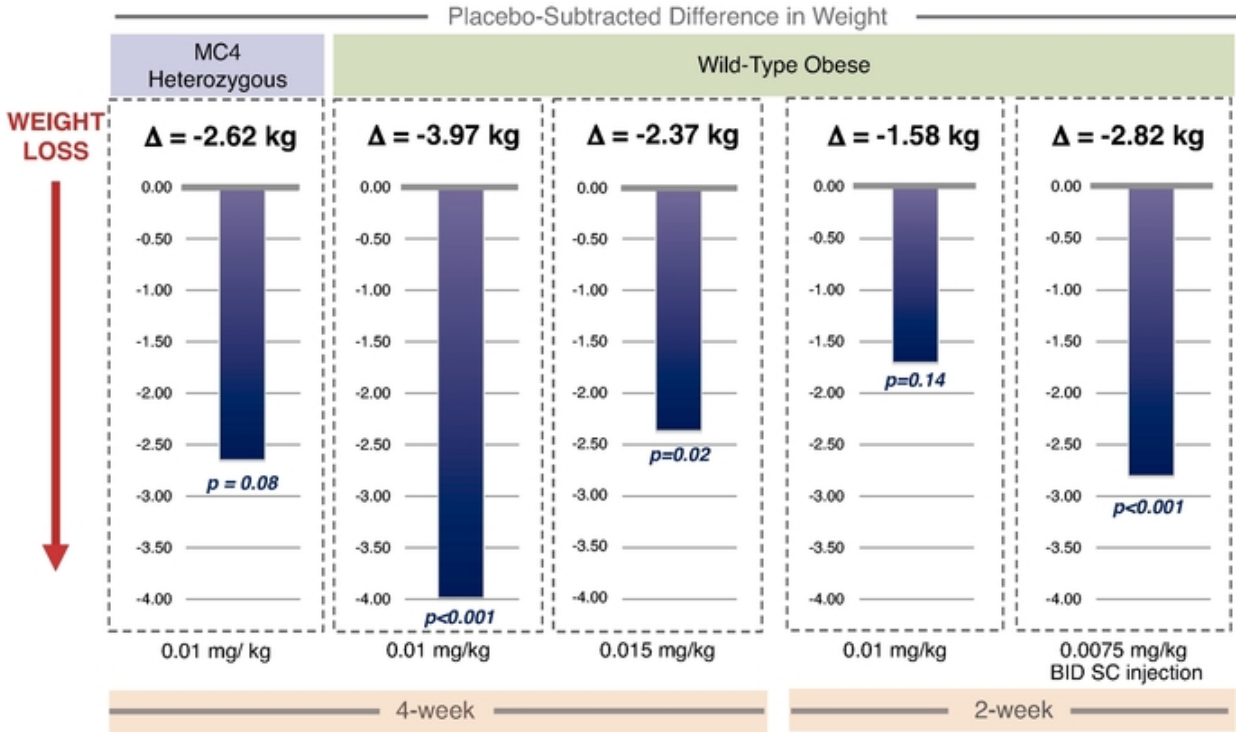
Phase 1 Clinical Development in the General Obese Population

We have completed a Phase 1 single-ascending dose, or SAD, clinical trial of setmelanotide, as well as five cohorts in a Phase 1 multiple-ascending dose, or MAD, clinical trial of setmelanotide. Both clinical trials were in healthy obese subjects, and included a double-blind, placebo-controlled randomized escalating dose design. Subjects received treatment in these Phase 1 clinical trials for one day at doses up to 0.1 mg/kg/day, which is a total daily dose of approximately 10 mg/day, and for up to 28 days at doses up to 0.015 mg/kg/day, which is a total daily dose of approximately 1.5 mg/day.

In the SAD clinical trial, our extensive monitoring of heart rate and blood pressure did not demonstrate any clinically meaningful changes with setmelanotide treatment compared with placebo. Similarly, in the MAD clinical trial, there was no evidence of any notable changes in cardiovascular parameters compared to placebo when assessed by 24-hour ambulatory blood pressure monitoring, or ABPM. We determined that the terminal half-life of setmelanotide is approximately nine to ten hours, making it suitable for once daily dosing.

Four cohorts of the Phase 1 MAD clinical trial that included doses of greater than 0.01 mg/kg/day, which is approximately 1 mg/day, for two to four weeks, demonstrated placebo subtracted weight loss differences. Most panels showed statistically significant, placebo subtracted weight reduction that ranged from 0.6 to 1.4 kg/week, with a mean of approximately 0.9 kg/week over the two to four weeks of treatment in Phase 1.

Setmelanotide: Phase 1b General Obesity Patients: Placebo Subtracted Differences[1][2]



(1) Over two to four weeks of treatment with setmelanotide by continuous SC infusion. Placebo subtracted differences are the FDA's primary weight loss analysis approach, assessing the weight difference between active and placebo treatment groups for changes from baseline for weight.

(2) Preliminary data.

D = Placebo subtracted weight loss from baseline.

BID = Two times per day.

Phase 1 Energy Expenditure Clinical Trial

In collaboration with the National Institute of Diabetes, Digestive and Kidney Diseases, we investigated setmelanotide in a Phase 1 clinical trial to determine the effects of setmelanotide on energy expenditure, a mechanism for weight loss, in addition to the well-known effects of MC4R agonists on appetite and food intake. Twelve obese adults were randomized to receive setmelanotide or placebo by continuous SC infusion over 72 hours, followed immediately by crossover to the other treatment. Setmelanotide showed statistically significant 6.85% increases in resting energy expenditure, supporting a role for setmelanotide in weight regulation. This trial provided the first clinical demonstration that MC4R activation with setmelanotide increases resting energy expenditure in obese humans.

Long-Acting Setmelanotide Pharmacokinetic Trial

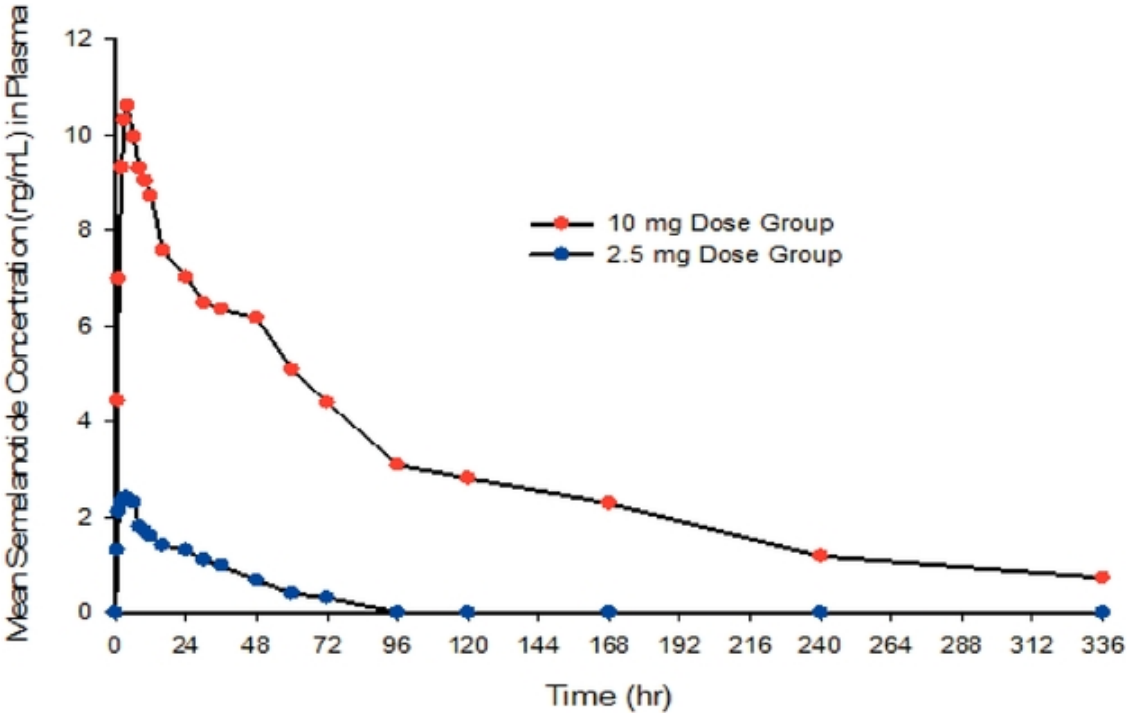
In addition to developing the once daily SC injectable formulation of setmelanotide that we are using in our ongoing clinical trials, in collaboration with Camurus AB, or Camurus, we have developed a once weekly, long-acting formulation using FluidCrystal® technology. When injected subcutaneously, aqueous body fluid is absorbed by the excipient lipid phase which forms a gel-like depot consisting of liquid crystals formed in situ leading to slow diffusion of setmelanotide from the depot.

We have compelling preclinical data with the long-acting formulation: in monkeys, the terminal half-life of the long-acting formulation is approximately 105 hours, and in rats, approximately 92 hours. Two-week toxicology studies in rats have been completed, and the long-acting formulation was well tolerated. During the two-week dosing period, animals given setmelanotide had dose-related, statistically significant lower body weights, from –9.8% to –11.7%, compared to those given placebo controls. Food consumption for animals given setmelanotide was also lower compared to controls, which decreased by approximately –20.5%.

A clinical pharmacokinetic trial is ongoing. It is an ascending-dose, placebo-controlled, up to three sequential panel PK trial, and PK and safety/tolerability will be collected for approximately 14 days. Dose for the three panels will range from 2.5 mg up to 30 mg given as a single SC injection.

The results from the 2.5 mg and 10 mg doses are now available. At these doses, setmelanotide long-acting formulation was well tolerated. The pharmacokinetic data from the 10 mg single subcutaneous dose showed a profile that was consistent with once weekly dosing with a mean pharmacokinetic half-life of 123 hours. While this data is preliminary, and this formulation is expected to be only ready for submission in 2019, or later, this simpler dosing regimen may provide improvements in patient convenience.

Mean Setmelanotide Concentrations (ng/mL) After a Single Subcutaneous Dose of the Long-Acting Camurus Formulation of Setmelanotide in Healthy Obese Subjects (N=8)



Safety and Tolerability

Historically, clinical data with other MC4R therapies suggested that MC4R-mediated side effects may include changes in blood pressure and heart rate, increased erections in males, changes in libido and sexual function in females and nausea and vomiting. As a result, primarily due to concerns about blood pressure and heart rate changes, none of these therapies have proceeded to commercialization and no other MC4R agonists are currently in the clinic for the treatment of obesity and/or hyperphagia. It is noteworthy that the pattern of effects differed among each of the other MC4R therapies, underscoring the complex physiology of MC4R. With setmelanotide, there has been little, if any, evidence of blood pressure or heart rate

changes, preliminarily supporting an important differentiation of setmelanotide from previous MC4R therapies. Careful monitoring for blood pressure and heart rate changes, as well as other potential adverse events, is included in all setmelanotide clinical trials.

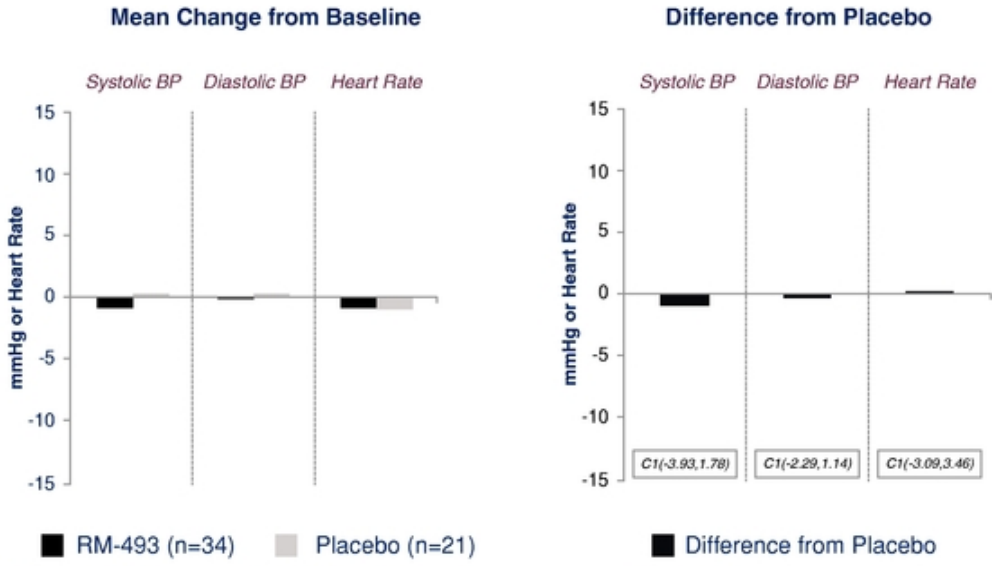
Because of these first generation MC4 therapy failures, the setmelanotide program employed an intensive preclinical screening program to assess clinical candidates for blood pressure and heart rate effects, along with efficacy. The cornerstone of this preclinical screening program was a significant investment in obese primate studies which validated setmelanotide as a promising compound for clinical development.

Setmelanotide was generally well tolerated in our Phase 1 and Phase 2 clinical trials. Overall, except as outlined below, the number and patterns of adverse events was generally low, and the intensity of the adverse events was generally mild, and infrequently led to clinical trial discontinuation.

There has been only a single serious adverse event possibly attributed to setmelanotide in our clinical trials. In our Phase 2 clinical trial with once daily SC injection, one patient was hospitalized for unusual chest pain, but no evidence of any serious respiratory or cardiac cause was found after careful evaluation, and the event was attributed to musculoskeletal pain. There were no treatment-related changes in physical examination, except as noted below, and few, if any, clinically relevant changes in electrocardiograms, laboratory data and/or anti-drug antibodies. Overall, there have been five other serious adverse events in the full development program, in addition to the serious adverse event described above: two others on setmelanotide, including left arm numbness and influenza immunization reaction, and three on placebo consisting of biliary dyskinesia, severe groin strain, and pelvic inflammatory disease. None of these five other serious experiences was considered related to setmelanotide treatment.

To demonstrate that setmelanotide has the potential to provide a safe cardiovascular profile, we extensively validated setmelanotide in obese primate preclinical studies, with special attention to cardiovascular effects. The results of these studies supported testing in clinical trials. In the clinical trials, we monitored blood pressure and heart rate extensively, primarily by 24-hour ABPM. In most clinical trials, there were multiple 24-hour ABPM periods, both on a pre-treatment and post-treatment basis. Trial-by-trial review of the 24-hour ABPM data shows little, if any, evidence of changes in heart rate and/or blood pressure even at the highest doses tested in Phase 1 and Phase 2 clinical trials. We have also conducted an analysis of 24-hour ABPMs that were obtained pre-dose and post-dose across completed studies, which was presented at the Obesity Society in 2015. This included 128 patients, of which 79 were active and 49 were on a placebo. Overall, there was little, if any, evidence of blood pressure or heart rate changes evident from baseline versus placebo in any trial, preliminarily supporting an important differentiation of setmelanotide from previous MC4 therapies. While the preliminary data are encouraging, there will be continued focus on potential cardiovascular risk until addressed in larger and longer clinical trials.

Setmelanotide Phase 2 SC Injection Trial: 24-hr ABPM (All Studied Patients), Showing No Adverse Effect of Setmelanotide on Blood Pressure or Heart Rate



24-hr Ambulatory Blood Pressure Monitoring (ABPM) performed predose and between Days 8 and 9 of dosing; Measurements obtained every 15-20 min throughout the 24-hrs.

In the majority of our trials, there was a small increase in penile erections in male patients, as well as signs of sexual arousal in a small number of female patients. These symptoms were infrequent, generally mild, not painful, and short-lived. Most often these symptoms were reported in the first week of treatment. There was a small incidence of nausea and vomiting, as well as injection site reactions, both of which usually were reported as mild, early in treatment, and short-lived. A small number of patients had dose reductions and/or discontinued treatment due to nausea and vomiting.

We also noted darkening of skin and skin lesions, such as moles and freckles, in most patients who received setmelanotide. This was likely caused by activation of the closely related MC1 receptor, the receptor that mediates skin darkening in response to sun exposure. This was observed generally after one to two weeks of treatment, most often plateaued by two to four weeks of treatment, and like sun-related tanning, generally returned to baseline after cessation of exposure.

Other effects, specifically back pain, headaches, fatigue, diarrhea and arthralgia, have been numerically more frequent in setmelanotide-treated patients as compared to placebo patients, but most investigators reported these effects to be unrelated to setmelanotide.

While general obese patients are not currently the focus of setmelanotide studies, the FDA and EMA consider the risk and benefit information observed to date with setmelanotide in general obese patients to be supportive of the continued development of this therapy. These data from general obese patients do not raise any new safety concerns and suggest that substantial benefit, as evidenced by weight loss, is possible.

Preclinical Development

Preclinical studies demonstrated the efficacy of setmelanotide in suppressing food intake and body weight gain in diet-induced obese mice, rats, dogs, and rhesus macaques, as well as in genetic models of obesity, including leptin-deficient ob/ob mice and obese Zucker, or fa/fa (leptin-receptor deficient), rats. Furthermore, setmelanotide is associated with restoring insulin sensitivity in nonclinical models of obesity in rodents and lowering of plasma triglycerides, cholesterol, and free fatty acids.

In particular, we demonstrated activity in obese non-human primates, where approximately 13% weight loss was demonstrated with eight weeks of treatment, without evidence of cardiovascular toxicity. We also studied obese primates in crossover studies to confirm the lack of cardiovascular toxicity by setmelanotide in obese primates. These preclinical studies also confirmed the cardiovascular effects of previous MC4 therapies that had produced cardiovascular toxicity in humans. In contrast, setmelanotide was without cardiovascular effects in head-to-head studies.

Lastly, the toxicology program to support the NDA filing of setmelanotide for POMC deficiency obesity is near completion. We completed three-month toxicology studies in rats and monkeys, with doses and exposures that are more than 300-fold greater than those at the anticipated clinical doses without evidence of clinically relevant toxicological findings. Similarly, we have also completed chronic toxicity studies (6-month rat, 9-month monkey), which in rats provided 219- (maximum concentration) and 106-times (area under the curve), respectively, and in monkeys 282- and 82-times, respectively, the exposures at the anticipated clinical doses compared to the No-Observed-Adverse-Effect-Level(s) in animals. We have evaluated the potential reproductive and development effects of setmelanotide in rats and rabbits with administration by SC injection, to support the administration of setmelanotide in women of child-bearing potential. In addition, a juvenile toxicology study has been completed that will support dosing in pediatric patients less than 12 years of age. In addition, we are planning carcinogenicity studies, the longest of which is expected to be two years. We believe that the FDA and EMA have each provided preliminary guidance that we may file our initial POMC deficiency obesity NDA and marketing authorization application, respectively, without the carcinogenicity studies for these rare disease populations, which we will then provide post-approval.

Competition

The biotechnology and pharmaceutical industries are intensely competitive and subject to rapid and significant technological change. We have competitors in a number of jurisdictions, many of which have substantially greater name recognition, commercial infrastructures and financial, technical and personnel resources than we have. Established competitors may invest heavily to quickly discover and develop compounds that could make setmelanotide obsolete or uneconomical. Any new product that competes with an approved product may need to demonstrate compelling advantages in efficacy, convenience, tolerability and safety to be commercially successful. Other competitive factors, including generic competition, could force us to lower prices or could result in reduced sales. In addition, new products developed by others could emerge as competitors to setmelanotide. If we are not able to compete effectively against our current and future competitors, our business will not grow and our financial condition and operations will suffer.

There are no current pharmacological treatments for regulating hunger and hyperphagia-related behaviors of patients with POMC deficiency obesity, LepR deficiency obesity, Bardet-Biedl syndrome, Alström syndrome, POMC heterozygous deficiency obesity or POMC epigenetic disorders. Bariatric surgery is not a treatment option for these genetic disorders of obesity because the severe obesity and hyperphagia associated with these disorders are considered to be risk factors for bariatric surgery.

Licensing Agreements

Ipsen Pharma S.A.S.

In February 2010, the Predecessor Company entered into a license agreement with Ipsen S.A.S., or Ipsen, pursuant to which Ipsen granted to it an exclusive, sublicensable, worldwide license to certain patents and other intellectual property rights to research, develop, and commercialize compounds that were discovered or researched by Ipsen in the course of conducting its MC4 program or that otherwise were covered by the licensed patents. Rights under the license included the right to research, develop and commercialize setmelanotide. Pursuant to the license, Ipsen also granted to the Predecessor Company a

non-exclusive, sublicensable, worldwide license to certain patents and other intellectual property rights that were licensed by Ipsen from a third party or that Ipsen may develop in the future to research, develop, and commercialize any of the compounds exclusively licensed by Ipsen pursuant to the license.

On March 21, 2013, the LLC entity completed the Corporate Reorganization pursuant to which, among other things, the existing license with Ipsen with respect to the MC4 program is now held separately by us. As a result we hold the rights to the MC4 program, including the rights to develop and commercialize setmelanotide.

Under the terms of the Ipsen license agreement, Ipsen will receive payments of up to $40.0 million upon the achievement of certain development and commercial milestones in connection with the development, regulatory approval and commercialization of applicable licensed products, and royalties on future sales of the licensed products. Substantially all of the aggregate payments under the Ipsen license agreement are for milestones that may be achieved no earlier than first commercial sale of the applicable licensed product. Royalties in the mid-single digits on future sales of the applicable licensed products will be due under the Ipsen license agreement on a licensed product-by-licensed product and country-by-country basis until the later of the date when sales of a licensed product in a particular country are no longer covered by patent rights licensed pursuant to the Ipsen license agreement and the tenth anniversary of the date of the first commercial sale of the applicable licensed product in the applicable country. The term of the Ipsen license agreement continues until the expiration of the applicable royalty term on a country-by-country and product-by- product basis. Upon expiration of the term of the agreement, the licensed rights granted to us under the agreement, to the extent they remain in effect at the time of expiration, will thereafter become irrevocable, perpetual and fully paid-up licenses that survive the expiration of the term. We have a right to terminate the license agreement at any time during the term for any reason on 180 days' written notice to Ipsen. Ipsen has a right to terminate the agreement prior to expiration of its term for our material breach of the agreement, our failure to initiate or complete development of a licensed product or our bringing an action seeking to have an Ipsen license patent right declared invalid. Upon any early termination of the license agreement not due to Ipsen's material breach, all licensed rights granted under the license agreement will terminate.

Camurus

In January 2016, we entered into a license agreement for the use of Camurus' drug delivery technology, FluidCrystal, to formulate setmelanotide with Camurus. Under the terms of the agreement, Camurus granted us a worldwide license to the FluidCrystal technology to formulate setmelanotide and to develop, manufacture, and commercialize this new formulation for once-weekly dosing, administered as a SC injection. The license granted to us is specific to the FluidCrystal technology incorporating setmelanotide. Under the terms of the license agreement, we are responsible for manufacturing, development, and commercialization of the setmelanotide FluidCrystal formulation worldwide. Camurus received a non-refundable and non-creditable upfront payment of $500,000 in January 2016, and is eligible to receive progressive payments of approximately $65.0 million, of which the majority are sales milestones. In addition, Camurus is eligible to receive tiered, mid to mid-high, single digit royalties on future sales of the product.

The term of the agreement continues until the expiration of the applicable royalty term on a country-by-country and product-by-product basis. Upon expiration of the term of the agreement, the licensed rights granted to us under the agreement, to the extent they remain in effect at the time of expiration, will thereafter become irrevocable, perpetual and fully paid-up licenses that survive the expiration of the term. We have a right to terminate the license agreement at any time during the term for any reason upon 90 days' written notice to Camurus. Camurus has a right to terminate the agreement prior to expiration of its term for our material breach of the agreement, if we voluntarily or involuntarily file for bankruptcy, or for our bringing an action seeking to have a Camurus license patent right declared invalid.

Upon any early termination of the license agreement not due to Camurus' material breach, all licensed rights granted under the license agreement will terminate.

Commercial Operations

Our commercial strategies center around creating a well-informed, supportive genetic obesity community of institutions, healthcare providers, patients, caregivers, and payers to support our ongoing research and development efforts to transform the care of patients with MC4 pathway deficiencies.

Our commercial priorities for the launch of setmelanotide include:

- Improving methods of evaluation and diagnosis of rare genetic obesity patients through enhanced diagnostic capabilities and partnership with key opinion leaders and pediatric endocrinologists in order to more clearly articulate the clinical presentation of these patients to referring physicians;
- Facilitating an integrated genetic obesity community through services that support patient awareness, education, advocacy, and treatment;
- Communicating the burden of rare genetic obesity syndromes to promote advocacy for patient sequencing and support for pricing and reimbursement of setmelanotide; and
- Building a global commercial organization to drive patient identification and enable a successful launch of setmelanotide.

Our management team understands the complexity of rare diseases and we believe has the necessary expertise to be a true partner to patients, caregivers, advocacy, and healthcare teams leading to shared success. We intend to establish a specialty sales force and develop an organizational infrastructure that will support an extensive network of endocrinologists and other physicians treating severe childhood obesity and rare genetic disorders of obesity which in turn we believe will help establish genetic obesity centers of excellence. Our goal is for our field personnel to work directly with patients, caregivers and healthcare providers to facilitate therapy initiation and adherence. We also expect to partner with existing and new advocacy organizations to further educate our patient population on genetic obesity and support coverage for setmelanotide. In addition, we intend to establish our own commercial sales and marketing organization in the United States and core strategic markets and to selectively establish partnerships in markets outside the United States for sales, marketing and distribution.

Patents and Proprietary Rights

We have in-licensed a large patent portfolio from Ipsen for our melanocortin programs. The portfolio includes multiple patent families, and all of these in-licensed patent families are being prosecuted or maintained by Ipsen in consultation with us. We have also filed patent applications in four families which are exclusively owned and maintained by us that relate to the melanocortin program.

Our MC4 portfolio of licensed and exclusively owned patent families, which includes setmelanotide, consists of 9 patent families currently being prosecuted or maintained, which include applications and patents directed to compositions of matter, formulations and methods of treatment using setmelanotide. As of May 10, 2017, the portfolio licensed for the MC-4 program consists of seven issued United States patents and 42 issued non-United States patents across four of the 9 families. We are actively pursuing six United States patent applications and 48 non-United States applications in 18 jurisdictions.

In the patent family directed to the composition of matter for setmelanotide, we have two issued United States patents and 21 issued non-United States patents, including Australia, Canada, China, Europe, Hong Kong, Israel, Japan, Korea, New Zealand, Russia and Singapore. The standard 20-year term for patents in this family would expire in 2026, but the United States patent will expire in 2027 due to a patent term adjustment. Patent term extensions for delays in marketing approval may also extend the terms of patents in this family.

In addition to the patents and patent applications discussed above, we have filed one application co-owned with Charité-Universitätsmedizin Berlin, that relates to the melanocortin program, which has not yet entered active prosecution.

Intellectual Property Protection Strategy

We currently seek, and intend to continue seeking, patent protection whenever commercially reasonable for any patentable aspects of setmelanotide and related technology or any new products or product candidates we acquire in the future. Where our intellectual property is not protected by patents, we may seek to protect it through other means, including maintenance of trade secrets and careful protection of our proprietary information. Our license from Ipsen for the melanocortin program require Ipsen, subject to certain exceptions and upon consultation with us, to prosecute and maintain its patent rights as they relate to the licensed compounds and methods. If Ipsen decides to cease prosecution or maintenance of any of the licensed patent rights, we have the option to take over prosecution and maintenance of those patents and Ipsen will assign to us all of its rights in such patents. For those patent rights that we own exclusively, we control all prosecution and maintenance activities.

The patent positions of biopharmaceutical companies are generally uncertain and involve complex legal, scientific and factual questions. In addition, the coverage claimed in a patent application can be significantly reduced before the patent is issued, and its scope can be reinterpreted after issuance. Consequently, we do not know whether the product candidate we in-license will be protectable or remain protected by enforceable patents. We cannot predict whether the patent applications we are currently pursuing will issue as patents in any particular jurisdiction, and furthermore, we cannot determine whether the claims of any issued patents will provide sufficient proprietary protection to protect us from competitors, or will be challenged, circumvented or invalidated by third parties. Because patent applications in the United States and certain other jurisdictions are maintained in secrecy for 18 months, and since publication of discoveries in the scientific or patent literature often lags behind actual discoveries, we cannot be certain of the priority of inventions covered by pending patent applications. This potential issue is exacerbated by the fact that, prior to March 16, 2013, in the United States, the first to make the claimed invention may be entitled to the patent. On March 16, 2013, the United States transitioned to a "first to file" system in which the first inventor to file a patent application may be entitled to the patent. Therefore, we may have to participate in interference proceedings declared by the United States Patent and Trademark Office, or PTO, or a foreign patent office to determine priority of invention. Moreover, we may have to participate in other proceedings declared by the United States PTO or a foreign patent office, such as post-grant proceedings and oppositions, that challenge the validity of a granted patent. Such proceedings could result in substantial cost, even if the eventual outcome is favorable to us.

Although we currently have issued patents directed to a number of different attributes of our products, and pending applications on others, there can be no assurance that any issued patents would be held valid by a court of competent jurisdiction. An adverse outcome could subject us to significant liabilities to third parties, require disputed rights to be licensed from third parties or require us to cease using specific compounds or technology. To the extent prudent, we intend to bring litigation against third parties that we believe are infringing our patents.

The term of individual patents depends upon the legal term of the patents in the countries in which they are obtained. In most countries in which we file, the patent term is 20 years from the earliest date of filing a non-provisional patent application. In the United States, a patent's term may be lengthened by patent term adjustment, which compensates a patentee for administrative delays by the United States PTO in granting a patent, or may be shortened if a patent is terminally disclaimed over another patent with an earlier expiration date.

As mentioned above, in the United States, the patent term of a patent that covers an FDA-approved drug may also be eligible for patent term extension, which permits patent term restoration as

compensation for the patent term lost during the FDA regulatory review process. In the future, if and when our pharmaceutical products receive FDA approval, we expect to apply for patent term extensions on patents covering those products. We intend to seek patent term adjustments and extensions to any of our issued patents in any jurisdiction where these are available, however there is no guarantee that the applicable authorities, including the FDA in the United States, will agree with our assessment of whether such extensions should be granted, and even if granted, the length of such adjustments or extensions.

To protect our rights to any of our issued patents and proprietary information, we may need to litigate against infringing third parties, or avail ourselves of the courts or participate in hearings to determine the scope and validity of those patents or other proprietary rights. These types of proceedings are often costly and could be very time-consuming to us, and we cannot be certain that the deciding authorities will rule in our favor. An unfavorable decision could result in the invalidation or a limitation in the scope of our patents or forfeiture of the rights associated with our patents or pending patent applications. Any such decision could result in our key technologies not being protectable, allowing third parties to use our technology without being required to pay us licensing fees or may compel us to license needed technologies from third parties to avoid infringing third-party patent and proprietary rights. Such a decision could even result in the invalidation or a limitation in the scope of our patents or could cause us to lose our rights under existing issued patents or not to have rights granted under our pending patent applications.

In addition, we intend to seek orphan drug exclusivity in jurisdictions in which it is available. A prerequisite to orphan drug exclusivity in the United States and in the European Union is orphan drug designation. An orphan drug designation may be granted where a drug is developed specifically to treat a rare or uncommon medical treatment. If a product which has an orphan drug designation subsequently receives the first regulatory approval for the indication for which it has such designation, the product is entitled to orphan exclusivity, meaning that the applicable regulatory authority may not approve any other applications to market the same drug for the same indication, except in certain very limited circumstances, for a period of seven years in the United States and 10 years in the European Union. Orphan drug exclusivity does not prevent competitors from developing or marketing different drugs for an indication.

We also rely on trade secret protection for our confidential and proprietary information. Although we take steps to protect our proprietary information and trade secrets, including through contractual means with our employees and consultants, no assurance can be given that others will not independently develop substantially equivalent proprietary information and techniques or otherwise gain access to our trade secrets or disclose such technology, or that we can meaningfully protect our trade secrets. It is our policy to require our employees, consultants, outside scientific collaborators, sponsored researchers and other advisors to execute confidentiality agreements upon the commencement of employment or consulting relationships with us. These agreements provide that all confidential information developed or made known to the individual during the course of the individual's relationship with us is to be kept confidential and not disclosed to third parties except in specific circumstances. In the case of employees, the agreements provide that all inventions conceived by the individual will be our exclusive property. There can be no assurance, however, that these agreements will provide meaningful protection or adequate remedies for our trade secrets in the event of unauthorized use or disclosure of such information.

Manufacturing

We currently contract with a third party for the manufacture of setmelanotide and intend to continue to do so in the future. We have entered into a process development and manufacturing services agreement with CordenPharma International, formerly Peptisyntha SA prior to its acquisition by CordenPharma International, or Peptisyntha, under which Peptisyntha will provide certain process development and manufacturing services in connection with the manufacture of setmelanotide. Under the agreement, we pay Peptisyntha for services in accordance with the terms of mutually agreed upon work orders, which we and Peptisyntha may enter into from time to time. The agreement also provides that, subject to certain conditions, for a period following each product launch date, we will source from Peptisyntha a portion of

our requirements for that product being sourced from non-affiliate third parties. Under the agreement, each party is subject to customary indemnification provisions.

The Peptisyntha agreement will continue, unless earlier terminated pursuant to its terms, until the later of six years from the July 17, 2013 effective date or the completion of all services under all work plans executed in accordance with the terms of the agreement prior to the sixth anniversary of its effective date. The agreement may be extended by us continuously for additional two-year periods upon written notice to Peptisyntha. We also may terminate the agreement or any work order thereunder upon at least 30 days' prior written notice to Peptisyntha.

We have also entered into a process development and manufacturing services agreement with Recipharm Monts S.A.S., or Recipharm, under which Recipharm will provide certain process development and manufacturing services in connection with the manufacture of setmelanotide. Under the agreement, we pay Recipharm for services in accordance with the terms of mutually agreed upon work orders, which we and Recipharm may enter into from time to time. Under the agreement, each party is subject to customary indemnification provisions. The Recipharm agreement will continue, unless earlier terminated pursuant to its terms, until the later of three years from the December 21, 2016 effective date or the completion of all services under all work plans executed in accordance with the terms of the agreement prior to the third anniversary of its effective date. The agreement may be extended by us continuously for additional two-year periods upon written notice to Recipharm. We also may terminate the agreement or any work order thereunder upon at least 60 days' prior written notice to Recipharm.

We currently have no plans to build our own clinical or commercial scale manufacturing capabilities. To meet our projected needs for clinical supplies to support our activities through regulatory approval and commercial manufacturing, the contract manufacturing organizations, or CMOs, with whom we currently work will need to increase scale of production or we expect that we will need to secure alternate suppliers. We have not currently identified alternate suppliers in the event the current CMOs we utilize are unable to scale production. Because we rely on these CMOs, we have personnel with pharmaceutical development and manufacturing experience who are responsible for maintaining our CMO relationships.

Regulatory Matters

Government Regulation and Product Approvals

Government authorities in the United States, at the federal, state and local level, and in other countries and jurisdictions, including the European Union, extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, packaging, storage, recordkeeping, labeling, advertising, promotion, distribution, marketing, post-approval monitoring and reporting, and import and export of pharmaceutical products. The processes for obtaining marketing approvals in the United States and in foreign countries and jurisdictions, along with subsequent compliance with applicable statutes and regulations and other competent authorities, require the expenditure of substantial time and financial resources.

Review and Approval of Drugs in the United States

In the United States, the FDA approves drug products under the Federal Food, Drug, and Cosmetic Act, or FDCA, and associated implementing regulations. Biological products, on the other hand, are licensed by the FDA under the Public Health Service Act, or PHSA. With passage of the Biologics Price Competition and Innovation Act of 2009, Congress amended the definition of "biological product" in the PHSA so as to exclude a chemically synthesized polypeptide from licensure under the PHSA. Rather, the Act provided that such products would be treated as drugs under the FDCA. Subsequently, through final guidance issued in April 2015, the FDA indicated that a "chemically synthesized polypeptide" is any alpha amino acid polymer that is made entirely by chemical synthesis and is less than 100 amino acids in size. Accordingly, based on this FDA guidance, we believe that our products will not be treated as biologics

subject to approval of a biologics license application, or BLA, by the FDA, and rather will be treated as drug products subject to approval of a new drug application, or NDA, by the FDA pursuant to the FDCA.

The failure to comply with applicable requirements under the FDCA and other applicable laws at any time during the product development process, approval process or after approval may subject an applicant and/or sponsor to a variety of administrative or judicial sanctions, including refusal by the FDA to approve pending applications, withdrawal of an approval, imposition of a clinical hold, issuance of warning letters and other types of letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement of profits, or civil or criminal investigations and penalties brought by the FDA and the Department of Justice or other governmental entities.

An applicant seeking approval to market and distribute a new drug product in the United States must typically undertake the following:

- completion of preclinical laboratory tests, animal studies and formulation studies in compliance with the FDA's good laboratory practice, or GLP, regulations;
- submission to the FDA of an IND, which must take effect before human clinical trials may begin;
- approval by an independent institutional review board, or IRB, representing each clinical site before each clinical trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with current Good Clinical Practices, or cGCPs, to establish the safety and efficacy of the proposed drug product for each proposed indication;
- preparation and submission to the FDA of an NDA requesting marketing for one or more proposed indications;
- review by an FDA advisory committee, where appropriate or if applicable, as may be requested by the FDA to assist with its review;
- satisfactory completion of one or more FDA inspections of the manufacturing facility or facilities at which the product, or components thereof, are produced to assess compliance with current Good Manufacturing Practices, or cGMP, requirements and to assure that the facilities, methods and controls are adequate to preserve the product's identity, strength, quality and purity;
- satisfactory completion of FDA audits of clinical trial sites to assure compliance with cGCPs and the integrity of the clinical data;
- payment of user fees, per published Prescription Drug User Fee Act, or PDUFA, guidelines for the relevant year, and securing FDA approval of the NDA; and
- compliance with any post-approval requirements, including the potential requirement to implement a Risk Evaluation and Mitigation Strategy, or REMS, and the potential requirement to conduct post-approval studies.

Preclinical Studies

Before an applicant begins testing a compound with potential therapeutic value in humans, the drug candidate enters the preclinical testing stage. Preclinical studies include laboratory evaluation of product chemistry, toxicity and formulation, as well as *in vitro* and animal studies to assess the potential safety and activity of the drug for initial testing in humans and to establish a rationale for therapeutic use. The conduct of preclinical studies is subject to federal regulations and requirements, including GLP regulations. The results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and plans for clinical trials, among other things, are submitted to

the FDA as part of an IND. Some long-term preclinical testing, such as animal tests of reproductive adverse events and carcinogenicity, may continue after the IND is submitted.

The IND and IRB Processes

An IND is an exemption from the FDCA that allows an unapproved drug to be shipped in interstate commerce for use in an investigational clinical trial and a request for FDA authorization to administer an investigational drug to humans. Such authorization must be secured prior to interstate shipment and administration of any new drug that is not the subject of an approved NDA. In support of a request for an IND, applicants must submit a protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. In addition, the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and plans for clinical trials, among other things, are submitted to the FDA as part of an IND. The FDA requires a 30-day waiting period after the filing of each IND before clinical trials may begin. This waiting period is designed to allow the FDA to review the IND to determine whether human research subjects will be exposed to unreasonable health risks. At any time during this 30-day period, the FDA may raise concerns or questions about the conduct of the trials as outlined in the IND and impose a clinical hold. In this case, the IND sponsor and the FDA must resolve any outstanding concerns before clinical trials can begin.

Following commencement of a clinical trial under an IND, the FDA may also place a clinical hold or partial clinical hold on that trial. A clinical hold is an order issued by the FDA to the sponsor to delay a proposed clinical investigation or to suspend an ongoing investigation. A partial clinical hold is a delay or suspension of only part of the clinical work requested under the IND. For example, a specific protocol or part of a protocol is not allowed to proceed, while other protocols may do so. No more than 30 days after imposition of a clinical hold or partial clinical hold, the FDA will provide the sponsor a written explanation of the basis for the hold. Following issuance of a clinical hold or partial clinical hold, an investigation may only resume after the FDA has notified the sponsor that the investigation may proceed. The FDA will base that determination on information provided by the sponsor correcting the deficiencies previously cited or otherwise satisfying the FDA that the investigation can proceed.

A sponsor may choose, but is not required, to conduct a foreign clinical study under an IND. When a foreign clinical study is conducted under an IND, all FDA IND requirements must be met unless waived. When the foreign clinical study is not conducted under an IND, the sponsor must ensure that the study complies with certain regulatory requirements in order to use the study as support for an IND or application for marketing approval. Specifically, on April 28, 2008, the FDA amended its regulations governing the acceptance of foreign clinical studies not conducted under an investigational new drug application as support for an IND or a new drug application. The final rule provides that such studies must be conducted in accordance with good clinical practice, or GCP, including review and approval by an independent ethics committee, or IEC, and informed consent from subjects. The GCP requirements in the final rule encompass both ethical and data integrity standards for clinical studies. The FDA's regulations are intended to help ensure the protection of human subjects enrolled in non-IND foreign clinical studies, as well as the quality and integrity of the resulting data. They further help ensure that non-IND foreign studies are conducted in a manner comparable to that required for IND studies.

In addition to the foregoing IND requirements, an IRB representing each institution participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that institution, and the IRB must conduct continuing review and reapprove the study at least annually. The IRB must review and approve, among other things, the study protocol and informed consent information to be provided to study subjects. An IRB must operate in compliance with FDA regulations. An IRB can suspend or terminate approval of a clinical trial at its institution, or an institution it represents, if the clinical trial is not being conducted in accordance with the IRB's requirements or if the product candidate has been associated with unexpected serious harm to patients.

Additionally, some trials are overseen by an independent group of qualified experts organized by the trial sponsor, known as a data safety monitoring board or committee. This group provides authorization for whether or not a trial may move forward at designated check points based on access that only the group maintains to available data from the study. Suspension or termination of development during any phase of clinical trials can occur if it is determined that the participants or patients are being exposed to an unacceptable health risk. Other reasons for suspension or termination may be made by us based on evolving business objectives and/or competitive climate.

Information about certain clinical trials must be submitted within specific timeframes to the National Institutes of Health, or NIH, for public dissemination on its ClinicalTrials.gov website.

Human Clinical Studies in Support of an NDA

Clinical trials involve the administration of the investigational product to human subjects under the supervision of qualified investigators in accordance with GCP requirements, which include, among other things, the requirement that all research subjects provide their informed consent in writing before their participation in any clinical trial. Clinical trials are conducted under written study protocols detailing, among other things, the inclusion and exclusion criteria, the objectives of the study, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated.

Human clinical trials are typically conducted in the following sequential phases, which may overlap or be combined:

- Phase 1: The drug is initially introduced into healthy human subjects or, in certain indications such as cancer, patients with the target disease or condition and tested for safety, dosage tolerance, absorption, metabolism, distribution, excretion and, if possible, to gain an early indication of its effectiveness and to determine optimal dosage.

- Phase 2: The drug is administered to a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage.

- Phase 3: The drug is administered to an expanded patient population, generally at geographically dispersed clinical trial sites, in well-controlled clinical trials to generate enough data to statistically evaluate the efficacy and safety of the product for approval, to establish the overall risk-benefit profile of the product, and to provide adequate information for the labeling of the product.

- Phase 4: Post-approval studies, which are conducted following initial approval, are typically conducted to gain additional experience and data from treatment of patients in the intended therapeutic indication.

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and more frequently if serious adverse events occur. In addition, IND safety reports must be submitted to the FDA for any of the following: serious and unexpected suspected adverse reactions; findings from other studies or animal or *in vitro* testing that suggest a significant risk in humans exposed to the drug; and any clinically important increase in the case of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, or at all. Furthermore, the FDA or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution, or an institution it represents, if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients. The FDA will typically inspect one or more clinical sites to assure compliance with GCP and the integrity of the clinical data submitted.

During the course of clinical development the sponsor often refines the indication and endpoints on which the NDA will be based. For endpoints based on PROs and OROs, the process typically is an iterative one. The FDA has issued guidance on the framework it uses to evaluate PRO instruments, and it may offer advice on optimizing PRO and ORO instruments during the clinical development process, but the FDA usually reserves final judgment until it reviews the NDA.

Concurrent with clinical trials, companies often complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the drug as well as finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the drug candidate and, among other things, must develop methods for testing the identity, strength, quality, purity and potency of the final drug. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the drug candidate does not undergo unacceptable deterioration over its shelf life.

In a general guidance meeting with FDA review staff in 2013, following the opening of our independent new drug application for the development of setmelanotide, the FDA provided us with general principles to follow in designing clinical studies for drugs intended for use in an indication targeted to a specific obese population. In 2015, we received further guidance from FDA review staff in a meeting to discuss clinical endpoints and trial design strategies for the study of setmelanotide in patients with rare genetic forms of obesity. At that meeting, the FDA noted its experience in applying regulatory flexibility for drugs intended to treat rare diseases. It indicated that it would take into account factors related to particular patient populations, such as the prevalence and severity of the disease, but also noted that the requirements for a phase 3 program would depend on the effect observed and the robustness of the results. The FDA also indicated that it would exercise flexibility regarding the timing and requirements for certain preclinical toxicology testing. In 2017, we intend to take advantage of our breakthrough therapy designation by meeting regularly with FDA review staff to discuss methods to shorten the development timeline for an indication in POMC deficiency obesity, and to use the knowledge gained to do likewise for other closely-related indications in rare genetic forms of obesity.

Submission and Review of an NDA by the FDA

Assuming successful completion of required clinical testing and other requirements, the results of the preclinical studies and clinical trials, together with detailed information relating to the product's chemistry, manufacture, controls and proposed labeling, among other things, are submitted to the FDA as part of an NDA requesting approval to market the drug product for one or more indications. Under federal law, the submission of most NDAs is additionally subject to an application user fee, and the sponsor of an approved NDA is also subject to annual product and establishment user fees. For federal fiscal year 2017, the submission of an NDA is subject to an application user fee of $2,038,100. The annual product and establishment user fees for fiscal year 2017 are $97,750 per product and $512,200 per establishment.

Certain exceptions and waivers are available for some of these fees, such as an exception from the application fee for drugs with orphan designation and a waiver for certain small businesses, an exception from the establishment fee when the establishment does not engage in manufacturing the drug during a particular fiscal year and an exception from the product fee for a drug that is the same as another drug approved under an abbreviated pathway. Each category of fees is typically increased annually.

The FDA conducts a preliminary review of an NDA generally within 60 calendar days of its receipt and strives to inform the sponsor by the 74th day after the FDA's receipt of the submission to determine whether the application is sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an NDA for filing. In this event, the application must be resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth

substantive review. The FDA has agreed to specified performance goals in the review process of NDAs. Under that agreement, 90% of applications seeking approval of New Molecular Entities, or NMEs, are meant to be reviewed within ten months from the date on which the FDA accepts the NDA for filing, and 90% of applications for NMEs that have been designated for "priority review" are meant to be reviewed within six months of the filing date. For applications seeking approval of drugs that are not NMEs, the ten-month and six-month review periods run from the date the FDA receives the application. The review process and the Prescription Drug User Fee Act goal date may be extended by the FDA for three additional months to consider new information or clarification provided by the applicant to address an outstanding deficiency identified by the FDA following the original submission.

Before approving an NDA, the FDA typically will inspect the facility or facilities where the product is or will be manufactured. These pre-approval inspections may cover all facilities associated with an NDA submission, including drug component manufacturing, e.g., active pharmaceutical ingredients, finished drug product manufacturing, and control testing laboratories. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA, the FDA will typically inspect one or more clinical sites to assure compliance with cGCP.

In addition, as a condition of approval, the FDA may require an applicant to develop a REMS. REMS use risk minimization strategies beyond the professional labeling to ensure that the benefits of the product outweigh the potential risks. To determine whether a REMS is needed, the FDA will consider the size of the population likely to use the product, seriousness of the disease, expected benefit of the product, expected duration of treatment, seriousness of known or potential adverse events, and whether the product is a new molecular entity. REMS can include medication guides, physician communication plans for healthcare professionals, and elements to assure safe use, or ETASU. ETASU may include, but are not limited to, special training or certification for prescribing or dispensing, dispensing only under certain circumstances, special monitoring, and the use of patient registries. The FDA may require a REMS before approval or post-approval if it becomes aware of a serious risk associated with use of the product. The requirement for a REMS can materially affect the potential market and profitability of a product.

The FDA is required to refer an application for a novel drug to an advisory committee or explain why such referral was not made. Typically, an advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

Fast Track, Breakthrough Therapy, Priority Review and Regenerative Advanced Therapy Designations

The FDA is authorized to designate certain products for expedited review if they are intended to address an unmet medical need in the treatment of a serious or life-threatening disease or condition. These programs are referred to as fast track designation, breakthrough therapy designation, priority review designation and regenerative advanced therapy designation.

Specifically, the FDA may designate a product for Fast Track review if it is intended, whether alone or in combination with one or more other products, for the treatment of a serious or life-threatening disease or condition, and it demonstrates the potential to address unmet medical needs for such a disease or condition. For Fast Track products, sponsors may have greater interactions with the FDA and the FDA may initiate review of sections of a Fast Track product's application before the application is complete. This rolling review may be available if the FDA determines, after preliminary evaluation of clinical data submitted by the sponsor, that a Fast Track product may be effective. The sponsor must also provide, and the FDA must approve, a schedule for the submission of the remaining information and the sponsor must

pay applicable user fees. However, the FDA's time period goal for reviewing a Fast Track application does not begin until the last section of the application is submitted. In addition, the Fast Track designation may be withdrawn by the FDA if the FDA believes that the designation is no longer supported by data emerging in the clinical trial process.

Second, a product may be designated as Breakthrough Therapy if it is intended, either alone or in combination with one or more other products, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The FDA may take certain actions with respect to Breakthrough Therapies, including holding meetings with the sponsor throughout the development process; providing timely advice to the product sponsor regarding development and approval; involving more senior staff in the review process; assigning a cross-disciplinary project lead for the review team; and taking other steps to design the clinical trials in an efficient manner.

Third, the FDA may designate a product for priority review if it is a product that treats a serious condition and, if approved, would provide a significant improvement in safety or effectiveness. The FDA determines, on a case- by-case basis, whether the proposed product represents a significant improvement when compared with other available therapies. Significant improvement may be illustrated by evidence of increased effectiveness in the treatment of a condition, elimination or substantial reduction of a treatment-limiting product reaction, documented enhancement of patient compliance that may lead to improvement in serious outcomes, and evidence of safety and effectiveness in a new subpopulation. A priority designation is intended to direct overall attention and resources to the evaluation of such applications, and to shorten the FDA's goal for taking action on a marketing application from ten months to six months.

With passage of the 21st Century Cures Act, or the Cures Act, in December 2016, Congress authorized the FDA to accelerate review and approval of products designated as regenerative advanced therapies. A product is eligible for this designation if it is a regenerative medicine therapy that is intended to treat, modify, reverse or cure a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the drug has the potential to address unmet medical needs for such disease or condition. The benefits of a regenerative advanced therapy designation include early interactions with the FDA to expedite development and review, benefits available to breakthrough therapies, potential eligibility for priority review and accelerated approval based on surrogate or intermediate endpoints.

Accelerated Approval Pathway

The FDA may grant accelerated approval to a drug for a serious or life-threatening condition that provides meaningful therapeutic advantage to patients over existing treatments based upon a determination that the drug has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit. The FDA may also grant accelerated approval for such a condition when the product has an effect on an intermediate clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality, or IMM, and that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity or prevalence of the condition and the availability or lack of alternative treatments. Drugs granted accelerated approval must meet the same statutory standards for safety and effectiveness as those granted traditional approval.

For the purposes of accelerated approval, a surrogate endpoint is a marker, such as a laboratory measurement, radiographic image, physical sign or other measure that is thought to predict clinical benefit, but is not itself a measure of clinical benefit. Surrogate endpoints can often be measured more easily or more rapidly than clinical endpoints. An intermediate clinical endpoint is a measurement of a therapeutic effect that is considered reasonably likely to predict the clinical benefit of a drug, such as an effect on IMM. The FDA has limited experience with accelerated approvals based on intermediate clinical endpoints, but has indicated that such endpoints generally may support accelerated approval where the

therapeutic effect measured by the endpoint is not itself a clinical benefit and basis for traditional approval, if there is a basis for concluding that the therapeutic effect is reasonably likely to predict the ultimate clinical benefit of a drug.

The accelerated approval pathway is most often used in settings in which the course of a disease is long and an extended period of time is required to measure the intended clinical benefit of a drug, even if the effect on the surrogate or intermediate clinical endpoint occurs rapidly. Thus, accelerated approval has been used extensively in the development and approval of drugs for treatment of a variety of cancers in which the goal of therapy is generally to improve survival or decrease morbidity and the duration of the typical disease course requires lengthy and sometimes large trials to demonstrate a clinical or survival benefit. Thus, the benefit of accelerated approval derives from the potential to receive approval based on surrogate endpoints sooner than possible for trials with clinical or survival endpoints, rather than deriving from any explicit shortening of the FDA approval timeline, as is the case with priority review.

The accelerated approval pathway is usually contingent on a sponsor's agreement to conduct, in a diligent manner, additional post-approval confirmatory studies to verify and describe the drug's clinical benefit. As a result, a drug candidate approved on this basis is subject to rigorous post-marketing compliance requirements, including the completion of Phase 4 or post-approval clinical trials to confirm the effect on the clinical endpoint. Failure to conduct required post-approval studies, or confirm a clinical benefit during post-marketing studies, would allow the FDA to initiate expedited proceedings to withdraw approval of the drug. All promotional materials for drug candidates approved under accelerated regulations are subject to prior review by the FDA.

The FDA's Decision on an NDA

On the basis of the FDA's evaluation of the NDA and accompanying information, including the results of the inspection of the manufacturing facilities, the FDA may issue an approval letter or a complete response letter. An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. A complete response letter generally outlines the deficiencies in the submission and may require substantial additional testing or information in order for the FDA to reconsider the application. If and when those deficiencies have been addressed to the FDA's satisfaction in a resubmission of the NDA, the FDA will issue an approval letter. The FDA has committed to reviewing such resubmissions in two or six months depending on the type of information included. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

If the FDA approves a product, it may limit the approved indications for use for the product, require that contraindications, warnings or precautions be included in the product labeling, require that post-approval studies, including Phase 4 clinical trials, be conducted to further assess the drug's safety after approval, require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution restrictions or other risk management mechanisms, including REMS, which can materially affect the potential market and profitability of the product. The FDA may prevent or limit further marketing of a product based on the results of post-market studies or surveillance programs. After approval, many types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further testing requirements and FDA review and approval.

Post-Approval Requirements

Drugs manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion and reporting of adverse experiences with the product. After approval, most changes to the approved product, such as adding new

indications or other labeling claims, are subject to prior FDA review and approval. There also are continuing, annual user fee requirements for any marketed products and the establishments at which such products are manufactured, as well as new application fees for supplemental applications with clinical data.

In addition, drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and state agencies, and are subject to periodic unannounced inspections by the FDA and these state agencies for compliance with cGMP requirements. Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting and documentation requirements upon the sponsor and any third-party manufacturers that the sponsor may decide to use. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance.

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess new safety risks; or imposition of distribution or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, suspension of the approval, or complete withdrawal of the product from the market or product recalls;
- fines, warning letters or holds on post-approval clinical trials;
- refusal of the FDA to approve pending NDAs or supplements to approved NDAs;
- product seizure or detention, or refusal to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates the marketing, labeling, advertising and promotion of prescription drug products placed on the market. This regulation includes, among other things, standards and regulations for direct-to-consumer advertising, communications regarding unapproved uses, industry-sponsored scientific and educational activities, and promotional activities involving the Internet and social media. Promotional claims about a drug's safety or effectiveness are prohibited before the drug is approved. After approval, a drug product generally may not be promoted for uses that are not approved by the FDA, as reflected in the product's prescribing information. In the United States, healthcare professionals are generally permitted to prescribe drugs for such uses not described in the drug's labeling, known as off-label uses, because the FDA does not regulate the practice of medicine. However, FDA regulations impose rigorous restrictions on manufacturers' communications, prohibiting the promotion of off-label uses. It may be permissible, under very specific, narrow conditions, for a manufacturer to engage in non-promotional, non-misleading communication regarding off-label information, such as distributing scientific or medical journal information. If a company is found to have promoted off-label uses, it may become subject to adverse public relations and administrative and judicial enforcement by the FDA, the Department of Justice, or the Office of the Inspector General of the Department of Health and Human Services, as well as state authorities. This could subject a company to a range of penalties that could have a significant commercial impact, including civil and criminal fines and agreements that materially restrict the manner in which a company promotes or distributes drug products. The federal government has levied large civil and criminal fines against companies for alleged improper promotion, and has also requested that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed.

In addition, the distribution of prescription pharmaceutical products is subject to the Prescription Drug Marketing Act, or PDMA, and its implementation regulations, as well as the Drug Supply Chain Security Act, or DSCSA, which regulate the distribution and tracing of prescription drugs and prescription drug samples at the federal level, and set minimum standards for the regulation of drug distributors by the states. The PDMA, its implementing regulations and state laws limit the distribution of prescription pharmaceutical product samples, and the DSCSA imposes requirements to ensure accountability in distribution and to identify and remove counterfeit and other illegitimate products from the market.

Abbreviated New Drug Applications for Generic Drugs

In 1984, with passage of the Hatch-Waxman Amendments to the FDCA, Congress established an abbreviated regulatory scheme allowing the FDA to approve generic drugs that are shown to contain the same active ingredients as, and to be bioequivalent to, drugs previously approved by the FDA pursuant to NDAs. To obtain approval of a generic drug, an applicant must submit an abbreviated new drug application, or ANDA, to the agency. An ANDA is a comprehensive submission that contains, among other things, data and information pertaining to the active pharmaceutical ingredient, bioequivalence, drug product formulation, specifications and stability of the generic drug, as well as analytical methods, manufacturing process validation data and quality control procedures. ANDAs are "abbreviated" because they generally do not include preclinical and clinical data to demonstrate safety and effectiveness. Instead, in support of such applications, a generic manufacturer may rely on the preclinical and clinical testing previously conducted for a drug product previously approved under an NDA, known as the reference-listed drug, or RLD.

Specifically, in order for an ANDA to be approved, the FDA must find that the generic version is identical to the RLD with respect to the active ingredients, the route of administration, the dosage form, the strength and the conditions of use of the drug. At the same time, the FDA must also determine that the generic drug is "bioequivalent" to the innovator drug. Under the statute, a generic drug is bioequivalent to a RLD if "the rate and extent of absorption of the drug do not show a significant difference from the rate and extent of absorption of the listed drug..."

Upon approval of an ANDA, the FDA indicates whether the generic product is "therapeutically equivalent" to the RLD in its publication "Approved Drug Products with Therapeutic Equivalence Evaluations," also referred to as the "Orange Book." Physicians and pharmacists consider a therapeutic equivalent generic drug to be fully substitutable for the RLD. In addition, by operation of certain state laws and numerous health insurance programs, the FDA's designation of therapeutic equivalence often results in substitution of the generic drug without the knowledge or consent of either the prescribing physician or patient.

Under the Hatch-Waxman Amendments, the FDA may not approve an ANDA until any applicable period of non-patent exclusivity for the RLD has expired. The FDCA provides a period of five years of non-patent data exclusivity for a new drug containing a new chemical entity. For the purposes of this provision, a new chemical entity, or NCE, is a drug that contains no active moiety that has previously been approved by the FDA in any other NDA. An active moiety is the molecule or ion responsible for the physiological or pharmacological action of the drug substance. In cases where such NCE exclusivity has been granted, an ANDA may not be filed with the FDA until the expiration of five years unless the submission is accompanied by a Paragraph IV certification, in which case the applicant may submit its application four years following the original product approval.

The FDCA also provides for a period of three years of exclusivity if the NDA includes reports of one or more new clinical investigations, other than bioavailability or bioequivalence studies, that were conducted by or for the applicant and are essential to the approval of the application. This three-year exclusivity period often protects changes to a previously approved drug product, such as a new dosage form, route of administration, combination or indication. Three-year exclusivity would be available for a

drug product that contains a previously approved active moiety, provided the statutory requirement for a new clinical investigation is satisfied. Unlike five-year NCE exclusivity, an award of three-year exclusivity does not block the FDA from accepting ANDAs seeking approval for generic versions of the drug as of the date of approval of the original drug product. The FDA typically makes decisions about awards of data exclusivity shortly before a product is approved.

Under FDARA, a priority review track will be established for certain generic drugs, requiring the FDA to review a drug application within eight months for a drug that has three or fewer approved drugs listed in the *Orange Book* and is no longer protected by any patent or regulatory exclusivities, or is on the FDA's drug shortage list. The new legislation also authorizes the FDA to expedite review of "competitor generic therapies" or drugs with inadequate generic competition, including holding meetings with or providing advice to the drug sponsor prior to submission of the application.

505(b)(2) NDAs

As an alternative path to FDA approval for modifications to formulations or uses of products previously approved by the FDA pursuant to an NDA, an applicant may submit an NDA under Section 505(b)(2) of the FDCA. Section 505(b)(2) was enacted as part of the Hatch-Waxman Amendments and permits the filing of an NDA where at least some of the information required for approval comes from studies not conducted by, or for, the applicant. If the 505(b)(2) applicant can establish that reliance on FDA's previous findings of safety and effectiveness is scientifically and legally appropriate, it may eliminate the need to conduct certain preclinical or clinical studies of the new product. The FDA may also require companies to perform additional studies or measurements, including clinical trials, to support the change from the previously approved reference drug. The FDA may then approve the new product candidate for all, or some, of the label indications for which the reference drug has been approved, as well as for any new indication sought by the 505(b)(2) applicant.

Hatch-Waxman Patent Certification and the 30-Month Stay

Upon approval of an NDA or a supplement thereto, NDA sponsors are required to list with the FDA each patent with claims that cover the applicant's product or an approved method of using the product. Each of the patents listed by the NDA sponsor is published in the Orange Book. When an ANDA applicant files its application with the FDA, the applicant is required to certify to the FDA concerning any patents listed for the reference product in the Orange Book, except for patents covering methods of use for which the ANDA applicant is not seeking approval. To the extent that the Section 505(b)(2) applicant is relying on studies conducted for an already approved product, the applicant is required to certify to the FDA concerning any patents listed for the approved product in the Orange Book to the same extent that an ANDA applicant would.

Specifically, the applicant must certify with respect to each patent that:

- the required patent information has not been filed;
- the listed patent has expired;
- the listed patent has not expired, but will expire on a particular date and approval is sought after patent expiration; or
- the listed patent is invalid, unenforceable or will not be infringed by the new product.

A certification that the new product will not infringe the already approved product's listed patents or that such patents are invalid or unenforceable is called a Paragraph IV certification. If the applicant does not challenge the listed patents or indicates that it is not seeking approval of a patented method of use, the application will not be approved until all the listed patents claiming the referenced product have expired, other than method of use patents involving indications for which the applicant is not seeking approval.

If the ANDA or 505(b)(2) applicant has provided a Paragraph IV certification to the FDA, the applicant must also send notice of the Paragraph IV certification to the NDA and patent holders once the ANDA or 505(b)(2) application has been accepted for filing by the FDA. The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice of the Paragraph IV certification. The filing of a patent infringement lawsuit within 45 days after the receipt of a Paragraph IV certification automatically prevents the FDA from approving the application until the earlier of 30 months after the receipt of the Paragraph IV notice, expiration of the patent, or a decision in the infringement case that is favorable to the applicant. The ANDA or 505(b)(2) application also will not be approved until any applicable non-patent exclusivity listed in the Orange Book for the branded reference drug has expired.

Pediatric Studies and Exclusivity

Under the Pediatric Research Equity Act, an NDA or supplement thereto must contain data that are adequate to assess the safety and effectiveness of the drug product for the claimed indications in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. With enactment of the FDASIA in 2012, sponsors must also submit pediatric study plans prior to the assessment data. Those plans must contain an outline of the proposed pediatric study or studies the applicant plans to conduct, including study objectives and design, any deferral or waiver requests, and any other information required by regulation. The applicant, the FDA, and the FDA's internal review committee must then review the information submitted, consult with each other, and agree upon a final plan. The FDA or the applicant may request an amendment to the plan at any time.

In addition, FDARA requires the FDA to meet early in the development process to discuss pediatric study plans with drug sponsors. The legislation requires the FDA to meet with drug sponsors by no later than the end-of-phase 1 meeting for serious or life-threatening diseases and by no later than 90 days after the FDA's receipt of the study plan.

The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements. Additional requirements and procedures relating to deferral requests and requests for extension of deferrals are contained in FDASIA. Unless and until the FDA promulgates a regulation stating otherwise, the pediatric data requirements do not apply to products with orphan designation.

Pediatric exclusivity is another type of non-patent marketing exclusivity in the United States and, if granted, provides for the attachment of an additional six months of marketing protection to the term of any existing regulatory exclusivity, including the non-patent and orphan exclusivity. This six-month exclusivity may be granted if an NDA sponsor submits pediatric data that fairly respond to a written request from the FDA for such data. The data do not need to show the product to be effective in the pediatric population studied; rather, if the clinical trial is deemed to fairly respond to the FDA's request, the additional protection is granted. If reports of requested pediatric studies are submitted to and accepted by the FDA within the statutory time limits, whatever statutory or regulatory periods of exclusivity or patent protection cover the product are extended by six months. This is not a patent term extension, but it effectively extends the regulatory period during which the FDA cannot approve another application. With regard to patents, the six-month pediatric exclusivity period will not attach to any patents for which a generic (ANDA or 505(b)(2) NDA) applicant submitted a paragraph IV patent certification, unless the NDA sponsor or patent owner first obtains a court determination that the patent is valid and infringed by a proposed generic product.

Orphan Drug Designation and Exclusivity

Under the Orphan Drug Act, the FDA may designate a drug product as an "orphan drug" if it is intended to treat a rare disease or condition, generally meaning that it affects fewer than 200,000 individuals in the United States, or more in cases in which there is no reasonable expectation that the cost of developing and making a drug product available in the United States for treatment of the disease or condition will be recovered from sales of the product. A company must request orphan drug designation before submitting an NDA for that drug for that rare disease or condition. If the request is granted, the FDA will disclose the identity of the therapeutic agent and its potential use. Orphan drug designation does not shorten the PDUFA goal dates for the regulatory review and approval process, although it does convey certain advantages, such as tax benefits and exemptions from the PDUFA application fee.

If a product with orphan designation receives the first FDA approval for the disease or condition for which it has such designation or for a select indication or use within the rare disease or condition for which it was designated, the product generally will receive orphan drug exclusivity. Orphan drug exclusivity means that the FDA may not approve another sponsor's marketing application for the same drug for the same indication for seven years, except in certain limited circumstances. Orphan drug exclusivity does not block the approval of a different drug for the same rare disease or condition, nor does it block the approval of the same drug for different indications. If a drug or drug product designated as an orphan product ultimately receives marketing approval for an indication broader than what was designated on its orphan product application, it may not be entitled to exclusivity.

Under FDARA, orphan exclusivity will not bar approval of another orphan drug under certain circumstances, including if a subsequent product with the same drug for the same indication is shown to be clinically superior to the approved product on the basis of greater efficacy or safety, or providing a major contribution to patient care, or if the company with orphan drug exclusivity is not able to meet market demand. The new legislation reverses prior precedent holding that the Orphan Drug Act unambiguously required the FDA to recognize orphan exclusivity regardless of a showing of clinical superiority.

Patent Term Restoration and Extension

A patent claiming a new drug product may be eligible for a limited patent term extension, also known as patent term restriction, under the Hatch-Waxman Act, which permits a patent restoration of up to five years for patent term lost during product development and the FDA regulatory review. Patent term extension is generally available only for drug products whose active ingredient has not previously been approved by the FDA. The restoration period granted is typically one-half the time between the effective date of an IND and the submission date of an NDA, plus the time between the submission date of an NDA and the ultimate approval date. Patent term extension cannot be used to extend the remaining term of a patent past a total of 14 years from the product's approval date. Only one patent applicable to an approved drug product is eligible for the extension, and the application for the extension must be submitted prior to the expiration of the patent in question. A patent that covers multiple drugs for which approval is sought can only be extended in connection with one of the approvals. The United States PTO reviews and approves the application for any patent term extension in consultation with the FDA.

FDA Approval and Regulation of Companion Diagnostics

If safe and effective use of a therapeutic product depends on an *in vitro* diagnostic medical device, then the FDA generally will require approval or clearance of that diagnostic, known as an *in vitro* companion diagnostic device, at the same time that the FDA approves the therapeutic product. In August 2014, the FDA issued final guidance clarifying the requirements that will apply to approval of therapeutic products and *in vitro* companion diagnostic devices. According to the guidance, for novel drugs, an *in vitro* companion diagnostic device and its corresponding therapeutic should be approved or cleared contemporaneously by the FDA for the use indicated in the therapeutic product's labeling.

If FDA determines that an *in vitro* companion diagnostic device is essential to the safe and effective use of a novel therapeutic product or indication, FDA generally will not approve the therapeutic product or new therapeutic product indication if the *in vitro* companion diagnostic device is not approved or cleared for that indication. Approval or clearance of the *in vitro* companion diagnostic device will ensure that the device has been adequately evaluated and has adequate performance characteristics in the intended population.

Under the FDCA, *in vitro* diagnostics, including *in vitro* companion diagnostic devices, are generally regulated as medical devices. In the United States, the FDCA and its implementing regulations, and other federal and state statutes and regulations govern, among other things, medical device design and development, preclinical and clinical testing, premarket clearance or approval, registration and listing, manufacturing, labeling, storage, advertising and promotion, sales and distribution, export and import, and post-market surveillance. Unless an exemption applies, diagnostic tests require marketing clearance or approval from the FDA prior to commercial distribution. The two primary types of FDA marketing authorization applicable to a medical device are premarket notification, also called 510(k) clearance, and premarket approval, or PMA approval. The FDA has generally required *in vitro* companion diagnostic devices intended to select the patients who will respond to a drug to obtain a PMA for that diagnostic simultaneously with approval of the drug.

The PMA process, including the gathering of clinical and preclinical data and the submission to and review by the FDA, can take several years or longer. It involves a rigorous premarket review during which the applicant must prepare and provide the FDA with reasonable assurance of the device's safety and effectiveness and information about the device and its components regarding, among other things, device design, manufacturing and labeling. PMA applications are subject to an application fee, which exceeds $250,000 for most PMAs. In addition, PMAs for certain devices must generally include the results from extensive preclinical and adequate and well-controlled clinical trials to establish the safety and effectiveness of the device for each indication for which FDA approval is sought. In particular, for a diagnostic, a PMA application typically requires data regarding analytical and clinical validation studies. As part of the PMA review, the FDA will typically inspect the manufacturer's facilities for compliance with the Quality System Regulation, or QSR, which imposes elaborate testing, control, documentation and other quality assurance requirements.

PMA approval is not guaranteed, and the FDA may ultimately respond to a PMA submission with a not approvable determination based on deficiencies in the application and require additional clinical trial or other data that may be expensive and time-consuming to generate and that can substantially delay approval. If the FDA's evaluation of the PMA application is favorable, the FDA typically issues an approvable letter requiring the applicant's agreement to specific conditions, such as changes in labeling, or specific additional information, such as submission of final labeling, in order to secure final approval of the PMA. If the FDA's evaluation of the PMA or manufacturing facilities is not favorable, the FDA will deny approval of the PMA or issue a not approvable letter. A not approvable letter will outline the deficiencies in the application and, where practical, will identify what is necessary to make the PMA approvable. The FDA may also determine that additional clinical trials are necessary, in which case the PMA approval may be delayed for several months or years while the trials are conducted and then the data submitted in an amendment to the PMA. If the FDA concludes that the applicable criteria have been met, the FDA will issue a PMA for the approved indications, which can be more limited than those originally sought by the applicant. The PMA can include post-approval conditions that the FDA believes necessary to ensure the safety and effectiveness of the device, including, among other things, restrictions on labeling, promotion, sale and distribution. Once granted, PMA approval may be withdrawn by the FDA if compliance with post approval requirements, conditions of approval or other regulatory standards are not maintained or problems are identified following initial marketing.

After a device is placed on the market, it remains subject to significant regulatory requirements. Medical devices may be marketed only for the uses and indications for which they are cleared or approved.

Device manufacturers must also establish registration and device listings with the FDA. A medical device manufacturer's manufacturing processes and those of its suppliers are required to comply with the applicable portions of the QSR, which cover the methods and documentation of the design, testing, production, processes, controls, quality assurance, labeling, packaging and shipping of medical devices. Domestic facility records and manufacturing processes are subject to periodic unscheduled inspections by the FDA. The FDA also may inspect foreign facilities that export products to the United States.

The 21st Century Cures Act

On December 13, 2016, President Obama signed the Cures Act into law. The Cures Act is designed to modernize and personalize healthcare, spur innovation and research, and streamline the discovery and development of new therapies through increased federal funding of particular programs. It authorizes increased funding for the FDA to spend on innovation projects. The new law also amends the Public Health Service Act to reauthorize and expand funding for the National Institutes of Health. The Act establishes the NIH Innovation Fund to pay for the cost of development and implementation of a strategic plan, early stage investigators and research. It also charges NIH with leading and coordinating expanded pediatric research. Further, the Cures Act directs the Centers for Disease Control and Prevention to expand surveillance of neurological diseases.

With amendments to the FDCA and the Public Health Service Act, or PHSA, Title III of the Cures Act seeks to accelerate the discovery, development, and delivery of new medicines and medical technologies. To that end, and among other provisions, the Cures Act reauthorizes the existing priority review voucher program for certain drugs intended to treat rare pediatric diseases until 2020; creates a new priority review voucher program for drug applications determined to be material national security threat medical countermeasure applications; revises the FDCA to streamline review of combination product applications; requires FDA to evaluate the potential use of "real world evidence" to help support approval of new indications for approved drugs; provides a new "limited population" approval pathway for antibiotic and antifungal drugs intended to treat serious or life-threatening infections; and authorizes FDA to designate a drug as a "regenerative advanced therapy," thereby making it eligible for certain expedited review and approval designations.

On August 3, 2017, Congress passed the FDARA. FDARA reauthorizes the various user fees to facilitate the agency's review and oversight relating to prescription drugs, generic drugs, medical devices, and biosimilars. The legislation also includes several policy riders that will impact an array of issues within the FDA's authority including, among others, pediatric study requirements, orphan drug exclusivity, and the approval process for generic drugs.

Regulation and Procedures Governing Approval of Medicinal Products in the European Union

In addition to regulations in the United States, we will be subject to a variety of foreign regulations governing clinical trials and commercial sales and distribution of setmelanotide to the extent we choose to sell any setmelanotide outside of the United States. Whether or not we obtain FDA approval for a product, we must obtain approval of a product by equivalent competent authorities in foreign jurisdictions before we can commence clinical trials or marketing of the product in those countries. The approval process varies from country to country and the time may be longer or shorter than that required for FDA approval. The requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary greatly from country to country. As in the United States, post-approval regulatory requirements, such as those regarding product manufacture, marketing, or distribution would apply to any product that is approved outside the United States.

The process governing the marketing authorization of medicinal products in the European Union entails satisfactory completion of preclinical studies and adequate and well-controlled clinical trials to establish the safety, quality and efficacy of the medicinal product for each proposed therapeutic indication.

It also requires the submission to the relevant competent authorities of a marketing authorization application, or MAA, and granting of a marketing authorization by these authorities before the product can be marketed and sold in the European Union.

Clinical Trial Approval

The Clinical Trials Directive 2001/20/EC, the Directive 2005/28/EC on Good Clinical Practice, or GCP, and the related national implementing provisions of the individual EU member states govern the system for the approval of clinical trials in the European Union. Under this system, an applicant must obtain prior approval from the competent national authority of the EU member states in which the clinical trial is to be conducted. Furthermore, the applicant may only start a clinical trial at a specific study site after the competent ethics committee has issued a favorable opinion. The clinical trial application must be accompanied by, among other documents, an investigational medicinal product dossier (the Common Technical Document) with supporting information prescribed by Directive 2001/20/EC, Directive 2005/28/EC, where relevant the implementing national provisions of the individual EU member states and further detailed in applicable guidance documents.

In April 2014, the new Clinical Trials Regulation, (EU) No 536/2014 (Clinical Trials Regulation) was adopted. The Regulation is anticipated to enter into force in 2019. The Clinical Trials Regulation will be directly applicable in all the EU member states, repealing the current Clinical Trials Directive 2001/20/EC. Conduct of all clinical trials performed in the European Union will continue to be bound by currently applicable provisions until the new Clinical Trials Regulation becomes applicable. The extent to which on-going clinical trials will be governed by the Clinical Trials Regulation will depend on when the Clinical Trials Regulation becomes applicable and on the duration of the individual clinical trial. If a clinical trial continues for more than three years from the day on which the Clinical Trials Regulation becomes applicable the Clinical Trials Regulation will at that time begin to apply to the clinical trial.

The new Clinical Trials Regulation aims to simplify and streamline the approval of clinical trials in the European Union. The main characteristics of the regulation include: a streamlined application procedure via a single entry point, the "EU portal"; a single set of documents to be prepared and submitted for the application as well as simplified reporting procedures for clinical trial sponsors; and a harmonized procedure for the assessment of applications for clinical trials, which is divided in two parts. Part I is assessed by the competent authorities of all EU member states in which an application for authorization of a clinical trial has been submitted (member states concerned). Part II is assessed separately by each member state concerned. Strict deadlines have been established for the assessment of clinical trial applications. The role of the relevant ethics committees in the assessment procedure will continue to be governed by the national law of the concerned EU member state. However, overall related timelines will be defined by the Clinical Trials Regulation.

Marketing Authorization

To obtain a marketing authorization for a product under European Union regulatory systems, an applicant must submit an MAA either under a centralized procedure administered by the European Medicines Agency, or EMA, or one of the procedures administered by competent authorities in the EU member states (decentralized procedure, national procedure or mutual recognition procedure). A marketing authorization may be granted only to an applicant established in the European Union. Regulation (EC) No 1901/2006 provides that prior to obtaining a marketing authorization in the European Union, applicants have to demonstrate compliance with all measures included in an EMA-approved Paediatric Investigation Plan, or PIP, covering all subsets of the pediatric population, unless the EMA has granted (1) a product-specific waiver, (2) a class waiver or (3) a deferral for one or more of the measures included in the PIP.

The centralized procedure provides for the grant of a single marketing authorization by the European Commission that is valid for all EU member states and three of the four European Free Trade Association, or EFTA, States, Iceland, Liechtenstein and Norway. Pursuant to Regulation (EC) No 726/2004, the centralized procedure is compulsory for specific products, including for medicines produced by certain biotechnological processes, products designated as orphan medicinal products, advanced therapy products and products with a new active substance indicated for the treatment of certain diseases, including products for the treatment of cancer. For products with a new active substance indicated for the treatment of other diseases and products that are highly innovative or for which a centralized process is in the interest of patients, the centralized procedure may be optional.

Under the centralized procedure, the Committee for Medicinal Products for Human Use, or the CHMP, established at the EMA is responsible for conducting the initial assessment of a product. The CHMP is also responsible for several post-authorization and maintenance activities, such as the assessment of modifications or extensions to an existing marketing authorization. Under the centralized procedure in the European Union, the maximum timeframe for the evaluation of an MAA is 210 days, excluding clock stops, when additional information or written or oral explanation is to be provided by the applicant in response to questions of the CHMP. Accelerated evaluation might be granted by the CHMP in exceptional cases, when a medicinal product is of major interest from the point of view of public health and in particular from the viewpoint of therapeutic innovation. If the CHMP accepts such request, the time limit of 210 days will be reduced to 150 days but it is possible that the CHMP can revert to the standard time limit for the centralized procedure if it considers that it is no longer appropriate to conduct an accelerated assessment. At the end of this period, the EMA's Committee for Medicinal Products for Human Use ("CHMP") provides a scientific opinion on whether or not a marketing authorization should be granted in relation to a medicinal product. Within 15 calendar days of receipt of a final opinion from the CHMP, the European Commission must prepare a draft decision concerning an application for marketing authorization. This draft decision must take the opinion and any relevant provisions of EU law into account. Before arriving at a final decision on an application for centralized authorization of a medicinal product the European Commission must consult the Standing Committee on Medicinal Products for Human Use. The Standing Committee is composed of representatives of the EU member states and chaired by a non-voting European Commission representative. The European Parliament also has a related "droit de regard". The European Parliament's role is to ensure that the European Commission has not exceeded its powers in deciding to grant or refuse to grant a marketing authorization.

Unlike the centralized authorization procedure, the decentralized marketing authorization procedure requires a separate application to, and leads to separate approval by, the competent authorities of each EU member state in which the product is to be marketed. This application is identical to the application that would be submitted to the EMA for authorization through the centralized procedure. The reference EU member state prepares a draft assessment and drafts of the related materials within 120 days after receipt of a valid application. The resulting assessment report is submitted to the concerned EU member states who, within 90 days of receipt, must decide whether to approve the assessment report and related materials. If a concerned EU member state cannot approve the assessment report and related materials due to concerns relating to a potential serious risk to public health, disputed elements may be referred to the European Commission, whose decision is binding on all EU member states.

The mutual recognition procedure similarly is based on the acceptance by the competent authorities of the EU member states of the marketing authorization of a medicinal product by the competent authorities of other EU member states. The holder of a national marketing authorization may submit an application to the competent authority of an EU member state requesting that this authority recognize the marketing authorization delivered by the competent authority of another EU member state.

Regulatory Data Protection in the European Union

In the European Union, innovative medicinal products approved on the basis of a complete independent data package qualify for eight years of data exclusivity upon marketing authorization and an additional two years of market exclusivity pursuant to Directive 2001/83/EC. Regulation (EC) No 726/2004 repeats this entitlement for medicinal products authorized in accordance the centralized authorization procedure. Data exclusivity prevents applicants for authorization of generics of these innovative products from referencing the innovator's data to assess a generic (abbreviated) application for a period of eight years. During an additional two-year period of market exclusivity, a generic marketing authorization application can be submitted and authorized, and the innovator's data may be referenced, but no generic medicinal product can be placed on the European Union market until the expiration of the market exclusivity. The overall ten-year period will be extended to a maximum of 11 years if, during the first eight years of those ten years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies. Even if a compound is considered to be a new chemical entity so that the innovator gains the prescribed period of data exclusivity, another company nevertheless could also market another version of the product if such company obtained marketing authorization based on an MAA with a complete independent data package of pharmaceutical tests, preclinical tests and clinical trials.

Periods of Authorization and Renewals

A marketing authorization has an initial validity for five years in principle. The marketing authorization may be renewed after five years on the basis of a re-evaluation of the risk-benefit balance by the EMA or by the competent authority of the EU member state. To this end, the marketing authorization holder must provide the EMA or the competent authority with a consolidated version of the file in respect of quality, safety and efficacy, including all variations introduced since the marketing authorization was granted, at least six months before the marketing authorization ceases to be valid. The European Commission or the competent authorities of the EU member states may decide, on justified grounds relating to pharmacovigilance, to proceed with one further five year period of marketing authorization. Once subsequently definitively renewed, the marketing authorization shall be valid for an unlimited period. Any authorization which is not followed by the actual placing of the medicinal product on the European Union market (in case of centralized procedure) or on the market of the authorizing EU member state within three years after authorization ceases to be valid (the so-called sunset clause).

Orphan Drug Designation and Exclusivity

Regulation (EC) No. 141/2000, as implemented by Regulation (EC) No. 847/2000 provides that a drug can be designated as an orphan drug by the European Commission if its sponsor can establish: that the product is intended for the diagnosis, prevention or treatment of (1) a life-threatening or chronically debilitating condition affecting not more than five in ten thousand persons in the European Union when the application is made, or (2) a life-threatening, seriously debilitating or serious and chronic condition in the European Union and that without incentives it is unlikely that the marketing of the drug in the European Union would generate sufficient return to justify the necessary investment. For either of these conditions, the applicant must demonstrate that there exists no satisfactory method of diagnosis, prevention or treatment of the condition in question that has been authorized in the European Union or, if such method exists, the drug will be of significant benefit to those affected by that condition.

Once authorized, orphan medicinal products are entitled to 10 years of market exclusivity in all EU member states and in addition a range of other benefits during the development and regulatory review process including scientific assistance for study protocols, authorization through the centralized marketing authorization procedure covering all member countries and a reduction or elimination of registration and marketing authorization fees. However, marketing authorization may be granted to a similar medicinal

product with the same orphan indication during the 10 year period with the consent of the marketing authorization holder for the original orphan medicinal product or if the manufacturer of the original orphan medicinal product is unable to supply sufficient quantities. Marketing authorization may also be granted to a similar medicinal product with the same orphan indication if this product is safer, more effective or otherwise clinically superior to the original orphan medicinal product. The period of market exclusivity may, in addition, be reduced to six years if it can be demonstrated on the basis of available evidence that the original orphan medicinal product is sufficiently profitable not to justify maintenance of market exclusivity

Regulatory Requirements after a Marketing Authorization has been Obtained

In case an authorization for a medicinal product in the European Union is obtained, the holder of the marketing authorization is required to comply with a range of requirements applicable to the manufacturing, marketing, promotion and sale of medicinal products. These include:

- Compliance with the European Union's stringent pharmacovigilance or safety reporting rules must be ensured. These rules can impose post-authorization studies and additional monitoring obligations.

- The manufacturing of authorized medicinal products, for which a separate manufacturer's license is mandatory, must also be conducted in strict compliance with the applicable European Union laws, regulations and guidance, including Directive 2001/83/EC, Directive 2003/94/EC, Regulation (EC) No 726/2004 and the European Commission Guidelines for Good Manufacturing Practice. These requirements include compliance with European Union cGMP standards when manufacturing medicinal products and active pharmaceutical ingredients, including the manufacture of active pharmaceutical ingredients outside of the European Union with the intention to import the active pharmaceutical ingredients into the European Union.

- The marketing and promotion of authorized drugs, including industry-sponsored continuing medical education and advertising directed toward the prescribers of drugs and/or the general public, are strictly regulated in the European Union notably under Directive 2001/83EC, as amended, and EU member state laws.

Regulatory Procedure Governing CE marking Companion Diagnostics in the European Union

In the European Union, *in vitro* medical devices are required to conform with the essential requirements of the European Union Directive on *in vitro* diagnostic medical devices (Directive No 98/79/EC, as amended). To demonstrate compliance with the essential requirements, the manufacturer must undergo a conformity assessment procedure. The conformity assessment varies according to the type of *in vitro* diagnostic medical device. The conformity assessment of *in vitro* diagnostic medical devices can require the intervention of a Notified Body, which is an organization designated by the competent authorities of an EU member state to conduct conformity assessments. The Notified Body will issue a CE Certificate of Conformity following successful completion of a conformity assessment procedure conducted in relation to the *in vitro* diagnostic medical device and its manufacturer and their conformity with the requirements of the Directive. This Certificate entitles the manufacturer to affix the CE mark to its medical device after having prepared and signed a related EC Declaration of Conformity. For *in vitro* diagnostic medical devices which do not require the intervention of a notified body, the manufacturer can issue an EC Declaration of Conformity based on a self-assessment of the conformity of its products with the Essential Requirements laid down in the *in vitro* diagnostic medical device Directive.

Brexit and the Regulatory Framework in the United Kingdom

On June 23, 2016, the electorate in the United Kingdom voted in favor of leaving the European Union, commonly referred to as Brexit. Thereafter, on March 29, 2017, the country formally notified the

European Union of its intention to withdraw pursuant to Article 50 of the Lisbon Treaty. The withdrawal of the United Kingdom from the European Union will take effect either on the effective date of the withdrawal agreement or, in the absence of agreement, two years after the United Kingdom provides a notice of withdrawal pursuant to the E.U. Treaty. Since the regulatory framework for pharmaceutical products in the United Kingdom. covering quality, safety and efficacy of pharmaceutical products, clinical trials, marketing authorization, commercial sales and distribution of pharmaceutical products is derived from European Union directives and regulations, Brexit could materially impact the future regulatory regime which applies to products and the approval of product candidates in the United Kingdom. It remains to be seen how, if at all, Brexit will impact regulatory requirements for product candidates and products in the United Kingdom.

Pharmaceutical Coverage and Reimbursement

In the United States and markets in other countries, patients who are prescribed treatments for their conditions and providers performing the prescribed services generally rely on third-party payors to reimburse all or part of the associated healthcare costs. Patients are unlikely to use setmelanotide unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of our products. Significant uncertainty exists as to the coverage and reimbursement status of products approved by the FDA and other government authorities. Even if setmelanotide is approved, sales will depend, in part, on the extent to which third-party payors, including government health programs in the United States such as Medicare and Medicaid, commercial health insurers and managed care organizations, provide coverage, and establish adequate reimbursement levels for, such products. The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the product once coverage is approved. Third-party payors are increasingly challenging the prices charged, examining the medical necessity, and reviewing the cost-effectiveness of medical products and services and imposing controls to manage costs. Third-party payors may limit coverage to specific products on an approved list, also known as a formulary, which might not include all of the approved products for a particular indication.

In order to secure coverage and reimbursement for any product that might be approved for sale, a company may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of the product, in addition to the costs required to obtain FDA or other comparable marketing approvals. Nonetheless, setmelanotide may not be considered medically necessary or cost effective. A decision by a third-party payor not to cover setmelanotide could reduce physician utilization of our products once approved and have a material adverse effect on our sales, results of operations and financial condition. Additionally, a payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. Further, one payor's determination to provide coverage for a drug product does not assure that other payors will also provide coverage and reimbursement for the product, and the level of coverage and reimbursement can differ significantly from payor to payor. Third-party reimbursement and coverage may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development.

The containment of healthcare costs also has become a priority of federal, state and foreign governments and the prices of drugs have been a focus in this effort. Governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit a company's revenue generated from the sale of any approved products. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which a company or its collaborators receive marketing approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

Outside the United States, ensuring adequate coverage and payment for setmelanotide will face challenges. Pricing of prescription pharmaceuticals is subject to governmental control in many countries. Pricing negotiations with governmental authorities can extend well beyond the receipt of regulatory marketing approval for a product and may require us to conduct a clinical trial that compares the cost effectiveness of setmelanotide or products to other available therapies. The conduct of such a clinical trial could be expensive and result in delays in our commercialization efforts.

In the European Union, pricing and reimbursement schemes vary widely from country to country. Some countries provide that products may be marketed only after a reimbursement price has been agreed. Some countries may require the completion of additional studies that compare the cost-effectiveness of a particular drug candidate to currently available therapies or so called Health Technology Assessments, in order to obtain reimbursement or pricing approval. For example, the European Union provides options for its member states to restrict the range of products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. EU member states may approve a specific price for a product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the product on the market. Other EU member states allow companies to fix their own prices for products, but monitor and control prescription volumes and issue guidance to physicians to limit prescriptions.

Healthcare Law and Regulation

Healthcare providers and third-party payors play a primary role in the recommendation and prescription of drug products that are granted marketing approval. Arrangements and interactions with healthcare professionals, third-party payors, and patients, among others, are subject to broadly applicable fraud and abuse, anti-kickback, false claims laws, patient privacy laws and regulations and other healthcare laws and regulations that may constrain our business and/or financial arrangements, particularly once third-party reimbursement, including under Medicare, Medicaid or other federally-funded health care programs, becomes available for one or more of our products. The federal and state healthcare laws and regulations that may affect our ability to operate include, but are not limited to the following:

- the United States federal Anti-Kickback Statute, which prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, paying, or receiving remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, lease, order or arranging for or recommending the purchase, lease, or order of any good or service, for which payment may be made, in whole or in part, by federal healthcare programs such as Medicare and Medicaid. This statute has been interpreted to apply to arrangements between pharmaceutical companies on one hand and prescribers, purchasers and formulary managers on the other. Liability under the Anti-Kickback Statute may be established without proving actual knowledge of the statute or specific intent to violate it. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal civil False Claims Act. Although there are a number of statutory exemptions and regulatory safe harbors to the federal Anti-Kickback Statute protecting certain common business arrangements and activities from prosecution or regulatory sanctions, the exemptions and safe harbors are drawn narrowly. Practices that involve remuneration to those who prescribe, purchase, or recommend pharmaceutical and biological products, including certain discounts, or engaging such individuals as consultants, advisors and speakers, may be subject to scrutiny if they do not fit squarely within an exemption or safe harbor. Our practices may not in all cases meet all of the criteria for safe harbor protection from anti-kickback liability. Moreover, there are no safe harbors for many common practices, such as educational and research grants, charitable donations, product support and patient assistance programs;

- the federal civil False Claims Act prohibits individuals or entities from, among other things, knowingly presenting, or causing to be presented, a false or fraudulent claim for payment of government funds, or knowingly making, using or causing to made or used a false record or statement material to an obligation to pay money to the government or knowingly concealing or knowingly and improperly avoiding, decreasing, or concealing an obligation to pay money to the federal government. Actions under the False Claims Act may be brought by the Attorney General or as a qui tam action by a private individual in the name of the government. Many pharmaceutical manufacturers have been investigated and have reached substantial financial settlements with the federal government under the civil False Claims Act for a variety of alleged improper activities including causing false claims to be submitted as a result of the marketing of their products for unapproved and thus non-reimbursable uses, inflating prices reported to private price publication services which are used to set drug payment rates under government healthcare programs, and other interactions with prescribers and other customers including those that may have affected their billing or coding practices and submission to the federal government. The government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal civil False Claims Act. Pharmaceutical and other healthcare companies also are subject to other federal false claims laws, including, among others, federal criminal healthcare fraud and false statement statutes that extend to non-government health benefit programs;

- the federal Health Insurance Portability and Accountability Act of 1996, as amended by the Health Information Technology for Economic and Clinical Health Act, or HIPAA, which imposes criminal and civil liability for, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, or knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement or representation, or making or using any false writing or document knowing the same to contain any materially false, fictitious or fraudulent statement or entry, in connection with the delivery of or payment for healthcare benefits, items or services;

- HIPAA and its implementing regulations, which impose obligations with respect to safeguarding the privacy, security and transmission of individually identifiable health information;

- the federal transparency requirements known as the federal Physician Payments Sunshine Act, being implemented as the Open Payments Program requires certain manufacturers of drugs, devices, biologics and medical supplies report payments and other transfers of value to physicians and teaching hospitals, as well as ownership and investments interests held by physicians and their immediate family members. Pharmaceutical and biological manufacturers with products for which payment is available under Medicare, Medicaid or the State Children's Health Insurance Program are required to submit a report to the Centers for Medicare and Medicaid Services within the U.S. Department of Health and Human Services on or before the 90th day of each calendar year disclosing reportable payments made in the previous calendar year; and

- analogous state laws and regulations, such as state anti-kickback and false claims laws, which may apply to healthcare items or services that are reimbursed by non-governmental third-party payors, including private insurers.

In addition to the foregoing requirements, several states now require prescription drug companies to report expenses relating to the marketing and promotion of drug products and to report gifts and payments to individual physicians in these states. Other states prohibit various other marketing-related activities. Still other states require the posting of information relating to clinical studies and their outcomes. In addition, California, Connecticut, Nevada, and Massachusetts require pharmaceutical companies to implement compliance programs and/or marketing codes. Several additional states are considering similar proposals. Numerous federal, state and foreign laws and regulations also govern the privacy and security of health

information and the collection, use, disclosure, and protection of health-related and other personal information, including state data breach notification laws, state health information privacy laws, and federal and state consumer protection laws, such as Section 5 of the FTC Act, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts. Compliance with these laws is difficult and time consuming, and companies that do not comply with these state laws may face civil penalties.

Compliance with such laws and regulations will require substantial resources. If our operations are found to be in violation of any of the laws described above or any other governmental regulations that apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, imprisonment, exclusion from government-funded healthcare programs like Medicare and Medicaid, and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our financial results.

For additional information regarding obligations under federal health care programs, refer to the risk factor entitled "*If we participate in the Medicaid Drug Rebate Progarm and fail to comply with our reporting and payment obligations under that program or other governmental pricing programs that we participate in, we could be subject to additional reimbursement requirements, penalties, sanctions and fines, which could have a material adverse effect on our business, financial condition, results of operations and growth prospects*."

Healthcare Reform

A primary trend in the United States healthcare industry and elsewhere is cost containment. There have been a number of federal and state proposals during the last few years regarding the pricing of pharmaceutical and biopharmaceutical products, limiting coverage and reimbursement for drugs and other medical products, government control and other changes to the healthcare system in the United States.

By way of example, the United States and state governments continue to propose and pass legislation designed to reduce the cost of healthcare. In March 2010, President Obama signed into law the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, or collectively the ACA, which, among other things, includes changes to the coverage and payment for products under government health care programs. Among the provisions of the ACA of importance to our potential drug candidates are:

- an annual, nondeductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government healthcare programs, although this fee does not apply to sales of certain products approved exclusively for orphan indications;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to certain individuals with income at or below 133% of the federal poverty level, thereby potentially increasing a manufacturer's Medicaid rebate liability;
- expansion of manufacturers' rebate liability under the Medicaid Drug Rebate Program by increasing the minimum rebate for both branded and generic drugs and revising the definition of "average manufacturer price," or AMP, for calculating and reporting Medicaid drug rebates on outpatient prescription drug prices and extending rebate liability to prescriptions for individuals enrolled in Medicare Advantage plans;
- introduction of a price reporting requirement for drugs that are inhaled, instilled, implanted, injected, or infused and not generally dispensed through retail community pharmacies;
- addition of more entity types eligible for participation in the Public Health Service 340B drug pricing program, or the 340B program;

- established the Medicare Part D coverage gap discount program by requiring manufacturers to provide a 50% point-of-sale-discount off the negotiated price of applicable brand drugs to eligible beneficiaries during their coverage gap period as a condition for the manufacturers' outpatient drugs to be covered under Medicare Part D;

- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research;

- the Independent Payment Advisory Board, or IPAB, which has authority to recommend certain changes to the Medicare program to reduce expenditures by the program that could result in reduced payments for prescription drugs. However, the IPAB implementation has been not been clearly defined. ACA provided that under certain circumstances, IPAB recommendations or recommendations of the Secretary of Health and Human Services will become law unless Congress enacts legislation that will achieve the same or greater Medicare cost savings; and

- established the Center for Medicare and Medicaid Innovation within CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending.

Other legislative changes have been proposed and adopted in the United States since the ACA was enacted. For example, beginning April 1, 2013, Medicare payments for all items and services, including drugs and biologics, were reduced by 2% under the sequestration (i.e., automatic spending reductions) required by the Budget Control Act of 2011, as amended by the American Taxpayer Relief Act of 2012. Subsequent legislation extended the 2% reduction, on average, to 2025.

- Legislative changes to or regulatory changes under the ACA remain possible and appear likely in the 115th U.S. Congress and under the Trump administration. The nature and extent of any legislative or regulatory changes to the ACA, including repeal and replacement initiatives, are uncertain at this time. It is possible that ACA repeal and replacement initiatives, if enacted into law, could ultimately result in fewer individuals having health insurance coverage or in individuals having insurance coverage with less generous benefits. The scope of potential future legislation to modify or repeal and replace ACA provisions is highly uncertain in many respects.

Employees

We have leveraged skilled experts, consultants, CROs, and contractors to manage our clinical operations, under the leadership and direction of our management. We will expand our infrastructure to manage our clinical, finance and commercial operations with additional full-time employees.

We have 15 employees who are directly employed by us, four of whom hold Ph.D. or M.D. degrees. Of these employees, ten are engaged in development and commercial activities and five are engaged in support administration, including business development and finance. None of these employees are represented by labor unions or covered by collective bargaining agreements. We consider our relationships with these employees to be good.

Facilities

Our offices are located at a 6,830 square foot facility in Boston, Massachusetts used primarily for corporate functions. The lease for this space expires in May 2021.

Legal Proceedings

We are not currently a party to any material legal proceedings.

MANAGEMENT

Executive Officers and Directors

The following table sets forth the names, ages and positions of our directors and executive officers. Each executive officer is employed by us pursuant to a letter agreement entered into as of November 2016 except for Hunter Smith and Nithya Desikan, who entered into letter agreements as of July 2017. Prior to November 2016, each executive officer other than Hunter Smith and Nithya Desikan provided services to us pursuant to the Payroll Services Agreement, which was terminated in November 2016. Each executive officer will be elected annually and will serve until his re-election, or earlier resignation or removal. The executive officers, other than Hunter Smith and Nithya Desikan and directors have served as executive officers and directors of us, the LLC entity, the Predecessor Company and/or the Relamorelin Company during the periods set forth below. We refer to each of these persons as our executive officers.

Name	Age	Position(s)
Keith M. Gottesdiener, M.D.	63	Chief Executive Officer, President and Director
Hunter Smith	49	Chief Financial Officer and Treasurer
Nithya Desikan	38	Chief Commercial Officer
Lex H.T. Van der Ploeg, Ph.D.	62	Chief Scientific Officer
Fred T. Fiedorek, M.D.	62	Chief Medical Officer
Todd Foley(1)	45	Director
Ed Mathers(3)	57	Director
Neil Exter(1)	58	Director
Christophe R. Jean(2)	61	Director
Jonathan T. Silverstein, J.D.(1)(4)	50	Director
David P. Meeker(2)(3)	62	Director and Chairman
David W.J. McGirr(2)(3)	62	Director

(1) Member of Compensation Committee.

(2) Member of Audit Committee.

(3) Member of Governance and Nominating Committee.

(4) Mr. Silverstein will step down from our board of directors effective as of the closing of this offering.

Keith M. Gottesdiener, M.D. | *Chief Executive Officer and President*

Dr. Gottesdiener has been Chief Executive Officer and a member of the board of directors since October 2011 and was chairman of the board of directors from that date until April 2017. He has been President since August 2017. He joined the Predecessor Company after 16 years at Merck Research Laboratories, or Merck. Dr. Gottesdiener joined Merck early clinical development in 1995, helping to transition compounds from the bench to the bedside and through to proof of concept. He held positions of increasing responsibility, eventually leading Merck's early clinical development across all therapeutic areas from 2001 through early 2006. From 2006 to 2011, he was a leader of Merck's late clinical development organization, first overseeing the development of Merck's infectious diseases and vaccine products through pivotal trials, registration, and life cycle management, including Gardasil™ (HPV Vaccine), Rotateq™ (rotavirus vaccine), Zostavax™ (zoster vaccine) and Isentress™ (HIV integrase inhibitor), among others. In 2008, Dr. Gottesdiener was appointed Late Stage Therapeutic Group Leader, and in that role led Merck's late-stage clinical development efforts (from Phase 2 thru patent expiry) across all therapeutic areas. After Merck's merger with Schering Plough in 2009, he continued as co-head of late development. Dr. Gottesdiener received his B.A. from Harvard College and his M.D. from the University of Pennsylvania. He completed his residency and fellowship at the Brigham and Women's Hospital-Beth Israel Medical Center-Dana Farber Cancer Institute Children's Hospital programs. After his fellowship,

Dr. Gottesdiener did postdoctoral research in the laboratory of Dr. Jack Strominger at Dana Farber Cancer Institute working on the molecular immunology of the T-cell receptor. In 1986, he joined the faculty as an assistant professor at Columbia University, started an independent research laboratory with NIH RO-1 funding, focusing on gene transcription, and was Associate Clinical Professor of Medicine at the time he left to join Merck in 1995. Dr. Gottesdiener was a director and the chief executive officer of the Relamorelin Company until December 2016. Dr. Gottesdiener is currently a director of Intercept Pharmaceuticals and the LLC entity. In addition, Dr. Gottesdiener is the chief executive officer of the LLC entity, a position from which he will resign prior to the consummation of this offering. We believe that Dr. Gottesdiener's detailed knowledge of our company, his extensive experience in the pharmaceutical industry as a senior executive, and his research work for both medical and academic institutions provide him with the qualifications to serve as director of our company.

Hunter Smith | *Chief Financial Officer and Treasurer*

Mr. Smith has been Chief Financial Officer since July 2017 and Treasurer since August 2017. He has more than 20 years of global finance and management experience across multiple industries and financial disciplines, including expertise in business analysis and planning, mergers and acquisitions, capital raising and investor relations. Previously, he was Vice President, Finance and Chief Financial Officer of the Inflammation and Immunology Business Unit at Celgene Corporation from 2013 to July 2017. In this role, Mr. Smith provided finance leadership for the global launch of Otezla®, co-led the integration of Receptos, Inc. following its acquisition by Celgene, and led global business planning and analysis for commercial affiliates and clinical study activities in over 16 countries. Before joining Celgene, Mr. Smith worked in roles of increasing responsibility at Bunge Limited from 1999 to 2013, including Director of Investor Relations, Chief Financial Officer—Asia, Corporate Treasurer, and Chief Financial Officer of Bunge's Sugar and Bioenergy Segment. Mr. Smith also serves as an Independent Director of Genessee & Wyoming Inc. and is a member of its compensation committee. Mr. Smith holds an MBA in Finance from New York University's Stern School of Business and a B.A. in History, with honors, from Northwestern University.

Nithya Desikan | *Chief Commercial Officer*

Ms. Desikan has been Chief Commercial Officer since July 2017. She has over 15 years of experience commercializing new therapies in domestic and global markets. Previously, Ms. Desikan worked at Biogen Inc., where she served most recently as Vice President and Asset Executive, from September 2016 to July 2017, overseeing global profit and loss account for TECFIDERA® and supporting the product's position as the #1 prescribed oral therapy in multiple sclerosis and from November 2015 to September 2016, building a team to support the Biogen pipeline for the clinical development of inflammatory bowel disease. Prior to that, Ms. Desikan held the role of Vice President and Program Executive from September 2014 to November 2015, where she led Biogen's Hematology business, now the Biogen spin-off, Bioverativ, to drive the growth of ALPROLIX® and ELOCTATE® and the development of multiple preclinical assets. Before that, from February 2012 to September 2014, Ms. Desikan built the strategy to support the U.S. launch of ALPROLIX, Biogen's first entrant into the orphan hemophilia market. Before joining Biogen Inc., Ms. Desikan spent 12 years at Johnson & Johnson in the United States and China, supporting brands including: XARELTO®, LEVAQUIN®, TOPAMAX®, ULTRACET®, NUCYNTA®, NUCYNTA®ER and VELCADE®. Ms. Desikan holds a B.S. in Material Science Engineering, with honors, from the University of Florida.

Lex H.T. Van der Ploeg, Ph.D. | *Chief Scientific Officer*

Dr. Van der Ploeg has been Chief Scientific Officer since October 2011. He has more than 25 years of drug development experience focused on obesity, metabolic disorders, oncology, and neurodegenerative diseases. Before joining the Predecessor Company, he was Senior Vice President of Integrative Medicine

and Translational Science at Abraxis Bioscience and Head of R&D at Abraxis Health; both companies were acquired by Celgene Corporation. Prior to that, he held R&D leadership roles at Merck directing drug development programs in metabolism, oncology, and neurodegenerative diseases as Vice President, Basic Research and Site Head, Merck Boston; Site Head, Merck San Diego; and Head, Obesity Research for Merck Rahway and Banyu, Japan. Previously, Dr. Van der Ploeg was an associate professor in the Department of Genetics and Development at Columbia University. He has received numerous awards and grants for his research and has published more than 200 peer-reviewed research papers. Dr. Van der Ploeg is a named inventor on more than 50 patents and patent applications. Dr. Van der Ploeg was the Chief Scientific Officer of the Relamorelin Company was until December 2016. Dr. Van der Ploeg is currently the Chief Scientific Officer of the LLC entity, a position from which he will resign prior to the consummation of this offering. He received an M.S. in Biochemistry from the University of Amsterdam and a Ph.D. in Biochemistry/Enzymology/Genetics from the University of Amsterdam/Netherlands Cancer Institute.

Fred T. Fiedorek, M.D. | *Chief Medical Officer*

Dr. Fiedorek has been Chief Medical Officer since October 2014, joining us after nearly 14 years at Bristol-Myers Squibb, or BMS. He has extensive drug development experience across many therapeutic areas, ranging from early development through Phase 4 and commercial launch. Dr. Fiedorek has particular expertise in diabetes, metabolic disorders and cardiovascular disease, most recently serving as Senior Vice President, Head of Cardiovascular and Metabolic Development at BMS, where he led Phase 2 through Phase 4 global development for these therapeutic areas. Under his leadership, several new medicines achieved successful marketing authorization, including Onglyza® (saxagliptin), Farxiga™ (dapagliflozin), Eliquis® (apixaban), Myalept™ (metreleptin), Bydureon® Dual Chamber Pen, and Glucovance® (metformin/glyburide). While at BMS, Dr. Fiedorek also co-led exploratory development, helping to transition compounds from discovery stage to proof of concept patient trials. In addition, Dr. Fiedorek co-directed the Clinical Science Committee charged with providing scientific, regulatory, and biostatistical review of Phase 1 through Phase 4 clinical trials; he was a member of the Medical Review Group charged with oversight of potential emerging safety signals from marketed medicines or compounds in development; and he participated in joint development committees for BMS alliances with Astra-Zeneca, Pfizer, Otsuka, KAI Pharmaceuticals, Solvay, and Merck. Prior to joining BMS, Dr. Fiedorek held positions of increasing responsibility at Glaxo-Wellcome in Research Triangle Park, or RTP, and was International Project Leader for a Phase 3 metabolic drug development program prior to his move to BMS. Dr. Fiedorek was the Chief Medical Officer of the Relamorelin Company until December 2016. Dr. Fiedorek is currently the Chief Medical Officer of the LLC entity, a position from which he will resign prior to consummation of this offering. Dr. Fiedorek received his B.A. from Yale University and his M.D. from Harvard Medical School. He completed residency and fellowship training in Internal Medicine and Endocrinology & Metabolism at Washington University in St. Louis, including post-doctoral research on the genetics of animal models of diabetes and obesity. He also served on the faculties at Washington University School of Medicine in St. Louis and the University of North Carolina in Chapel Hill School of Medicine, including an adjunct clinical appointment while at Glaxo-Wellcome in RTP.

Todd Foley

Mr. Foley has served as a member of our board of directors since July 2014. Mr. Foley is a managing director with MPM Capital, a venture capital firm, which he joined in 1999. Prior to joining MPM, Mr. Foley worked in business development at Genentech and in management consulting with Arthur D. Little. Mr. Foley currently serves as a member of the board of directors of Chiasma, Inc., Clinical Ink, Inc., Iconic Therapeutics, Inc., Repare Therapeutics Inc., Semma Therapeutics, Inc., Switch Bio, Inc. and Tetherex Pharmaceuticals, Inc. Mr. Foley received a B.S. in chemistry from the Massachusetts Institute of Technology and an MBA from Harvard Business School. We believe that Mr. Foley's broad experience in

the life sciences industry as a venture capitalist, as well as his service on the boards of directors of numerous companies provide him with the qualifications to serve as a director of our company.

Ed Mathers

Mr. Mathers has served as a member of our board of directors since March 2013. He has been a Partner at New Enterprise Associates, or NEA, a venture capital firm, since August 2008. Mr. Mathers currently serves on the boards of directors of Amplyx Pharmaceuticals, Inc., Envisia Therapeutics Inc., Intarcia Therapeutics, Inc., Inozyme Pharma, Inc., Liquidia Technologies, Inc., Lumos Pharma, Inc., Lumena Pharmaceuticals, Inc., Mirna Therapeutics, Inc., ObsEva SA, Ra Pharmaceuticals, Inc., Satori Pharmaceuticals Incorporated, Senti Biosciences and Synlogic, LLC, all of which are biotechnology companies. In addition, Mr. Mathers is a member of the Biotechnology Industry Organization board, the Southeast BIO board and the North Carolina State Physical and Mathematical Sciences Foundation board. Prior to joining NEA, Mr. Mathers served in various corporate development roles at MedImmune, Inc., a biotechnology company that was acquired by AstraZeneca PLC in 2007, culminating in the position of Executive Vice President, Corporate Development and Venture. In this role, he also led the company's venture capital subsidiary, MedImmune Ventures, Inc., from 2002 to 2008. Mr. Mathers was a director of MedImmune, LLC, from 2007 to 2008. From 2000 to 2002, Mr. Mathers was Vice President, Marketing and Corporate Licensing and Acquisitions at Inhale Therapeutic Systems, Inc., a biopharmaceutical company, which is now known as Nektar Therapeutics, Inc. Previously, for 15 years, Mr. Mathers was at Glaxo Wellcome, Inc., where he held sales and marketing positions of increasing responsibility. Mr. Mathers received a B.S. in chemistry from North Carolina State University. We believe that Mr. Mather's extensive experience in the life sciences industry as a venture capitalist and senior executive, as well as his service on the boards of directors of numerous companies provide him with the qualifications to serve as a director of our company.

Neil Exter

Mr. Exter has served as a member of our board of directors since April 2014. He is a partner at Third Rock Ventures, where he plays an integral role in the formation, development, business strategy, and business development efforts of portfolio companies. He has more than 20 years of business development and strategic experience, facilitating the successful development and implementation of operations and collaborations across the spectrum of newly emerging and established biotech companies. Mr. Exeter is currently the interim chief operating officer of Goldfinch Bio. Prior to joining Third Rock Ventures, Mr. Exter was CBO of Alantos Pharmaceuticals and led the sale of that company to Amgen. Previously, he served as Vice President of Business Development for Millennium Pharmaceuticals. Mr. Exter is a board member of CytomX Therapeutics, Cibiem, Lotus Tissue Repair, Coridea NC1, Coridea NC2, Element Science, Goldfinch Bio, Pliant Therapeutics, Revolution Medicine, and Seventh Sense. He is a member of the Research Committee of Children's Hospital Boston, the investment committee of the Innovation Research Fund at Partners Healthcare, the Board of Directors of the New England Venture Capital Association, the Advisory Council of the Electrical and Computer Engineering Department at Cornell University, and the Board of Visitors of Columbia College. He holds an MBA as a Baker Scholar from Harvard Business School, an M.S. from Stanford University, and a B.S. from Cornell University. We believe that Mr. Exter's extensive experience in the life sciences industry as a venture capitalist and senior executive, as well as his service on the boards of directors of numerous companies provide him with the qualifications to serve as a director of our company.

Christophe R. Jean

Mr. Jean has served as a member of our board of directors since April 2015. He is Executive Vice President of Corporate Strategy, Business Development, Alliances and M&A for the Ipsen Group, a position he assumed in 2013 after serving for 11 years in the position of Executive Vice-President, Chief

Operating Officer, with responsibility for all commercial operations and medical affairs worldwide as well as Ipsen's therapeutic area franchises. Prior to joining Ipsen, Mr. Jean was President and CEO for the pharmaceutical activities of the Pierre Fabre Group and President of Europe, Middle East, and Africa for Novartis' Pharmaceutical Division. Prior to the merger of Ciba-Geigy and Sandoz that formed Novartis, he held a number of marketing and management positions in Europe and Latin America for Ciba-Geigy, culminating as Head of Finance and IT Worldwide and Member of the Pharma Executive Committee. Mr. Jean is a member of the Ipsen Group Executive Committee, the Supervisory Board of Diaxonhit, and the European Biopharmaceutical Enterprises Board. He holds an MBA from Harvard Business School. We believe that Mr. Jean's extensive experience in the life sciences industry as a senior executive provides him with the qualifications to serve as a director of our company.

Jonathan T. Silverstein, J.D.

Mr. Silverstein has served as a member of our board of directors since August 2015. He is a Partner and a Co-Head of Global Private Equity at OrbiMed, the world's largest fully dedicated healthcare fund manager. Mr. Silverstein joined OrbiMed in 1999 to focus on private equity and structured transactions in small-capitalization public biotechnology and medical device companies. From 2012 through 2016, *Forbes*® magazine has named Mr. Silverstein one of the top 100 venture capitalists in the world in its "Forbes Midas List" of top technology investors. Mr. Silverstein has a J.D. and an M.B.A. from the University of San Diego, and a B.A. in Economics from Denison University. We believe that Mr. Silverstein's extensive experience in life sciences venture capital provides him with the qualifications to serve as a director for our company. Mr. Silverstein will step down from our board of directors effective as of the closing of this offering.

David P. Meeker

Dr. Meeker has served as a member of our board of directors since November 2015 and became chairman of the board in April 2017. Dr. Meeker has served as President and Chief Executive officer of Genzyme, a unit of Sanofi, a global biotechnology company, since October 2011. Dr. Meeker oversees the company's two business units—Rare Diseases and Multiple Sclerosis. As an Executive Vice President of Sanofi, he is a member of Sanofi's Executive Committee. Dr. Meeker joined Genzyme in 1994 as Medical Director to work on the Cystic Fibrosis Gene Therapy program. Subsequently, as Vice President, Medical Affairs, he was responsible for the development of rare disease therapies that today represent transformative and life-saving advancements in medicine for patients. Prior to Genzyme's merger with Sanofi in 2011, Dr. Meeker was Genzyme's Chief Operating Officer, responsible for its commercial organization, overseeing its business units, country management organization and global market access functions. He played an important role in the integration with Sanofi. Prior to joining Genzyme, Dr. Meeker was the director of the Pulmonary Critical Care Fellowship at the Cleveland Clinic and an assistant professor of medicine at Ohio State University. Dr. Meeker is currently a member of the board of directors of MyoKardia, Inc. He has authored more than 40 articles and multiple book chapters. Dr. Meeker received his M.D. from the University of Vermont Medical School. He completed the Advanced Management Program at Harvard Business School in 2000. We believe that Dr. Meeker's deep experience as a senior executive at global pharmaceutical companies and involvement in the development and commercialization of pharmaceutical product candidates for the treatment of rare and ultra-rare diseases provide him with the qualifications to serve as a director of our company.

David W.J. McGirr

Mr. McGirr has served as a member of our board of directors since November 2015. Mr. McGirr serves as a director of Relypsa, Inc., a pharmaceutical company focused on polymer science, Insamed Incorporated, a pharmaceutical company devoted to the treatment of rare diseases, and Roka Bioscience, a molecular diagnostics company. From March 2013 until June 2014, Mr. McGirr was Senior Advisor to

the chief executive officer of Cubist Pharmaceuticals and from November 2002 to March 2013, Mr. McGirr was Senior Vice President and Chief Financial Officer of Cubist. Prior to joining Cubist in 2002, Mr. McGirr was the President and Chief Operating Officer of hippo inc, an internet technology, venture-financed company. Mr. McGirr served as a member of hippo's board of directors from 1999 to 2003. From 1996 to 1999, he was the President of GAB Robins North America, Inc., a risk management company, serving also as Chief Executive Officer from 1997 to 1999. Mr. McGirr was a private equity investor from 1995 to 1996. From 1978 to 1995, Mr. McGirr served in various positions within the S.G. Warburg Group, ultimately as Chief Financial Officer, Chief Administrative Officer and Managing Director of S.G. Warburg & Co., Inc., a position held from 1992 to 1995. Mr. McGirr received a B.Sc. in Civil Engineering from the University of Glasgow and received an M.B.A. from The Wharton School at the University of Pennsylvania. Mr. McGirr has been designated an audit committee financial expert as defined in applicable SEC rules. We believe that Mr. McGirr's senior-level executive experience in a variety of industries, including in the life sciences industry, provides him with the qualifications to serve as a director of our company.

Composition of the Board of Directors after this Offering

Our amended and restated bylaws will provide that our board of directors will consist of such number of directors as our board of directors may determine from time to time. Our board of directors currently consists of eight directors. Immediately upon the consummation of this offering, our board of directors will consist of (i) one director designated by MPM Capital, who is currently Todd Foley, and who will be continuing as a director following the offering, (ii) one director designated by NEA, who is currently Ed Mathers, and who will be continuing as a director following the offering, (iii) one director designated by Third Rock Ventures, who is currently Neil Exter, and who will be continuing as a director following the offering, (iv) one director designated by Sutrepa SAS, who is currently Christophe Jean, and who will be continuing as a director following the offering, and (v) David Meeker, David McGirr and our chief executive officer, each of whom will be continuing as a director following the offering. Our board of directors has determined that all of our directors, other than Dr. Gottesdiener, our chief executive officer, are independent for the purpose of serving on our board of directors under the independence standards promulgated by NASDAQ.

Our amended and restated certificate of incorporation and amended and restated bylaws that will become effective upon the closing of this offering will provide that our board of directors will be divided into three classes, Class I, Class II and Class III, with members of each class serving staggered three-year terms. Upon the closing of this offering, the members of the classes will be divided as follows

- our Class I directors will be Keith Gottesdiener and Christophe Jean, and their terms will expire at the annual meeting of stockholders to be held in 2018;
- our Class II directors will be Ed Mathers, Todd Foley and Neil Exter, and their terms will expire at the annual meeting of stockholders to be held in 2019; and
- our Class III directors will be David Meeker and David McGirr, and their terms will expire at the annual meeting of stockholders to be held in 2020.

Upon the expiration of the term of a class of directors, directors in that class will be eligible to be elected for a new three-year term at the annual meeting of stockholders in the year in which their term expires.

Board Leadership Structure

The positions of chairman of the board and chief executive officer are presently separated. Our board of directors recognizes the time, effort and energy that the chief executive officer is required to devote to his position in the current business environment, as well as the commitment required to serve as our

chairman, particularly as the board of directors' oversight responsibilities continue to grow. Our board of directors believes that having separate positions is the appropriate leadership structure for us at this time and demonstrates our commitment to good corporate governance.

Board Committees

Our board of directors has established the following committees: an audit committee, a compensation committee and a governance and nominating committee. The initial composition and responsibilities of each committee are described below. Members will serve on these committees until their resignation or until otherwise determined by our board of directors.

Audit Committee

Our audit committee will provide oversight of our accounting and financial reporting process, the audit of our financial statements and our internal control function. Among other matters, the audit committee will be responsible for the following: assisting the board of directors in oversight of the independent auditors' qualifications, independence and performance; the engagement, retention and compensation of the independent auditors; reviewing the scope of the annual audit; reviewing and discussing with management and the independent auditors the results of the annual audit and the review of our quarterly financial statements, including the disclosures in our annual and quarterly reports filed with the SEC; reviewing our risk assessment and risk management processes; establishing procedures for receiving, retaining and investigating complaints received by us regarding accounting, internal accounting controls or audit matters; and approving audit and permissible non-audit services provided by our independent auditor.

The current members of our audit committee are David McGirr, who is the chair of the committee, Christophe Jean, and David Meeker. All members of our audit committee meet the requirements for financial literacy under the applicable rules and regulations of the SEC and NASDAQ. Our board of directors has determined that David McGirr is an audit committee financial expert as defined under the applicable rules of the SEC and has the requisite financial sophistication as defined under the applicable rules and regulations of NASDAQ. All of the members of our audit committee are independent directors as defined under the applicable rules and regulations of the SEC and NASDAQ.

Compensation Committee

Our compensation committee will adopt and administer the compensation policies, plans and benefit programs for our executive officers and all other members of our executive team. Our compensation committee will also be responsible for making recommendations regarding non-employee director compensation to the full board of directors. In addition, among other things, our compensation committee will evaluate annually, in consultation with the board of directors, the performance of our chief executive officer, review and approve corporate goals and objectives relevant to compensation of our chief executive officer and other executives and evaluate the performance of these executives in light of those goals and objectives. Our compensation committee will also adopt and administer our equity compensation plans. The current members of our compensation committee are Neil Exter, who is the chair of the committee, Todd Foley, and Jonathan Silverstein. Following consummation of this offering Messrs. Exter and Foley will comprise our compensation committee. All of the members of our compensation committee are independent under the applicable rules and regulations of the SEC and NASDAQ, and qualify as outside directors under Section 162(m) of the Code.

Governance and Nominating Committee

Our governance and nominating committee will be responsible for, among other things, making recommendations regarding corporate governance, the composition of our board of directors, the

identification, evaluation and nomination of director candidates and the structure and composition of committees of our board of directors. In addition, our governance and nominating committee will oversee our corporate governance guidelines, approve our committee charters, oversee compliance with our code of business conduct and ethics, contribute to succession planning, review policies and procedures with respect to our related party transactions policy and oversee the board self-evaluation process. The current members of our governance and nominating committee are David Meeker, who is the chair of the committee, Ed Mathers, and David McGirr. All of the members of our governance and nominating committee are independent under the applicable rules and regulations of NASDAQ.

Compensation Committee Interlocks and Insider Participation

None of the members of our compensation committee is or has at any time during the past year been one of our officers or employees. None of our executive officers currently serves or in the past year has served as a member of the board of directors or compensation committee of any entity that has one or more executive officers serving on our board of directors or compensation committee.

Role of the Board in Risk Oversight

The audit committee of the board of directors is primarily responsible for overseeing our risk management processes on behalf of the board of directors. Going forward, we expect that the audit committee will receive reports from management at least quarterly regarding our assessment of risks. In addition, the audit committee reports regularly to the board of directors, which also considers our risk profile. The audit committee and the board of directors focus on the most significant risks we face and our general risk management strategies. While the board of directors oversees our risk management, management is responsible for day-to-day risk management processes. Our board of directors expects management to consider risk and risk management in each business decision, to proactively develop and monitor risk management strategies and processes for day-to-day activities and to effectively implement risk management strategies adopted by the audit committee and the board of directors. We believe this division of responsibilities is the most effective approach for addressing the risks we face and that the leadership structure of our board of directors, which also emphasizes the independence of the board of directors in its oversight of its business and affairs, supports this approach.

Scientific Advisory Board

Our management team is supported by a scientific advisory board composed of leading academic and industry scientists. This group generally meets quarterly with our management team either as a group or

individually to provide advice and guidance on our development programs. Our scientific advisory board consists of:

John Amatruda, M.D.	Dr. Amatruda has broad clinical development expertise in metabolic disease. Most recently, he was Senior Vice President and Franchise Head for Diabetes and Obesity at Merck & Co., Inc.
Michael Camilleri, M.D.	Dr. Camilleri is a Professor of Medicine and Physiology in the Mayo Clinic College of Medicine. He is a leading expert in gastroenterology, with a research focus on enteric neurosciences and the physiology, pathophysiology, and treatment of diseases that affect gastrointestinal motility, including gastroparesis, diabetes, obesity, and irritable bowel syndrome.
William Chin, M.D.	Dr. Chin is Chief Medical Officer and Executive Vice President at PhRMA. Formerly, he was Executive Dean for Research at Harvard Medical School, following a 10-year career at Eli Lilly and Company, where he was most recently Senior Vice President for Discovery Research and Clinical Investigation.
Lee Kaplan, M.D., Ph.D. *Chairman*	Dr. Kaplan is Director of the Obesity, Metabolism, & Nutrition Institute and was Founding Director of the Weight Center at the Massachusetts General Hospital. He is an Associate Professor of Medicine at Harvard Medical School.
Elizabeth Stoner, M.D.	Dr. Stoner is a founder of the LLC entity and served as our Chief Development Officer from 2010 through 2014. Dr. Stoner previously served in various roles at Merck, most recently as Senior Vice President of Global Clinical Development Operations, and is a Managing Director at MPM Ventures.

Code of Business Conduct and Ethics

We have adopted a code of business conduct and ethics that will apply to all of our employees, including our executive officers, and directors, and those employees responsible for financial reporting. The code of business conduct and ethics will be available on our website. We expect that, to the extent required by law, any amendments to the code, or any waivers of its requirements, will be disclosed on our website.

EXECUTIVE AND DIRECTOR COMPENSATION

This section discusses the material elements of compensation for our named executive officers and the most important factors relevant to an analysis of these policies. It provides qualitative information regarding the manner and context in which compensation is awarded to and earned by our executive officers named in the "Summary Compensation Table" below, or our named executive officers, and is intended to place in perspective the data presented in the following tables and the corresponding narrative. Our named executive officers are Keith M. Gottesdiener, M.D., Bart Henderson, our former president, and Fred T. Fiedorek, M.D. Each of our named executive officers is or was an employee of us pursuant to a letter agreement entered into November 2016, or the letter agreements. Prior to entering into the letter agreements, each of our named executive officers was an employee of the Relamorelin Company and provided services to us pursuant to a Payroll Services Agreement with the Relamorelin Company. The compensation discussed below was paid to our executive officers by us and/or the Relamorelin Company and the compensation decisions discussed below were made either by the compensation committee of the LLC entity's board of managers, which we refer to as the LLC committee, or the compensation committee of our board of directors, which we refer to as the committee.

In preparing to become a public company, we have begun a thorough review of all elements of the compensation of our executives, including our compensation philosophy and the function and design of our equity incentive programs. We have begun and expect to continue to evaluate the existing executive compensation program to ensure our program is competitive with the companies with which we compete for executive talent and is appropriate for a public company.

Summary Compensation Table

The following table presents compensation awarded in 2016 and 2015, to our named executive officers or accrued for those executive officers for services rendered during 2016 and 2015.

Name & Principal Position	Year	Salary ($)	Stock Awards ($)[1]	Option Awards ($)[2]	Non-Equity Incentive Plan Compensation ($)[3]	Total ($)[4]
Keith M. Gottesdiener, M.D.	2016	$ 476,500	—	—	$ 85,770	$ 562,270
Chief Executive Officer and President	2015	$ 463,508	—	$ 1,282,757	$ 231,754	$ 1,978,019
Bart Henderson	2016	$ 339,000	—	—	$ 54,240	$ 393,240
Former President	2015	$ 329,772	—	$ 579,871	$ 131,909	$ 1,041,552
Fred T. Fiedorek, M.D.	2016	$ 344,400	—	—	$ 37,195	$ 381,595
Chief Medical Officer	2015	$ 335,000	$ 567,934	$ 349,164	$ 117,250	$ 1,369,348

(1) Reflects the full grant date fair value of restricted common units of the LLC entity granted by the LLC entity in 2015.

(2) The amounts reflect the full grant date fair value for awards granted during 2015. The grant date fair value was computed in accordance with ASC Topic 718, Compensation—Stock Compensation. The assumptions we used in valuing options are described in Note 7 to our audited financial statements contained herein.

(3) Amounts represent incentive payments earned in 2016 and paid during 2017, or earned in 2015 and paid during 2016, as applicable, based on achievement of performance goals and other factors.

(4) Reflects compensation for services by the named executive officers. Pursuant to the Payroll Services Agreement, the 2015 and part of the 2016 costs were shared with the Relamorelin Company on a proportional use basis. Costs have been allocated consistent with Staff Accounting Bulletin Topic 1B.

Executive Compensation

Overview

Our executive compensation program is based on a pay-for-performance philosophy. The committee designed our executive compensation program to achieve the following primary objectives: provide compensation and benefit levels that will attract, retain, motivate and reward a highly talented executive team within the context of responsible cost management; establish a direct link between our individual/team performance and results and our executives' compensation; and align the interests and objectives of our executives with those of our stockholders by linking executive equity awards to stockholder value creation. The compensation program for our executive officers is composed primarily of the following three main components: base salary, annual cash incentives and long-term equity incentives.

Base Salary

The 2016 base salaries were determined for each named executive officer by the committee, which gives consideration to each officer's experience, expertise and performance, as well as market compensation levels for similar positions.

Name	2016 Base Salary ($)
Keith M. Gottesdiener, M.D.	476,500
Bart Henderson	339,000
Fred T. Fiedorek, M.D.	344,400

The 2016 base salary for each named executive officer became effective on January 1, 2016.

Annual Performance-Based Incentive Opportunity

In addition to base salaries, our named executive officers are eligible to receive annual performance-based cash incentives, which are designed to motivate our executives to achieve defined annual corporate goals and to reward our executives for their contributions towards achievement of these goals. The annual performance-based incentive each named executive officer was eligible to receive in 2016 was generally based on the extent to which the officer achieved the corporate goals that the LLC committee established at the beginning of 2016. After the end of 2016, the committee reviewed performance against each goal and determined the extent to which each goal was achieved.

The committee generally considered each named executive officer's individual contributions towards reaching the annual corporate goals but did not establish specific individual goals for each of them. Pursuant to the terms of their respective agreements governing their employment relationship, described below under "Agreements with our Named Executive Officers," Dr. Gottesdiener is eligible to receive a target bonus of up to 50% of his base salary, Mr. Henderson while serving as an executive officer, was eligible to receive a target bonus of up to 50% of his base salary, and Dr. Fiedorek is eligible to receive a target bonus of up to 35% of his base salary. However, there is no minimum bonus percentage or amount established for the named executive officers and, as a result, the bonus amounts have varied from year to year based on corporate and individual performance.

In December 2016, the committee reviewed the 2016 corporate goals and determined that on an overall basis, significant progress had been made towards achieving all of those goals. In recognition of this achievement and the efforts of each executive, the committee awarded each of our named executive officers eligible for performance bonuses a portion of their target bonus opportunity for 2016. For 2016, Dr. Gottesdiener received an aggregate bonus of $246,589, $160,819 of which was paid by the Relamorelin Company and $85,770 of which was paid by us. Mr. Henderson received an aggregate bonus of $155,940, $101,700 of which was paid by the Relamorelin Company and $54,240 of which was paid by us, and

Dr. Fiedorek received an aggregate bonus of $114,685, $77,490 of which was paid by the Relamorelin Company and $37,195 of which was paid by us.

Outstanding Equity Awards at End of 2016

The following table provides information about outstanding equity awards held by each of our named executive officers at December 31, 2016. All options were granted under the Plan.

	Option Awards[1][2]				Stock Awards	
Name	Number of Securities Underlying Unexercised Options (#) Exercisable	Number of Securities Underlying Unexercised Options (#) Unexercisable	Option Exercise Price ($)	Option Expiration Date	Number of Shares or Units of Stock That Have Not Vested	Market Value of Shares or Units or Other Rights That Have Not Vested
Keith M. Gottesdiener, M.D.	839,991(3)	1,531,747	$ 0.50	11/16/2025	—	—
	185,938(3)	339,062	$ 0.82	12/30/2025	—	—
	—	—	—	—	23,000(5)	$ 421,130
Bart Henderson	386,842(3)	705,418	$ 0.50	11/16/2025	—	—
	79,688(3)	145,312	$ 0.82	12/30/2025	—	—
	—	—	—	—	12,000(5)	$ 219,720
Fred T. Fiedorek, M.D.	259,219(3)	472,693	$ 0.50	11/16/2025	—	—
	31,875(4)	58,125	$ 0.82	12/30/2025	—	—
	—	—	—	—	51,443(6)	$ 941,921

(1) These options vest in 48 equal monthly installments, starting on August 3, 2015, except that the last installment, if necessary, may be smaller.

(2) Upon an option holder's termination of employment on account of the option holder's death or disability, these options expire on the first anniversary of the option holder's termination. If an option holder's employment terminates for any other reason, these options expire three months after the option holder's termination.

(3) If the option holder's employment is terminated within the three months preceding or the 12 months immediately following a change of control of us, 100% of the option holder's equity awards will become immediately exercisable.

(4) If the option holder's employment is terminated within the three months preceding or the 12 months immediately following a sale of us (as defined in his previous letter agreement with the Relamorelin Company and his current letter agreement with us), the vesting of all of the option holder's equity awards, including these options, will be accelerated such that up to 50% of the option holder's equity awards will become immediately exercisable. If, at the time of the change of control, 50% of the option holder's equity awards are already vested, there will be no further acceleration of vesting.

(5) Represents the unvested portion of restricted common units of the LLC entity granted by the LLC entity on March 21, 2013. The restricted common units vested fully upon the Distribution.

(6) Represents the unvested portion of restricted common units of the LLC entity granted by the LLC entity on June 1, 2015. The restricted common units vest in 48 equal monthly installments beginning October 21, 2014.

(7) Mr. Henderson resigned from employment with us in June 2017, but pursuant to the terms of his consulting agreement with us, he will continue to vest in any restricted equity held by him through and including December 31, 2017.

Pension Benefits

Our named executive officers did not participate in, or otherwise receive any benefits under, any pension or retirement plan during 2016, other than pursuant to the 401(k) plan described under "401(k) Plan."

Nonqualified Deferred Compensation

Our named executive officers did not participate in, or earn any benefits under, a nonqualified deferred compensation plan during 2016.

Agreements with our Named Executive Officers

In November 2016, each named executive officer entered into a letter agreement with us on the terms as described below. We anticipate that, prior to this offering, upon the recommendation of our committee as we prepare to become a public company, our named executive officers will enter into new letter agreements with us on terms substantially similar to those described below.

Agreement with Dr. Gottesdiener. Under Dr. Gottesdiener's letter agreement, he is entitled to an annual base salary of $476,500, subject to adjustment in the committee's sole discretion, is eligible to receive an annual target performance bonus of up to 50% of his base salary, as determined by the committee, and is entitled to certain severance benefits, the terms of which are described below under "—Potential Payments Upon Termination or Change of Control."

Agreement with Mr. Henderson. Under Mr. Henderson's letter agreement, he is entitled to an annual base salary of $335,000, subject to adjustment in the committee's sole discretion, is eligible to receive an annual target performance bonus of up to 50% of his base salary, as determined by the committee, and is entitled to certain severance benefits, the terms of which are described below under "—Potential Payments Upon Termination or Change of Control."

On June 12, 2017, Mr. Henderson resigned his employment and entered into a consulting agreement with us to provide transition services.

Agreement with Dr. Fiedorek. Under Dr. Fiedorek's letter agreement, he is entitled to an annual base salary of $344,400, subject to adjustment in the committee's sole discretion, is eligible to receive an annual target performance bonus of up to 35% of his base salary, as determined by the committee, and is entitled to certain severance benefits, the terms of which are described below under "—Potential Payments Upon Termination or Change of Control."

Potential Payments Upon Termination or Change of Control

Regardless of the manner in which a named executive officer's employment terminates, each named executive officer is entitled to receive amounts earned during his term of employment, including salary and unused vacation pay. In addition, each of our named executive officers is eligible to receive certain benefits pursuant to his letter agreement as described below.

Dr. Gottesdiener. Under the terms of Dr. Gottesdiener's letter agreement, upon termination without "cause," as defined below, or for "good reason," as defined below, subject to customary conditions, including his execution and nonrevocation of an acceptable release, Dr. Gottesdiener will be entitled to receive a severance payment in an aggregate amount equal to 12 months of his base salary then in effect, paid in substantially equal installments over a period of 12 months in accordance with ordinary payroll practices.

Upon a termination without "cause" or for "good reason" within the three months immediately preceding or the 12 months immediately following a "sale of the company" as defined in the letter

agreement, subject to customary conditions, including his execution and nonrevocation of an acceptable release, Dr. Gottesdiener, in lieu of the above benefits, will be entitled to receive a severance payment in an aggregate amount equal to 12 months of his base salary then in effect, paid in substantially equal installments over a period of 12 months in accordance with ordinary payroll practices, and a payment equal to 100% of his annual target bonus for the year in which the termination occurs. In addition, each unvested equity award held by Dr. Gottesdiener granted by both us or the LLC entity will immediately become fully vested.

Upon termination, Dr. Gottesdiener is entitled to reimbursement of his medical benefit premiums for so long as he is either entitled to severance under his letter agreement or otherwise becomes ineligible for COBRA, whichever is earlier.

Mr. Henderson. Under the terms of Mr. Henderson's letter agreement, upon termination without "cause," as defined below, or for "good reason," as defined below, subject to customary conditions, including his execution and nonrevocation of an acceptable release, Mr. Henderson will be entitled to receive a severance payment in an aggregate amount equal to six months of his base salary then in effect, paid in substantially equal installments over a period of six months in accordance with ordinary payroll practices.

Upon a termination without "cause" or for "good reason" within the three months immediately preceding or the 12 months immediately following a "sale of the company" as defined in his letter agreement, subject to customary conditions, including his execution and nonrevocation of an acceptable release. Mr. Henderson, in lieu of the above benefits, will be entitled to receive a severance payment in an aggregate amount equal to 12 months of his base salary then in effect, paid in substantially equal installments, over a period of 12 months in accordance with ordinary payroll practices, and a payment equal to 100% of his annual target bonus for the year in which the termination occurs. In addition, each unvested equity award held by Mr. Henderson granted by both us or the LLC entity will immediately become fully vested.

Upon termination, Mr. Henderson is entitled to reimbursement of his medical benefit premiums for so long as he is either entitled to severance under his letter agreement or otherwise becomes ineligible for COBRA, whichever is earlier.

On June 12, 2017, Mr. Henderson resigned his employment and entered into a consulting agreement with us to provide transition services.

Dr. Fiedorek. Under the terms of Dr. Fiedorek's letter agreement, upon termination without "cause," as defined below, or for "good reason," as defined below, subject to customary conditions, including his execution and nonrevocation of an acceptable release, Dr. Fiedorek will be entitled to receive a severance payment in an aggregate amount equal to six months of his base salary then in effect, paid in substantially equal installments over a period of six months in accordance with ordinary payroll practices.

Upon a termination without "cause" or for "good reason" within the three months immediately preceding or the 12 months immediately following a "sale of the company" as defined in his letter agreement, subject to customary conditions, including his execution and nonrevocation of an acceptable release. Dr. Fiedorek, in lieu of the above benefits, will be entitled to receive a severance payment in an aggregate amount equal to 12 months of his base salary then in effect, paid in substantially equal installments, over a period of 12 months in accordance with ordinary payroll practices, and a payment equal to 100% of his annual target bonus for the year in which the termination occurs. In addition, up to 50% of the unvested equity awards held by Dr. Fiedorek granted by both us or the LLC entity will immediately become fully vested. However, if 50% or more of Dr. Fiedorek's equity awards have already vested, there will be no further acceleration of vesting.

Upon termination, Dr. Fiedorek is entitled to reimbursement of his medical benefit premiums for so long as he is either entitled to severance under his letter agreement or otherwise becomes ineligible for COBRA, whichever is earlier.

For purposes of these letter agreements and those we intend to enter into with our named executive officers, "cause" generally means the occurrence of any of the following events by the individual: (i) commission of any crime involving fraud, breach of trust, or physical or emotional harm to any person, moral turpitude or dishonesty; (ii) any unauthorized use or disclosure of proprietary information (other than any such use or disclosure that is not intentional and is not material); (iii) any intentional misconduct or gross negligence that has a material adverse effect on business or reputation; (iv) any material breach by the executive of any agreement that is not cured within 30 days after receipt of notice; or (v) repeated and willful failure to perform the duties, functions and responsibilities of his position after a written warning from us.

For purposes of the letter agreements, "good reason" generally means resignation by the executive from all positions if, without the executive's written consent, there is a (i) material diminution of duties or authority; (ii) material reduction of the executive's base salary not pursuant to a program affecting all or substantially all employees unless the executive is affected to a greater extent than other similarly situated employees pursuant to such a program; or (iii) requirement to relocate the primary work location to a location that would increase the one way commute distance by more than 35 miles from the executive's primary work location as of immediately prior to such change, in each case, provided that the executive provides written notice within 30 days following such event, and failure to remedy the event within 30 days following receipt of such notice and the executive's resignation is effective no more than 30 days following the expiration of a cure period. Good reason may also occur if the executive resigns from all positions on the one year anniversary of a change in control if the executive has not entered into a written letter or agreement providing for the executive's continued employment with us or our successor.

Employee Benefit and Stock Plans

Amended and Restated 2015 Equity Incentive Plan

We currently have an amended and restated 2015 equity incentive plan which was subsequently amended as of January 2017 and is in effect prior to the closing of this offering, or the Plan, which we expect our board of directors and our stockholders to amend and restate effective immediately prior to the completion of this offering. The following summary of the material terms of the Plan does not purport to be complete and is qualified by reference to the full text of the Plan, which we will file as an exhibit to our registration statement of which this prospectus is a part.

The Plan provides for the grant of incentive stock options and nonstatutory stock options, stock appreciation rights, restricted stock and restricted stock unit awards, performance units, stock grants and qualified performance-based awards (that is, any of the foregoing that are intended to constitute performance-based compensation under Section 162(m) of the Code), which we collectively refer to as "awards" in connection with the Plan. Our directors, officers and other employees, as well as others performing consulting or advisory services for us, are eligible for grants under the Plan. The purpose of the Plan is to provide incentives that will attract, retain and motivate highly competent officers, directors, employees and consultants and advisors to promote the success of our business and align employees' interests with stockholders' interests.

Administration

Under its terms, the Plan is administered by the compensation committee of our board of directors which is made up of independent outside non-employee directors for purposes of applicable securities and tax laws. The board of directors itself may also exercise any of the powers and responsibilities under the Plan. The compensation committee may delegate to an executive officer or officers the authority to grant

awards under the Plan subject to applicable law and to guidelines specified by the compensation committee. Subject to the terms of the Plan, the compensation committee will select the recipients of awards and determine, among other things, the:

- number of shares of common stock covered by awards and the dates upon which such awards become exercisable or any restrictions to which they are subject lapse, as applicable;
- type of award and the exercise or purchase price and method of payment for each such award;
- vesting period for awards, risks of forfeiture and any potential acceleration of vesting or lapses in risks of forfeiture; and
- duration of awards.

All decisions, determinations and interpretations made in good faith by the compensation committee with respect to the Plan and the terms and conditions of or operation of any award are final and binding on all participants, beneficiaries, heirs, assigns or other persons holding or claiming rights under the Plan or any award.

Available Shares

Subject to the following sentence, the aggregate number of shares of our common stock which may be issued under the Plan or with respect to which awards may be granted may not exceed shares (including pursuant to incentive stock options), which may be either authorized and unissued shares of our common stock or shares of common stock held in or acquired for our treasury. The number of shares authorized under the Plan will be increased each January 1, commencing on the first January 1 following consummation of our initial public offering, by an amount equal to 4% of outstanding shares of stock as of the end of the immediately preceding fiscal year. Notwithstanding the foregoing, our board of directors may act prior to January 1 of a given year to provide that there will be no such January 1 increase in the number of shares of stock authorized under the Plan for such year or that the increase in the number of shares of stock authorized under the Plan for such year will be a lesser number than would otherwise occur pursuant to the preceding sentence. Notwithstanding the preceding sentences, in no event shall the number of shares available for issuance pursuant to incentive options over the term of the Plan exceed shares of stock. In general, if awards under the Plan are for any reason cancelled, or expire or terminate unexercised, the number of shares covered by such awards will again be available for the grant of awards under the Plan.

Eligibility for Participation

Members of our board of directors, as well as employees of, and consultants and advisors to, us or any of our subsidiaries and affiliates are eligible to receive awards under the Plan. The selection of participants is within the sole discretion of the compensation committee.

Individual Limitations

The maximum number of shares of common stock that may be subject to options or stock appreciation rights or any combination thereof granted to any one person during any single calendar year shall be . The maximum number of shares of common stock that may be subject to all other awards granted to any one person during any single calendar year that are intended to be qualified performance-based awards shall be . The maximum value of awards denominated in cash granted to any one person other than a non-employee member of our board of directors during any single calendar year and that are intended to be qualified performance-based awards shall be $. The maximum value of awards denominated in cash granted to any non-employee member of our board of directors during any single calendar year shall be $. Each of the foregoing limitations shall be doubled with respect to awards granted to an individual during the first calendar year in which he or she commences employment.

Incentive Stock Options

Incentive stock options are options that are intended to qualify as incentive stock options under Section 422 of the Code, and will be granted pursuant to incentive stock option agreements. Only our employees or employees of our parent or subsidiary corporations, as contemplated by the Code, are eligible to receive incentive stock options. The compensation committee will determine the exercise price for an incentive stock option, which may not be less than 100% of the fair market value of the stock underlying the option on the date of grant. In addition, incentive options granted to employees who own, or are deemed to own, more than 10% of our voting stock, must have an exercise price not less than 110% of the fair market value of the stock underlying the option on the date of grant. No incentive stock option may be exercised on or after the tenth anniversary of the date of grant, or after the fifth anniversary of the date of grant for employees who own, or are deemed to own, more than 10% of our voting stock.

Nonstatutory Stock Options

Nonstatutory stock options are not intended to qualify as incentive stock options under Section 422 of the Code and will be granted pursuant to nonstatutory stock option agreements. The compensation committee will determine the exercise price and term of a nonstatutory stock option.

Stock Appreciation Rights

A stock appreciation right, or a SAR, entitles a participant to receive a payment equal in value to the difference between the fair market value of a share of stock on the date of exercise of the SAR over a specified exercise price of the SAR. SARs may be granted in tandem with a stock option, such that the recipient has the opportunity to exercise either the stock option or the SAR, but not both. The exercise price (above which any appreciation is measured) will not be less than 100% of the fair market value of the common stock on the date of grant of the SAR or, in the case of an SAR granted in tandem with a stock option, the exercise price will be the same as the exercise price of the related stock option. The compensation committee may settle a SAR amount in cash, in shares of our common stock, or a combination of cash and shares of our common stock as determined by the compensation committee at or after grant but subject to the terms of the applicable aware agreement. The terms, methods of exercise, and any other terms and conditions of any SAR will be determined by the compensation committee at the time of the grant of the award and will be reflected in the award agreement.

Restricted Stock and Restricted Stock Units

A restricted stock award or restricted stock unit award is the grant of shares of our common stock either currently (in the case of restricted stock) or at a future date (in the case of restricted stock units) at a price determined by the compensation committee (including zero), based on satisfaction of certain vesting conditions, including continuing employment or other service, or achievement of performance goals. During the vesting period, participants holding shares of restricted stock shall, except as otherwise provided in the Plan or an individual award agreement, have full voting and dividend rights with respect to such shares but any stock dividends or other distributions payable in shares of stock or other securities of ours will be subject to the same vesting conditions that apply to the shares of restricted stock in respect of which the dividend was made. The receipt of cash dividends may also be deferred or required to be invested in additional shares of restricted stock. Participants holding restricted stock units may be entitled to receive payments equivalent to any dividends declared with respect to the common stock referenced in the grant of the restricted stock units, but only following the close of the applicable restriction period and then only if the employment or other service and/or performance goals have been met. The restrictions will lapse in accordance with a schedule or other conditions determined by the compensation committee. The compensation committee may settle restricted stock units in cash, in shares of our common stock, or a combination of cash and shares of our common stock as determined by the compensation committee at or after grant but subject to the terms of the applicable award agreement.

Performance Units

A performance unit award is a contingent right to receive the value of a specified number of shares of our common stock over an initial value for such number of shares (which may be zero) established by the compensation committee at the time of grant if certain performance goals or other business objectives are met with the specified performance period. The value of performance units will depend on the degree to which the specified performance goals are achieved. The compensation committee may, in its discretion, pay earned performance units in cash, in shares of our common stock, or a combination of both cash and shares of our common stock as determined by the compensation committee at or after grant but subject to the terms of the applicable award agreement.

The compensation committee has discretion to select the length of any applicable restriction or performance period, the kind and/or level of the applicable performance goal and whether the performance goal is to apply to us, to one of our subsidiaries or any division or business unit or to the recipient.

Stock Grants

A stock grant is an award of shares of common stock without restriction. Stock grants may only be made in limited circumstances, such as in lieu of other earned compensation or as an inducement to employment. Stock grants are made without any forfeiture conditions.

Qualified Performance-Based Awards

Qualified performance-based awards are earned based on the achievement of certain performance criteria intended to satisfy Section 162(m) of the Code. Section 162(m) of the Code limits our federal income tax deduction for compensation to certain of our executive officers to $1.0 million dollars, but excludes from that limit "performance-based compensation." Any form of award permitted under the Plan other than a stock grant may be granted as a qualified performance-based award, but, in the case of awards other than stock options and SARs, will be subject to satisfaction of pre-established, objective performance goals. Qualified performance-based awards include any of the foregoing awards that are granted subject to vesting and/or payment based on the attainment of specified performance goals. Performance criteria upon which performance goals are established by the plan administrator may include but are not limited to: (i) net earnings (either before or after one or more of (A) interest, (B) taxes, (C) depreciation and (D) amortization); (ii) gross or net sales or revenue; (iii) net income (either before or after taxes); (iv) adjusted net income; (v) operating earnings or profit; (vi) cash flow (including, but not limited to, operating cash flow and free cash flow); (vii) return on assets; (viii) return on capital; (ix) return on stockholders' equity; (x) total stockholder return; (xi) return on sales; (xii) gross or net profit or operating margin; (xiii) costs; (xiv) expenses; (xv) working capital; (xvi) earnings per share; (xvii) adjusted earnings per share; (xviii) price per share; (xix) regulatory body approval for commercialization of a product; (xx) implementation, completion or attainment of objectives relating to research, development, regulatory, commercial or strategic milestones or developments; (xxi) market share; (xxii) economic value; (xxiii) revenue; (xxiv) revenue growth; and (xxv) operational and organizational metrics.

Transferability

Awards, other than stock grants, granted under the Plan are generally nontransferable (other than by will or the laws of descent and distribution), except that the compensation committee may, at the time of grant or thereafter, provide for the transferability of nonstatutory stock options or restricted stock to certain family members and/or certain trusts, foundations or other entities owned or controlled by such family members.

Adjustment for Corporate Actions

In the event of any change in the outstanding shares of common stock as a result of a reorganization, recapitalization, reclassification, stock dividend, stock split, reverse stock split or other similar distribution with respect to the shares of common stock, an appropriate and proportionate adjustment will be made in (i) the maximum numbers and kinds of shares subject to the Plan, (ii) the numbers and kinds of shares or other securities subject to then outstanding awards, (iii) the exercise price for each share or unit of any other securities subject to then outstanding stock options or SARs (without change in the aggregate purchase price as to which such stock options or SARs remain exercisable), and (iv) the repurchase price of each share of restricted stock then subject to a risk of forfeiture in the form of a company repurchase right. Any such adjustment in awards will be determined and made by the compensation committee in its sole discretion.

Transactions

In the event of a transaction, including (i) any merger or consolidation of our company with or into another entity as a result of which our stock is converted into or exchanged for the right to receive cash, securities or other property or is cancelled, (ii) any sale or exchange of all or substantially all of our common stock for cash, securities, or other property, (iii) any sale, transfer or other disposition of all or substantially all of our assets to one or more other persons in a single transaction or series of related transactions, or (iv) any liquidation or dissolution of our company, the compensation committee may, (1) provide that awards will be assumed, or substantially equivalent rights shall be provided in substitution therefor by the acquiring or succeeding entity (or an affiliate thereof), (2) upon written notice to the recipient, provide that the recipient's unexercised outstanding stock options and SARs will terminate immediately prior to the consummation of such transaction unless exercised within a specified period following the date of such written notice, (3) provide that all or any unvested restricted stock or restricted stock unit awards will terminate immediately prior to the consummation of such transaction, (4) provide that all or any outstanding stock options and SARs shall become exercisable in whole or in part prior to or upon the transaction, (5) provide that the vesting of all or any unrestricted stock or restricted stock unit awards shall accelerate and any restrictions applicable to such awards shall lapse prior to or upon such transaction, (6) provide for cash payments, net of applicable tax withholdings, to be made to the recipients, (7) provide that, in connection with our liquidation or dissolution, awards other than awards of restricted stock or stock grants shall convert into the right to receive liquidation proceeds net of the exercise price of the awards and any applicable tax withholdings, or (8) any combination of the foregoing. With respect to outstanding awards other than stock options or SARs, that are not terminated prior to or upon the transaction, upon the occurrence of a transaction other than our liquidation or dissolution which is not part of another form of transaction, our repurchase and other rights under each such award will transfer to our successor and inure to the benefit of our successor, and shall, unless the compensation committee determines otherwise, apply to the cash, securities or other property which the stock was converted into or exchanged for pursuant to such transaction in the same manner and to the same extent as they applied to the award. In taking any of the actions described in the event of a transaction, the compensation committee is not obligated to treat all awards, all awards held by a participant or all awards of the same type identically.

Change of Control

Except as otherwise provided in the Plan or in the applicable award agreement, in the event of a change of control, to the extent that the surviving entity declines to continue, convert, assume or replace outstanding awards, then all such awards shall become fully vested and exercisable and any restrictions applicable to any such awards shall lapse in connection with the transaction.

A change of control is defined as the occurrence of any of the following: (1) a transaction, as described above, unless securities possessing more than 50% of the total combined voting power of the

resulting entity or acquiror's outstanding securities (or the securities of any parent thereof) are held by a person or persons who held securities possessing more than 50% of the total combined voting power of our outstanding securities immediately prior to the transaction; (2) any person or group of persons, excluding our company and certain other related entities or any of its affiliates, directly or indirectly acquires, including but not limited to by means of a merger or consolidation, beneficial ownership of securities possessing more than 50% of the total combined voting power of our outstanding securities, unless pursuant to a tender or exchange offer made directly to our stockholders that our board of directors recommends such stockholders accept; or (3) over a period of no more than 36 consecutive months there is a change in the composition of our board such that a majority of the board members ceases to be composed of individuals who either (i) have been board members continuously since the beginning of that period, or (ii) have been elected or nominated for election as board members during such period by at least a majority of the remaining board members who have been board members continuously since the beginning of that period; or (4) a majority of the board of directors votes in favor of a decision that a change of control has occurred.

Amendment and Termination

Our board of directors may at any time amend any or all of the provisions of the Plan, or suspend or terminate it entirely, retroactively or otherwise. However, except as set forth in the Plan, we must obtain stockholder approval to increase the number of shares available under the Plan, or to change the description of persons eligible for awards, or as otherwise required by law or applicable stock exchange rules. Unless otherwise required by law or specifically provided in the Plan, the rights of a participant under awards granted prior to any amendment, suspension or termination may not be adversely affected without the consent of the participant. Unless the Plan is earlier terminated by our board of directors, the Plan terminates immediately prior to the tenth anniversary of the earlier of the adoption of the Plan by our board of directors and approval of the Plan by our stockholders.

Allocation of Awards; Plan Benefits.

It is not presently possible to determine the dollar value of award payments that may be made or the number of options, shares of restricted stock, restricted stock units, or other awards that may be granted under the Plan in the future, or the individuals who may be selected to receive such awards because awards under the Plan are granted at the discretion of the compensation committee.

2017 Employee Stock Purchase Plan

We expect our board of directors to adopt and our stockholders to approve the 2017 employee stock purchase plan, or the ESPP, which will become effective immediately prior to the completion of this offering. The following summary of the material terms of the ESPP does not purport to be complete and is qualified by reference to the full text of the ESPP, which we will file as an exhibit to our registration statement of which this prospectus is a part.

The ESPP provides an incentive to, and encourages stock ownership by, all of our eligible employees and those of our participating subsidiaries so that they may share in our growth by acquiring or increasing their share ownership in us. It is intended that the ESPP constitute an "employee stock purchase plan" within the meaning of Section 423 of the Code. Under the ESPP, eligible employees may purchase shares of our common stock at a discount through payroll deductions.

Administration

The ESPP is administered by the compensation committee of our board of directors. The board of directors itself may exercise any of the powers and responsibilities under the ESPP. The compensation committee may delegate its duties in order to facilitate the purchase and transfer of shares of our common

stock and for the day-to-day administration of the ESPP. The compensation committee, has the discretion, subject to the provisions of the ESPP, to make or to select the manner of making all determinations with respect to options granted under the ESPP. Further, the compensation committee has complete authority to interpret the ESPP, to prescribe, amend and rescind rules and regulations relating to it, and to make all other determinations necessary or advisable for the administration of the ESPP. All decisions, determinations and interpretations made in good faith by the compensation committee with respect to the ESPP are final and binding on all persons having or claiming any interest in the ESPP or any option granted under the ESPP.

Shares Subject to the Plan

The shares issued or to be issued under the ESPP are authorized but unissued shares of our common stock or are shares held by us in our treasury. Subject to the following sentence, the ESPP authorizes the issuance of up to shares of common stock. The number of shares authorized under the ESPP will be increased each January 1, commencing on the first January 1 following consummation of our initial public offering and ending on (and including) January 1, 2027, by an amount equal to 1% of outstanding shares as of the end of the immediately preceding fiscal year. Notwithstanding the foregoing, our board of directors may act prior to January 1 of a given year to provide that there will be no such January 1 increase in the number of shares authorized under the ESPP for such year, or that the increase in the number of shares authorized under the ESPP for such year will be a lesser number than would otherwise occur pursuant to the preceding sentence.

Terms of Participation

The ESPP will be implemented through a series of purchase periods called "plan periods." The initial plan period shall commence on May 1 or November 1 of the calendar year as the Committee may determine, and will continue for six months. After the initial plan period, there will be two consecutive six-month plan periods, during each twelve month period thereafter, beginning on May 1 and ending on the immediately following October 31, and beginning on November 1 and ending on the immediately following April 30. An eligible employee will be granted an option at the beginning of the plan period, and can accumulate money to pay the exercise price for the option by electing to have payroll deductions taken from each payroll during a plan period of an amount, in whole percentages, between 1% and 15% of his or her compensation, but will not exceed $25,000 on an annual basis. At the end of each plan period, unless the participating employee has withdrawn from the ESPP, the option will be exercised by applying the employee's accumulated payroll deductions to the purchase of shares of our common stock. The exercise price paid by the employee will be the lower of 85% of the fair market value of our common stock at (i) the commencement of the plan period and (ii) the end of the plan period.

Withdrawal

An employee may withdraw from participation in an offering up to two weeks prior to the plan period termination date and permanently draw out the balance accumulated in his or her account. In such case, the employee's option for the plan period he or she is withdrawing from will be automatically terminated. A participant's withdrawal from a plan period will not have any effect upon his or her eligibility to participate in a succeeding plan period or in any similar plan which we may adopt. If a participant's employment ends prior to a plan period termination date for any reason, including retirement or death, the contributions credited to his or her account will be returned to him or her or, in the case of his or her death, to his or her designated beneficiaries, and his or her option will be automatically terminated.

Eligibility

Our employees and those of a participating subsidiary are eligible to participate in the ESPP if we customarily employ them for at least 20 hours per week and more than five months per year. However, no

employee shall be granted an option under the ESPP if, immediately after the grant, the employee would own stock, including any outstanding options to purchase stock, equaling 5% or more of the total voting power or value of all classes of our stock. In addition, the ESPP provides that no employee may be granted an option if the option would permit the employee to purchase stock under all of our employee stock purchase plans in an amount that exceeds $25,000 of the fair market value of such stock, determined as of the date(s) of grant, for each calendar year in which the option is outstanding.

Adjustment for Corporate Actions

In the event of any change in the outstanding shares of common stock as a result of a reorganization, recapitalization, reclassification, stock dividend, stock split, reverse stock split, or other similar distribution with respect to the shares of common stock, an appropriate and proportionate adjustment will be made in (i) the maximum numbers and kinds of shares subject to the ESPP, (ii) the numbers and kinds of shares or other securities subject to the then outstanding options, and (iii) the exercise price for each share or other unit of any other securities subject to then outstanding options.

Corporate Transactions

In the event of our dissolution or liquidation, the plan period then in progress will terminate unless otherwise provided by the compensation committee. In the event of another significant corporate transaction such as a merger or consolidation of us with and into another person or entity or the sale or transfer of all or substantially all of our assets, each right to purchase stock under the ESPP may be assumed, or an equivalent right substituted by, the successor corporation or a parent or subsidiary of the successor corporation. In the event that the successor corporation refuses to assume each purchase right or to substitute an equivalent right, any ongoing offering period will be shortened so that employees' rights to purchase stock under the ESPP are exercised prior to the transaction, unless the employee has withdrawn.

Amendment and Termination

Our board of directors has the power to amend or terminate the ESPP and to change or terminate plan periods as long as any such action does not adversely affect any outstanding rights to purchase stock; provided, however, that the board of directors may amend or terminate the ESPP or a plan period even if it would adversely affect outstanding options in order to avoid our incurring adverse accounting charges or if the board of directors determines that termination of the ESPP and/or plan period is in our best interest and the best interest of our stockholders. The ESPP will continue in effect until the tenth anniversary of the closing of the offering described in this prospectus, unless earlier terminated by the board of directors.

Amount of Benefits

The dollar value of benefits that will be received by any employee or group of employees in the ESPP is not determinable due to the voluntary nature of the ESPP and the variables involved in the calculation of any such benefits (including our stock price).

401(k) Plan

We maintain a tax-qualified retirement plan that provides eligible U.S. employees with an opportunity to save for retirement on a tax advantaged basis. Eligible employees are able to defer eligible compensation up to certain Code limits, which are updated annually. We have the ability to make matching and discretionary contributions to the 401(k) plan but have not done so to date. Employee contributions are allocated to each participant's individual account and are then invested in selected investment alternatives according to the participants' directions. Employees are immediately and fully vested in their own contributions. The 401(k) plan is intended to be qualified under Section 401(a) of the Code, with the related trust intended to be tax exempt under Section 501(a) of the Code. As a tax-qualified retirement

plan, contributions to the 401(k) plan are deductible by us when made, and contributions and earnings on those amounts are not taxable to the employees until withdrawn or distributed from the 401(k) plan.

Non-Employee Director Compensation

The following table sets forth the compensation we paid to our non—employee directors during 2016. Other than as set forth in the table below, we did not pay any compensation, make any equity awards or non-equity awards to, or pay any other compensation to any non-employee directors in 2016.

Prior to this offering, we did not have a formal policy for compensating our non-employee directors but the board determined to pay our outside directors cash and equity awards in 2016 as compensation for their services. However, non-employee directors may receive stock options and other equity awards under the Plan from time to time as determined by our board of directors. We also reimburse non-employee directors for travel expenses incurred in connection with their duties as directors.

Name	Fees Earned or Paid in Cash ($)	Option Awards Compensation ($)[1]	Total ($)
Neil Exter	—	—	—
Todd Foley	—	—	—
Christophe R. Jean	—	—	—
David W. J. McGirr	$ 25,000	180,000	$ 205,000
David P. Meeker	$ 12,500	180,000	$ 192,500
Ed Mathers	—	—	—
Jonathan T. Silverstein, J.D.	—	—	—

(1) As of December 31, 2016, David McGirr and David Meeker each had 600,000 outstanding options, 200,000 of which were vested options and 400,000 of which were unvested options. The aggregate grant date fair value was $0.30.

In August 2017, our board of directors adopted a non-employee director compensation policy that will be effective upon completion of this offering. We retained an independent compensation consultant to help us determine the terms of the non-employee director compensation policy. Our non-employee director compensation policy is designed to provide a total compensation package that enables us to attract and retain, on a long-term basis, skilled non-employee directors. Under the policy, all non-employee directors will be paid an annual retainer fee of $35,000 and such additional fees as are set forth in the following table. All payments will be made quarterly in arrears.

Non-Employee Director	Annual Fee
Lead Director	$ 25,000
Non-Executive Chair	$ 30,000
Chairman of the audit committee	$ 15,000
Member of the audit committee (other than chairman)	$ 7,500
Chairman of the compensation committee	$ 10,000
Member of the compensation committee (other than chairman)	$ 5,000
Chairman of the governance and nominating committee	$ 8,000
Member of the governance and nominating committee (other than chairman)	$ 4,000

Under the non-employee director compensation policy, each individual who is initially appointed or elected to the board of directors will be eligible to receive an option to purchase up to 200,000 shares of our common stock under the Plan on the date he or she first becomes a nonemployee director. These option grants will vest annually over a three-year period from the date of grant, subject to continued

service as a non-employee director through that vesting date. In addition, on the date of the annual meeting of stockholders, each continuing non-employee director who has served on the board of directors for a minimum of six months will be eligible to receive an option grant to purchase up to 100,000 shares of our common stock, which will vest in full upon the earlier of the first anniversary of the date of grant or the date of the next annual meeting of stockholders. The exercise price for each of these option grants will be equal to the fair market value of our common stock on the date of grant. These new director grants and annual grants will be subject to approval by our board of directors at the time of grant.

Limitation on Liability and Indemnification Matters

Section 145 of the Delaware General Corporation Law authorizes a corporation's board of directors to grant, and authorizes a court to award, indemnity to officers, directors and other corporate agents.

As permitted by Delaware law, our amended and restated certificate of incorporation provides that, to the fullest extent permitted by Delaware law, no director will be personally liable to us or our stockholders for monetary damages for breach of fiduciary duty as a director. Pursuant to Delaware law, such protection would be not available for liability:

- for any breach of a duty of loyalty to us or our stockholders;
- for acts or omissions not in good faith or that involve intentional misconduct or a knowing violation of law;
- for any transaction from which the director derived an improper benefit; or
- for an act or omission for which the liability of a director is expressly provided by an applicable statute, including unlawful payments of dividends or unlawful stock repurchases or redemptions as provided in Section 174 of the Delaware General Corporation Law.

Our amended and restated certificate of incorporation also provides that if Delaware law is amended after the approval by our stockholders of the amended and restated certificate of incorporation to authorize corporate action further eliminating or limiting the personal liability of directors, then the liability of our directors will be eliminated or limited to the fullest extent permitted by Delaware law.

Our amended and restated bylaws further provide that we must indemnify our directors and officers to the fullest extent permitted by Delaware law. Our amended and restated bylaws also authorize us to indemnify any of our employees or agents and permit us to secure insurance on behalf of any officer, director, employee or agent for any liability arising out of his or her action in that capacity, whether or not Delaware law would otherwise permit indemnification.

In addition, our amended and restated bylaws provide that we are required to advance expenses to our directors and officers as incurred in connection with legal proceedings against them for which they may be indemnified and that the rights conferred in the amended and restated bylaws are not exclusive.

We intend to enter into indemnification agreements with each of our directors and executive officers. These agreements, among other things, would require us to indemnify each director and officer to the fullest extent permitted by Delaware law, the amended and restated certificate of incorporation and amended and restated bylaws, for expenses such as, among other things, attorneys' fees, judgments, fines and settlement amounts incurred by the director or executive officer in any action or proceeding, including any action by or in our right, arising out of the person's services as our director or executive officer or as the director or executive officer of any subsidiary of ours or any other company or enterprise to which the person provides services at our request. Upon consummation of the offering, we intend to obtain and maintain directors' and officers' liability insurance.

The SEC has taken the position that personal liability of directors for violation of the federal securities laws cannot be limited and that indemnification by us for any such violation is unenforceable.

The limitation of liability and indemnification provisions in our amended and restated certificate of incorporation and amended and restated bylaws may discourage stockholders from bringing a lawsuit against our directors and officers for breach of their fiduciary duty. They may also reduce the likelihood of derivative litigation against our directors and officers, even though an action, if successful, might benefit us and other stockholders. Further, a stockholder's investment may be adversely affected to the extent that we pay the costs of settlement and damage awards against directors and officers as required by these indemnification provisions.

Rule 10b5-1 Sales Plans

Our directors and executive officers may adopt written plans, known as Rule 10b5-1 plans, pursuant to which, if adopted, they would contract with a broker to buy or sell shares of our common stock on a periodic basis. Under a Rule 10b5-1 plan, a broker executes trades pursuant to parameters established by the director or officer when entering into the plan, without further direction from them. The director or officer may amend a Rule 10b5-1 plan in some circumstances and may terminate a plan at any time. Our directors and executive officers also may buy or sell additional shares outside of a Rule 10b5-1 plan when they are not in possession of material nonpublic information subject to compliance with the terms of our insider trading policy. Prior to 180 days after the date of this offering (subject to early termination), the sale of any shares under such plan would be subject to the lock-up agreement that the director or officer has entered into with the underwriters.

CERTAIN RELATIONSHIPS AND RELATED PARTY TRANSACTIONS

We describe below transactions and series of similar transactions, during our last three fiscal years, to which we were a party or will be a party, in which:

- the amounts involved exceeded or will exceed $120,000; and
- any of the directors, executive officers or holders of more than 5% of our voting equity, or any member of the immediate family of the foregoing persons, had or will have a direct or indirect material interest.

Compensation arrangements for our directors and named executive officers are described elsewhere in this prospectus.

Series A Preferred Stock Financing

In August 2015 and December 2015, pursuant to the series A preferred stock purchase agreement we issued an aggregate of 40,000,000 shares of series A preferred stock, par value $0.001 per share, at a purchase price of $1.00 per share, resulting in aggregate gross proceeds of $40.0 million to us.

In January 2017 and August 2017, pursuant to the series A preferred stock purchase agreement we issued an aggregate of 40,949,999 shares of series A preferred stock, par value $0.001 per share, at a purchase price of $1.00 per share, resulting in aggregate gross proceeds of $40.9 million to us.

Following the closing of this offering and upon the expiration of the lock-up period, holders of our series A preferred stock will be entitled to certain registration rights with respect to the resale of such shares under the Securities Act, pursuant to the investors' rights agreement entered into between us and certain of our stockholders. See "Description of Capital Stock—Registration Rights."

The following table summarizes the participation in the series A preferred stock financing by our directors, executive officers, holders of more than 5% of our voting securities, or any member of the

immediate family of the foregoing persons. For further information on the ownership of securities of holders of more than 5% of our voting securities, see "Principal Stockholders."

Name	Shares of Series A Preferred Stock	Date(s) Purchased
OrbiMed Private Investments V, LP	10,937,500	August 3, 2015
667 L.P. and Baker Brothers Life Sciences, L.P.	5,000,000	August 3, 2015
New Enterprise Associates 13, L.P.	1,706,250	August 3, 2015
MPM BioVentures V, L.P. and MPM Asset Management Investors BV5 LLC	1,012,500	August 3, 2015
Pfizer Inc.	550,000	August 3, 2015
Third Rock Ventures, L.P.	143,750	August 3, 2015
OrbiMed Private Investments V, LP	6,562,500	December 1, 2015
667 L.P. and Baker Brothers Life Sciences, L.P.	3,000,000	December 1, 2015
New Enterprise Associates 13, L.P.	1,023,750	December 1, 2015
MPM BioVentures V, L.P. and MPM Asset Management Investors BV5 LLC	607,500	December 1, 2015
Pfizer Inc.	330,000	December 1, 2015
Third Rock Ventures, L.P.	86,250	December 1, 2015
New Enterprise Associates 13, L.P.	5,067,162	January 6, 2017
Third Rock Ventures, L.P.	4,624,751	January 6, 2017
MPM BioVentures V, L.P. and MPM Asset Management Investors BV5 LLC	3,015,916	January 6, 2017
OrbiMed Private Investments V, LP	2,924,766	January 6, 2017
Pfizer Inc.	1,611,852	January 6, 2017
667 L.P. and Baker Brothers Life Sciences, L.P.	1,337,036	January 6, 2017
David P. Meeker	250,000	January 6, 2017
Keith M. Gottesdiener, M.D.	125,000	January 6, 2017
Bart Henderson	100,000	January 6, 2017
New Enterprise Associates 13, L.P.	5,067,162	August 18, 2017
Third Rock Ventures, L.P.	4,624,751	August 18, 2017
MPM BioVentures V, L.P. and MPM Asset Management Investors BV5 LLC	3,015,915	August 18, 2017
OrbiMed Private Investments V, LP	2,924,765	August 18, 2017
Pfizer Inc.	1,611,852	August 18, 2017
667 L.P. and Baker Brothers Life Sciences, L.P.	1,337,035	August 18, 2017
David P. Meeker	250,000	August 18, 2017
Keith M. Gottesdiener, M.D.	125,000	August 18, 2017
Bart Henderson	100,000	August 18, 2017

Indemnification Agreements

We currently have an indemnification agreement with Jonathan T. Silverstein. Upon the completion of this offering, we intend to enter into new indemnification agreements with each of our directors and executive officers. These agreements, among other things, will require us to indemnify each director and officer to the fullest extent permitted by Delaware law, our amended and restated certificate of incorporation and amended and restated bylaws, for expenses such as, among other things, attorneys' fees, judgments, fines, and settlement amounts incurred by the director or executive officer in any action or proceeding, including any action by or in our right, arising out of the person's services as our director or executive officer or as the director or executive officer of any subsidiary of ours or any other company or

enterprise to which the person provides services at our request. Upon consummation of the offering, we intend to obtain and maintain directors' and officers' liability insurance. See "Executive and Director Compensation—Limitation on Liability and Indemnification Matters."

Employment and Board Arrangements

Our executive officers have employment letters with us for their services. For information about the employment letters with our named executive officers, refer to "Executive and Director Compensation—Agreements with our Executive Officers."

Consulting Agreement with Mr. Henderson

Mr. Henderson resigned from employment with us and thereafter entered into a consulting agreement with us. Under the terms of Mr. Henderson's consulting agreement, he is entitled to a consulting fee on an hourly basis, subject to adjustment by us. In consideration of Mr. Henderson's prior service to us as a founder and former officer and employee, under the terms of Mr. Henderson's consulting agreement with us, Mr. Henderson will continue to vest in any unvested equity awards held by him granted by both us or the LLC entity, through and including December 31, 2017, with a right to exercise any vested equity through and including October 1, 2018.

Related Party Transactions Policy

Our board of directors has adopted a policy, effective upon the closing of this offering, that our executive officers, directors, nominees for election as a director, beneficial owners of more than 5% of any class of our common stock and any members of the immediate family of any of the foregoing persons are not permitted to enter into a related person transaction with us without the prior review and approval of our governance and nominating committee. Any request for us to enter into a transaction with an executive officer, director, nominee for election as a director, beneficial owner of more than 5% of any class of our common stock or any member of the immediate family of any of the foregoing persons in which the amount involved exceeds $120,000 and such person would have a direct or indirect material interest must first be presented to our governance and nominating committee for review, consideration and approval. In approving or rejecting any such proposal, our governance and nominating committee is to consider the material facts of the transaction, including, but not limited to, whether the transaction is on terms no less favorable than terms generally available to an unaffiliated third party under the same or similar circumstances and the extent of the related person's interest in the transaction. We did not have a formal review and approval policy for related party transactions at the time of any of the transactions described above. However, the transactions described above under "Certain Relationships and Related Party Transactions" were entered into after presentation, consideration and approval by our board of directors.

PRINCIPAL STOCKHOLDERS

The following table sets forth information regarding the beneficial ownership of our common stock as of August 21, 2017, after giving effect to the conversion of our outstanding shares of preferred stock into shares of common stock, by:

- each of our directors and named executive officers;
- all of our directors and executive officers as a group; and
- each person, or group of affiliated persons, who is known by us to beneficially own more than 5% of our common stock.

Beneficial ownership is determined according to the rules of the SEC and generally means that a person has beneficial ownership of a security if he, she or it possesses sole or shared voting or investment power of that security, and of convertible securities that are currently exercisable or exercisable within 60 days after August 21, 2017. Shares of our common stock issuable pursuant to options or warrants, if any, are deemed outstanding for computing the percentage of the person holding such options or warrants and the percentage of any group of which the person is a member but are not deemed outstanding for computing the percentage of any other person. Except as indicated by the footnotes below, we believe, based on the information furnished to us, that the persons named in the table below have sole voting and investment power with respect to all shares of common stock shown that they beneficially own, subject to community property laws where applicable. The information does not necessarily indicate beneficial ownership for any other purpose, including for purposes of Section 13(d) and 13(g) of the Securities Act.

Our calculation of the percentage of beneficial ownership prior to this offering is based on shares of common stock outstanding as of August 21, 2017, assuming the conversion of our outstanding preferred stock into common stock, as if the conversion had occurred as of August 21, 2017. Our calculation of the percentage of beneficial ownership after this offering is based on shares of common stock outstanding immediately after the closing of this offering (assuming no exercise of the underwriters' option to purchase additional shares of our common stock).

Except as otherwise noted below, the address for persons listed in the table is c/o Rhythm Pharmaceuticals, Inc., 500 Boylston Street, Eleventh Floor, Boston, MA 02116.

	Prior to the Offering		After the Offering	
Name and Address of Beneficial Owner	Number of shares of common stock	Percent of class	Number of shares of common stock	Percent of class
5% Stockholders:				
New Enterprise Associates 13, L.P.[1] 2855 Sand Hill Road Menlo Park, CA 94025	40,002,369	20.77%		
Third Rock Ventures, L.P.[2] 29 Newbury Street Boston, MA 02116	36,509,787	18.96%		
MPM BioVentures V, L.P. and MPM Asset Management Investors BV5 LLC[3] 450 Kendall Street Cambridge, MA 02142	23,808,938	12.36%		
OrbiMed Private Investments V, LP[4] 601 Lexington Avenue, 54th Floor New York, NY 10022-4629	23,349,531	12.13%		%
Pfizer Inc.[5] 235 East 42nd Street New York, NY 10017	12,724,656	6.61%		
667, L.P. and Baker Brothers Life Sciences, L.P.[6] 667 Madison Avenue, 21st Floor New York, NY 10065	10,674,071	5.54%		%
Directors and Named Executive Officers:				
Keith M. Gottesdiener[7]	6,111,324	3.17%		%
Bart Henderson[8]	2,798,054	1.45%		%
Fred T. Fiedorek, M.D.[9]		*		%
Todd Foley	—	—		%
Ed Mathers	—	—		%
Neil Exter	—	—		%
Christophe R. Jean	—	—		%
Jonathan T. Silverstein, J.D.	—	—		%
David Meeker[10]		*		%
David McGirr[11]		*		%
All executive officers and directors as a group (13 persons)[12]	11,499,677	5.97%		%

* Represents beneficial ownership of less than 1%.

(1) Consists of (i) 269,404 shares of common stock and (ii) 39,732,965 shares of common stock underlying shares of convertible preferred stock directly held by New Enterprise Associates 13, L.P., or NEA 13, and are indirectly held by NEA Partners 13, L.P., or Partners 13, which is the sole general partner of NEA 13; NEA 13 GP, LTD, or NEA 13 LTD, which is the sole general partner of Partners 13; and each of the individual directors of NEA 13 LTD. The individual Directors of NEA 13 LTD, or the NEA 13 Directors, are M. James Barrett, Peter J. Barris, Forest Baskett, Patrick J. Kerins, David M. Mott, Scott D. Sandell and Ravi Viswanathan. NEA Partners 13, NEA 13 LTD, and the NEA 13 Directors share voting and dispositive power with regard to the shares owned directly by NEA 13. All

indirect holders of the above referenced shares disclaim beneficial ownership of all applicable shares except to the extent of their actual pecuniary interest therein.

(2) Consists of (i) 161,643 shares of common stock and (ii) 36,348,144 shares of common stock underlying shares of convertible preferred stock held directly by Third Rock Ventures, L.P., or TRV LP. Each of Third Rock Ventures GP, LP, or TRV GP, the general partner of TRV LP, and Third Rock Ventures GP, LLC, TRV LLC, the general partner of TRV GP, and Mark Levin, Kevin Starr and Robert Tepper, the managers of TRV LLC, may be deemed to share voting and investment power over the shares held by TRV LP. Each of the reporting persons disclaims beneficial ownership of such shares, except to the extent of their proportionate pecuniary interest therein, if any.

(3) Consists of (i) 269,404 shares of common stock and (ii) 23,539,534 shares of common stock underlying shares of convertible preferred stock held directly by MPM BioVentures V, L.P. and MPM Asset Management Investors BV5 LLC. MPM BioVentures V LLC is the Managing Member of MPM BioVentures V GP LLC, which is the General Partner of MPM BioVentures V, L.P. MPM BioVentures V LLC is the Manager of MPM Asset Management Investors BV5 LLC. Todd Foley, one of our directors, is a Member of MPM BioVentures V LLC and shares the power to vote, hold and dispose of the shares held by MPM BioVentures V, L.P., and MPM Asset Management Investors BV5 LLC. Mr. Foley and each such other Member of MPM BioVentures V LLC disclaims beneficial ownership of the securities reported herein except to the extent of his respective pecuniary interest therein.

(4) Consists of shares of common stock underlying 23,349,531 shares of series A preferred stock held by OrbiMed Private Investments V, LP, or OPI V. OrbiMed Capital GP V LLC, or GP V, is the sole general partner of OPI V, and OrbiMed Advisors LLC, or Advisors, a registered adviser under the Investment Advisers Act of 1940, as amended, is the sole managing member of GP V. Samuel D. Isaly, or Isaly, a natural person, is the managing member of, and holder of a controlling interest in, Advisors. By virtue of such relationships, GP V, Advisors and Isaly may be deemed to have voting and investment power with respect to the shares of series A preferred stock held by OPI V noted above and as a result may be deemed to have beneficial ownership over such shares of series A preferred stock. Jonathan T. Silverstein, one of our directors, is a Member of Advisors. Each of GP V, Advisors, Mr. Isaly and Mr. Silverstein disclaims beneficial ownership of the shares held by OPI V, except to the extent of its or his pecuniary interest therein if any.

(5) Consists of shares of common stock underlying shares of convertible preferred stock held by Pfizer Inc. As of August 15, 2017, the board of directors of Pfizer Inc. is comprised of the following individuals: Dennis A. Ausiello, Ronald E. Blaylock, W. Don Cornwell, Joseph J. Echevarria, Frances D. Fergusson, Helen H. Hobbs, James M. Kilts, Shantanu Narayen, Suzanne Nora Johnson, Ian C. Read, Stephen W. Sanger and James C. Smith. Pfizer Inc. is a publicly-traded company.

(6) Consists of shares of common stock underlying shares of series A preferred stock held by 667, L.P., or 667 LP, and Baker Brothers Life Sciences, L.P., or Baker Brothers Life Sciences. Baker Bros. Advisors LP, or Baker Bros. Advisors, is the investment adviser to 667 LP and Baker Brothers Life Sciences and, pursuant to amended and restated management agreements between Baker Bros. Advisors, 667 LP and Baker Brothers Life Sciences and the respective general partners of 667 LP and Baker Brother Life Sciences, Baker Bros. Advisors has complete and unlimited discretion and authority with respect to the investments and voting power over investments of 667 LP and Baker Brothers Life Sciences. Baker Bros. Advisors disclaims beneficial ownership of all shares of series A preferred stock held by 667 LP and Baker Brothers Life Sciences except to the extent of any pecuniary interest therein.

(7) Consists of (i) 3,919,408 shares of common stock, (ii) 250,000 shares of common stock underlying shares of series A preferred stock, and (iii) includes 1,941,916 shares of common stock underlying options that are exercisable within 60 days of August 21, 2017.

(8) Consists of (i) 1,805,012 shares of common stock, (ii) 200,000 shares of common stock underlying shares of series A preferred stock, and (iii) includes 793,042 shares of common stock underlying options that are exercisable within 60 days of August 21, 2017.

(9) Consists of (i) 907,140 shares of common stock, and (ii) includes 483,159 shares of common stock underlying options that are exercisable within 60 days of August 21, 2017.

(10) Consists of (i) 200,000 shares of common stock, and (ii) 500,000 shares of common stock underlying shares of series A preferred stock.

(11) Includes 200,000 shares of common stock underlying options that are exercisable within 60 days of August 21, 2017.

(12) Consists of (i) 6,831,560 shares of common stock, (ii) 950,000 shares of common stock underlying shares of series A preferred stock, and (iii) includes 3,718,117 shares of common stock underlying options that are exercisable within 60 days of August 21, 2017.

DESCRIPTION OF CAPITAL STOCK

The following description of our capital stock and provisions of our amended and restated certificate of incorporation and amended and restated bylaws as they will be in effect upon the consummation of this offering are summaries and are qualified in their entirety by reference to our amended and restated certificate of incorporation and amended and restated bylaws that will be in effect upon the closing of this offering, the forms of which are filed as exhibits to the registration statement of which this prospectus forms a part, and by applicable law.

In August 2015, we effected a 93,500-for-1 forward stock split of our then-outstanding common stock. Also in August 2015, December 2015, January 2017 and August 2017, we sold 25,000,000 shares, 15,000,000 shares, 20,475,001 shares and 20,474,998 shares, respectively, of our series A preferred stock to certain investors. Following the stock split and the closing of our series A preferred stock financings, the LLC entity remained our largest stockholder, with the balance of our stock being owned by our series A investors. In August 2017, the LLC entity exchanged 78,666,209 of its shares of our common stock for an equal number of newly-issued shares of our series A-1 junior preferred stock and the LLC entity distributed all of its shares of our series A-1 junior preferred stock to the holders of its preferred units and the remaining 14,833,791 shares of our common stock to the holders of its common units. We refer to the exchange and distribution as the Distribution. The series A-1 junior preferred stock will convert into shares of our common stock on a one to one basis upon the closing of this offering. See "Corporate Reorganization."

Upon consummation of this offering, our authorized capital stock will consist of shares of common stock, par value $0.001 per share and shares of preferred stock, par value $0.001 per share. Unless our board of directors determines otherwise, we will issue all shares of our capital stock in uncertificated form. Assuming (1) the conversion of all outstanding shares of our preferred stock into shares of our common stock and (2) the issuance by us of shares of common stock in this offering, there will be shares of common stock and no shares of preferred stock outstanding upon closing of this offering.

Common Stock

Holders of shares of our common stock are entitled to one vote for each share held of record on all matters submitted to a vote of stockholders. The holders of a plurality of the shares of our common stock entitled to vote in any election of directors can elect all of the directors standing for election.

Holders of shares of our common stock are entitled to receive dividends when and if declared by our board of directors out of funds legally available therefor, subject to any statutory or contractual restrictions on the payment of dividends and to any restrictions on the payment of dividends imposed by the terms of any outstanding preferred stock.

Upon our dissolution or liquidation or the sale of all or substantially all of our assets, after payment in full of all amounts required to be paid to creditors and to the holders of preferred stock having liquidation preferences, if any, the holders of shares of our common stock will be entitled to receive pro rata our remaining assets available for distribution.

Holders of shares of our common stock do not have preemptive, subscription, redemption or conversion rights.

Preferred Stock

Upon consummation of this offering, each share of our preferred stock will be converted into one share of our common stock.

Our amended and restated certificate of incorporation authorizes our board of directors to establish one or more series of preferred stock (including convertible preferred stock). Unless required by law or by

any stock exchange, the authorized shares of preferred stock will be available for issuance without further action by our stockholders. Our board of directors is able to determine, with respect to any series of preferred stock, the terms and rights of that series, including:

- the designation of the series;
- the number of shares of the series, which our board may, except where otherwise provided in the preferred stock designation, increase or decrease, but not below the number of shares then outstanding;
- the voting rights, if any, of the holders of the series;
- whether dividends, if any, will be cumulative or non-cumulative and the dividend rate of the series;
- the dates at which dividends, if any, will be payable;
- the rights of priority and amounts payable, if any, on shares of the series in the event of any voluntary or involuntary liquidation, dissolution or winding-up of the affairs of our company;
- the redemption rights and price or prices, if any, for shares of the series;
- the terms of any purchase, retirement or sinking fund, if any, provided for shares of the series;
- the terms, if any, upon which the shares of the series will be convertible into or exchangeable for shares of any other class, classes or series or other securities, whether or not issued by our company or any other entity;
- restrictions, if any, upon issuance of indebtedness of our company so long as any shares of the series are outstanding; and
- restrictions, if any, on the issuance of shares of the same series or of any other class or series.

We could issue a series of preferred stock that could, depending on the terms of the series, impede or discourage an acquisition attempt or other transaction that some, or a majority, of our stockholders might believe to be in their best interests or in which our stockholders might receive a premium for their shares of common stock over the market price of the shares of common stock.

Options

Upon completion of the offering, we will have options to purchase our common stock outstanding. See "Executive and Director Compensation—Employee Benefit and Stock Plans" for a discussion of the terms of the Plan.

Authorized but Unissued Capital Stock

The Delaware General Corporation Law does not require stockholder approval for any issuance of authorized shares. However, the listing requirements of NASDAQ, which would apply so long as our common stock remains listed on NASDAQ, require stockholder approval of certain issuances equal to or exceeding 20% of the then outstanding voting power or then outstanding number of shares of common stock. These additional shares may be used for a variety of corporate purposes, including future public offerings, to raise additional capital or to facilitate acquisitions.

One of the effects of the existence of unissued and unreserved common stock or preferred stock may be to enable our board of directors to issue shares to persons friendly to current management, which issuance could render more difficult or discourage an attempt to obtain control of our company by means of a merger, tender offer, proxy contest or otherwise, and thereby protect the continuity of our management and possibly deprive our stockholders of opportunities to sell their shares of common stock at prices higher than prevailing market prices.

Anti-Takeover Effects of Provisions of Delaware Law and Our Amended and Restated Certificate of Incorporation and Amended and Restated Bylaws

Undesignated Preferred Stock

The ability to authorize undesignated preferred stock will make it possible for our board of directors to issue preferred stock with super voting, special approval, dividend or other rights or preferences on a discriminatory basis that could impede the success of any attempt to acquire us or otherwise effect a change in control of us. These and other provisions may have the effect of deferring, delaying or discouraging hostile takeovers, or changes in control or management of our company.

Requirements for Advance Notification of Stockholder Meetings, Nominations and Proposals

Our amended and restated certificate of incorporation provides that special meetings of the stockholders may be called only by or at the direction of our board of directors, two or more of our directors, the chairman of our board, our chief executive officer or one or more holders of at least a minimum percentage of the voting power of the outstanding shares of our capital stock. This minimum will initially be 25% and will automatically increase to 51% on the first date on which the holders of outstanding shares of our common stock hold more than 51% of the voting power of all outstanding shares of our capital stock. Our amended and restated bylaws prohibit the conduct of any business at a special meeting other than as specified in the notice for such meeting. These provisions may have the effect of deferring, delaying or discouraging hostile takeovers, or changes in control or management of our company.

Our amended and restated bylaws establish advance notice procedures with respect to stockholder proposals and the nomination of candidates for election as directors, other than nominations made by or at the direction of the board of directors or a committee of the board of directors. In order for any matter to be "properly brought" before a meeting, a stockholder will have to comply with advance notice requirements and provide us with certain information. Additionally, vacancies and newly created directorships may be filled only by a vote of a majority of the directors then in office, even though less than a quorum, and not by the stockholders. Our amended and restated bylaws will allow the presiding officer at a meeting of the stockholders to adopt rules and regulations for the conduct of meetings which may have the effect of precluding the conduct of certain business at a meeting if the rules and regulations are not followed. These provisions may also defer, delay or discourage a potential acquirer from conducting a solicitation of proxies to elect the acquirer's own slate of directors or otherwise attempting to obtain control of our company.

Our amended and restated certificate of incorporation provides that the board of directors is expressly authorized to adopt, amend or repeal our amended and restated bylaws.

No Cumulative Voting

The Delaware General Corporation Law provides that stockholders are not entitled to cumulate votes in the election of directors unless our amended and restated certificate of incorporation provides otherwise. Our amended and restated certificate of incorporation does not expressly provide for cumulative voting.

Removal of Directors

In accordance with the terms of our amended and restated certificate of incorporation and amended and restated bylaws that will become effective upon the closing of this offering, our board of directors will be divided into three staggered classes of directors of the same or nearly the same number and each will be assigned to one of the three classes. At each annual meeting of the stockholders, a class of directors will be elected for a three-year term to succeed the directors of the same class whose terms are then expiring. The initial term of office of the directors of Class I shall expire as of the first annual meeting of our

stockholders following the closing of this offering; the initial term of office of the directors of Class II shall expire as of the second annual meeting of our stockholders following the closing of this offering; and the initial term of office of the directors of Class III shall expire as of the third annual meeting of our stockholders following the closing of this offering.

- Our Class I directors will be Keith Gottesdiener and Christophe Jean;
- Our Class II directors will be Ed Mathers, Todd Foley, and Neil Exter; and
- Our Class III directors will be David Meeker and David McGirr.

Our amended and restated certificate of incorporation and amended and restated bylaws provide that the number of our directors shall be fixed from time to time by a resolution of the majority of our board of directors. Any additional directorships resulting from an increase in the number of directors will be distributed among the three classes so that, as nearly as possible, each class shall consist of one third of the board of directors.

The division of our board of directors into three classes with staggered three-year terms may delay or prevent stockholder efforts to effect a change of our management or a change in control.

Our amended and restated certificate of incorporation and amended and restated bylaws that will become effective upon the closing of this offering also provide that our directors may be removed only for cause by the affirmative vote of the holders of at least 75% of the outstanding shares of capital stock entitled to vote in the election of directors or class of directors, voting together as a single class, at a meeting of the stockholders called for that purpose. This requirement of a supermajority vote to remove directors could enable a minority of our stockholders to prevent a change in the composition of our board. Any vacancy on our board of directors, including a vacancy resulting from an enlargement of our board of directors, may be filled only by the vote of a majority of the remaining directors then in office, although less than a quorum, or by the sole remaining director.

Amendments to Amended and Restated Certificate of Incorporation and Amended and Restated Bylaws

The Delaware General Corporation Law provides that, unless a corporation's certificate of incorporation provides otherwise, the affirmative vote of holders of shares constituting a majority of the votes of all shares entitled to vote may approve amendments to the certificate of incorporation.

Our amended and rested certificate of incorporation and amended and restated bylaws will provide that the affirmative vote of holders of at least 75% of the outstanding shares of capital stock, voting together as a single class, and entitled to vote in the election of directors will be required to amend, alter, change or repeal the amended and restated certificate of incorporation and the amended and restated bylaws. This requirement of a supermajority vote to approve amendments to our amended and restated certificate of incorporation and amended and restated bylaws could enable a minority of our stockholders to exercise veto power over such amendments.

Stockholder Action by Written Consent

Pursuant to Section 228 of the Delaware General Corporation Law, any action required to be taken at any annual or special meeting of the stockholders may be taken without a meeting, without prior notice and without a vote if a consent or consents in writing, setting forth the action so taken, is signed by the holders of outstanding stock having not less than the minimum number of votes that would be necessary to authorize or take such action at a meeting at which all shares of our stock entitled to vote thereon were present and voted, unless the corporation's certificate of incorporation provides otherwise. Our amended and restated certificate of incorporation will prohibit the taking of any action of our stockholders by written consent without a meeting.

Delaware Anti-Takeover Statute

We have not opted out of, and therefore are subject to, Section 203 of the Delaware General Corporation Law. Section 203 provides that, subject to certain exceptions specified in the law, a publicly-held Delaware corporation shall not engage in certain "business combinations" with any "interested stockholder" for a three-year period after the date of the transaction in which the person became an interested stockholder unless:

- prior to the date of the transaction, the board of directors of the corporation approved either the business combination or the transaction that resulted in the stockholder becoming an interested stockholder;
- upon completion of the transaction that resulted in the stockholder becoming an interested stockholder, the stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the number of shares outstanding (1) shares owned by persons who are directors and also officers and (2) shares owned under employee stock plans in which employee participants do not have the right to determine confidentially whether shares held subject to the plan will be tendered in a tender or exchange offer; or
- on or subsequent to the date of the transaction, the business combination is approved by the board and authorized at an annual or special meeting of stockholders, and not by written consent, by the affirmative vote of at least $66^{2}/_{3}\%$ of the outstanding voting stock which is not owned by the interested stockholder.

Generally, a business combination includes a merger, asset or stock sale, or other transaction resulting in a financial benefit to the interested stockholder. An interested stockholder is a person who, together with affiliates and associates, owns or, within three years prior to the determination of interested stockholder status, did own 15% or more of a corporation's outstanding voting stock. Since Section 203 will apply to us, we expect that it would have an anti-takeover effect with respect to transactions our board of directors does not approve in advance. In such event, we would also anticipate that Section 203 could discourage attempts that might result in a premium over the market price for the shares of common stock held by stockholders.

Under certain circumstances, Section 203 makes it more difficult for a person who would be an "interested stockholder" to effect various business combinations with a corporation for a three-year period. The provisions of Section 203 may encourage companies interested in acquiring our company to negotiate in advance with our board of directors because the stockholder approval requirement would be avoided if our board of directors approves either the business combination or the transaction that results in the stockholder becoming an interested stockholder. These provisions also may make it more difficult to accomplish transactions that stockholders may otherwise deem to be in their best interests.

Registration Rights

Following the closing of this offering, the holders of shares of our common stock, or their transferees, will be entitled to the registration rights set forth below with respect to registration of the resale of such shares under the Securities Act pursuant to the investors' rights agreement, by and among us and certain of our stockholders.

Demand Registration Rights

At any time after 180 days after the effective date of this public offering as set forth on the cover page of this prospectus, upon the written request of at least a majority of the holders of the registrable securities then outstanding that we file a registration statement under the Securities Act covering the registration of registrable securities owned by such holder(s) having an anticipated aggregate offering price, net of selling expenses, of at least $15.0 million, we will be obligated to notify all holders of registrable securities of such

request. As soon as practicable thereafter, and in any event within 60 days after the date such request is received, we will be required to register the sale on a registration statement on Form S-1 of all registrable securities that holders may request to be registered, subject to specified exceptions, conditions and limitations. We may postpone the filing of a registration statement for up to 120 days once in any 12-month period if in the good faith judgment of our board of directors such registration would be materially detrimental to us, and we are not required to effect the filing of a registration statement during the period starting with the date that is 60 days prior to our good faith estimate of the date of filing of a registration statement initiated by us and ending on a date 180 days after the effective date of a registration statement initiated by us. The underwriters of any underwritten offering will have the right to limit the number of shares having registration rights to be included in the registration statement.

"Piggyback" Registration Rights

If we register any securities for public sale, holders of registration rights will have the right to include their shares in the registration statement. The underwriters of any underwritten offering will have the right to limit the number of registrable securities to be included in the registration statement, but such number may not be below 30% of the total number of shares included in such registration statement. The holders of registration rights have waived any and all rights to which they would otherwise be entitled to have their shares included in this offering.

Form S-3 Registration Rights

If we are eligible to file a registration statement on Form S-3, holders of at least 10% of our registrable securities then outstanding have the right to request that we file a registration statement on Form S-3, so long as the aggregate price to the public of the securities to be sold under the registration statement on Form S-3 is at least $10.0 million or consists of all the remaining registrable securities, and subject to specified exceptions, conditions and limitations.

Expenses of Registration

Pursuant to the investors' rights agreement, we are generally required to bear all registration expenses, including the fees and expenses of one counsel, not to exceed $50,000, representing the selling holders, incurred in connection with the demand, piggyback and Form S-3 registrations described above. We are not required to bear selling expenses, which include all underwriting discounts, selling commissions, stock transfer taxes applicable to the sale of registrable securities and fees and disbursements of any additional counsel for any selling holder. We are not required to pay registration expenses if the registration request under the investors' rights agreement is withdrawn at the request of the holders of a majority of the registrable securities unless (i) the holders of a majority of the registrable securities then outstanding agree to forfeit their right to one registration under the investors' rights agreement or (ii) the withdrawal is due to the discovery of a material adverse change in our business.

Termination of Registration Rights

The demand, piggyback and Form S-3 registration rights discussed above will terminate as to a given holder of registrable securities upon the earlier of (i) five years following the closing of this offering or (ii) such time as SEC Rule 144 or another similar exemption under the Securities Act is available for the sale of all shares held by the holder during a three-month period without registration and without the requirement for us to be in compliance with the current public information required under SEC Rule 144(c)(1).

Limitations of Liability and Indemnification

See "Executive and Director Compensation—Limitation on Liability and Indemnification Matters."

Market Listing

We have applied to list our common stock on the NASDAQ Global Market under the symbol "RYTM."

Transfer Agent and Registrar

Upon the completion of this offering, the transfer agent and registrar for our common stock will be Computershare.

MATERIAL UNITED STATES FEDERAL INCOME AND ESTATE TAX CONSEQUENCES TO NON-U.S. HOLDERS OF OUR COMMON STOCK

The following is a discussion of the material U.S. federal income and estate tax consequences of the acquisition, ownership, and disposition of our common stock to a non-U.S. holder that purchases shares of our common stock for cash in this offering. For purposes of this discussion, a "non-U.S. holder" means a beneficial owner (other than a partnership or other pass-through entity) of our common stock that is not, for U.S. federal income tax purposes:

- an individual who is a citizen or resident alien of the United States;
- a corporation or any other organization taxable as a corporation for U.S. federal income tax purposes, created or organized in the United States or under the laws of the United States or of any state thereof or the District of Columbia;
- an estate, the income of which is subject to U.S. federal income tax regardless of its source; or
- a trust if (i) the trust is subject to the primary supervision of a U.S. court and all substantial decisions of the trust are controlled by one or more U.S. persons or (ii) the trust has a valid election in effect under applicable U.S. Treasury regulations to be treated as a U.S. person.

This discussion does not address the tax treatment of partnerships (or other entities that are treated as partnerships, grantor trusts, or other pass-through entities for U.S. federal income tax purposes) or persons that hold their common stock through partnerships, grantor trusts or such other pass-through entities. The tax treatment of a partner in a partnership or a holder of an interest in another pass-through entity that will hold our common stock generally will depend upon the status of the partner or interest holder and the activities of the partner or interest holder and the partnership or other pass-through entity, as applicable. Such a partner or interest holder should consult his, her, or its own tax advisor regarding the tax consequences of the acquisition, ownership and disposition of our common stock through a partnership or other pass-through entity, as applicable.

This discussion is based upon the provisions of the Code, the U.S. Treasury regulations promulgated thereunder, judicial decisions, and published rulings, administrative procedures and other guidance of the Internal Revenue Service, which we refer to as the IRS, all as in effect as of the date hereof. These authorities are subject to change and to differing interpretations, possibly with retroactive effect, which could result in U.S. federal income or estate tax consequences different from those summarized below. No ruling has been or will be sought from the IRS with respect to the matters summarized below, and there can be no assurance that the IRS will not take a contrary position regarding the U.S. federal income or estate tax consequences of the acquisition, ownership, or disposition of our common stock, or that any such contrary position would not be sustained by a court.

This discussion is not a complete analysis of all of the potential U.S. federal income and estate tax consequences relating to the acquisition, ownership, and disposition of our common stock by non-U.S. holders, nor does it address any U.S. federal gift tax or generation-skipping transfer tax consequences, any tax consequences arising under any state, local, or non-U.S. tax laws, the impact of any applicable tax treaty, any consequences under the Medicare contribution tax on net investment income, the alternative minimum tax, or any consequences under other U.S. federal tax laws. In addition, this discussion does not address tax consequences resulting from a non-U.S. holder's particular circumstances or to non-U.S. holders that may be subject to special tax rules, including, without limitation:

- non-U.S. governments, agencies or instrumentalities thereof, or entities they control;
- "controlled foreign corporations" and their shareholders;
- "passive foreign investment companies" and their shareholders;
- partnerships, grantor trusts or other entities that are treated as pass-through entities for U.S. federal income tax purposes, and their owners;

- corporations that accumulate earnings to avoid U.S. federal income tax;
- former citizens or former long-term residents of the United States;
- banks, insurance companies or other financial institutions;
- tax-exempt pension funds or other tax-exempt organizations;
- persons who acquired our common stock pursuant to the exercise of employee stock options or otherwise as compensation;
- tax-qualified retirement plans;
- traders, brokers or dealers in securities, commodities or currencies;
- persons who hold our common stock as a position in a hedging transaction, wash sale, "straddle," "conversion transaction" or other risk reduction transaction or synthetic security;
- persons who do not hold our common stock as a capital asset within the meaning of Section 1221 of the Code (generally, for investment purposes);
- persons who own or have owned, or are deemed to own or to have owned, more than 5% of our common stock (except to the extent specifically set forth below); or
- persons deemed to sell our common stock under the constructive sale provisions of the Code.

Prospective investors should consult their tax advisors regarding the particular U.S. federal income, estate, gift, and generation-skipping transfer tax consequences to them of acquiring, owning and disposing of our common stock, as well as any tax consequences arising under any state, local or foreign tax laws and any other U.S. federal tax laws. Prospective investors should also consult their tax advisors regarding the potential impact of any applicable income or estate tax treaty between the United States and such prospective investor's country of residence and of the rules described below under the heading "Foreign Account Tax Compliance Act."

Distributions on Common Stock

As described in the section entitled "Dividend Policy," we currently intend to retain all available funds and any future earnings for use in the operation of our business and do not anticipate paying any dividends on our common stock in the foreseeable future. The disclosure in this section addresses the consequences should our board of directors, in the future, determine to make a distribution of cash or property with respect to our common stock (other than certain distributions of stock which may be made free of tax), or to effect a redemption that is treated for tax purposes as a distribution. Any such distribution will generally constitute a dividend for U.S. federal tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. To the extent such a distribution exceeds both our current and our accumulated earnings and profits, such excess will be allocated ratably among the shares of common stock with respect to which the distribution is made, will constitute a return of capital, and will first be applied against and reduce the non-U.S. holder's adjusted tax basis in those shares of common stock, but not below zero. Distributions in excess of our current and accumulated earnings and profits and in excess of a non-U.S. holder's tax basis in that non-U.S. holder's shares of common stock then will be treated as gain from the sale of that common stock, subject to the tax treatment described below under "Gain on Disposition of Common Stock." A non-U.S. holder's adjusted tax basis in a share of common stock is generally the purchase price of the share, reduced by the amount of any distributions constituting a return of capital with respect to that share.

Any dividend paid to a non-U.S. holder of our common stock generally will be subject to U.S. federal withholding tax at a rate of 30% of the gross amount of the dividend, or such lower rate as may be specified by an applicable income tax treaty between the United States and such non-U.S. holder's country of residence. If a non-U.S. holder is eligible for benefits under an income tax treaty and wishes to claim a reduced rate of withholding, the non-U.S. holder generally will be required to provide us or our paying

agent with a properly completed IRS Form W-8BEN, Form W-8BEN-E, or other applicable form, certifying under penalties of perjury the non-U.S. holder's qualification for the reduced rate. This certification must be provided to us or our paying agent prior to the payment of the dividend and may be required to be updated periodically. Special certification requirements apply to non-U.S. holders that hold common stock through certain foreign intermediaries. Non-U.S. holders that do not timely provide the required certifications, but that qualify for a reduced treaty rate, may obtain a refund of any excess amounts withheld by timely filing an appropriate claim for refund with the IRS. If we are not able to determine whether or not a distribution will exceed current and accumulated earnings and profits at the time the distribution is made, we may withhold tax on the entire amount of any distribution at the same rate as we would withhold on a dividend. However, a non-U.S. holder may obtain a refund of amounts that we withhold to the extent attributable to the portion of the distribution in excess of our current and accumulated earnings and profits.

If a non-U.S. holder holds our common stock in connection with the conduct of a trade or business in the U.S., and dividends paid on the common stock are effectively connected with the non-U.S. holder's U.S. trade or business (and, if required by an applicable income tax treaty between the United States and such non-U.S. holder's country of residence, are attributable to a permanent establishment or fixed base maintained by the non-U.S. holder in the U.S., as defined under the applicable treaty), the non-U.S. holder will be exempt from U.S. federal withholding tax on the dividends. To claim the exemption, the non-U.S. holder must furnish a properly executed IRS Form W-8ECI (or other applicable form) prior to the payment of the dividends. Any dividends paid on our common stock that are effectively connected with a non-U.S. holder's U.S. trade or business (and satisfy any other applicable treaty requirements) generally will be subject to U.S. federal income tax on a net income basis at the regular graduated U.S. federal income tax rates generally applicable to U.S. persons (as defined in the Code). A non-U.S. holder that is treated as a corporation for U.S. federal income tax purposes also may be subject to an additional branch profits tax equal to 30% (or such lower rate as is specified by an applicable income tax treaty between the United States and such non-U.S. holder's country of residence) of a portion of its earnings and profits for the taxable year that are effectively connected with a U.S. trade or business, as adjusted for certain items.

Gain on Disposition of Common Stock

Subject to the discussion below regarding backup withholding and foreign accounts, a non-U.S. holder generally will not be subject to U.S. federal income tax on any gain realized upon the sale, exchange, or other taxable disposition of our common stock unless:

- the gain is effectively connected with the non-U.S. holder's conduct of a U.S. trade or business (and, if required by an applicable income tax treaty between the United States and such non-U.S. holder's country of residence, the gain is attributable to a permanent establishment or fixed base maintained by the non-U.S. holder in the United States), in which case the non-U.S. holder will generally be required to pay tax on the gain derived from the sale, exchange, or other taxable disposition (net of certain deductions or credits) under regular graduated U.S. federal income tax rates generally applicable to U.S. persons, and in the case of a non-U.S. holder that is treated as a corporation for U.S. federal income tax purposes, such non-U.S. holder may be subject to a branch profits tax at a 30% rate or such lower rate as may be specified by an applicable income tax treaty between the United States and such non-U.S. holder's country of residence;

- the non-U.S. holder is an individual who is present in the U.S. for a period or periods aggregating 183 days or more during the taxable year in which the sale, exchange, or other taxable disposition occurs and certain other conditions are met, in which case the non-U.S. holder will be subject to U.S. federal income tax at a flat 30% rate (or such lower rate as is specified by an applicable income tax treaty between the United States and such non-U.S. holder's country of residence) on the net gain derived from the sale, exchange, or other taxable disposition, which gain may be offset by U.S. source capital losses (even though the non-U.S. holder is not considered a resident of the United

States) provided that the non-U.S. holder has timely filed U.S. federal income tax returns reporting those losses; or

- our common stock is a "United States real property interest" by reason of our status as a "United States real property holding corporation," or USRPHC, for U.S. federal income tax purposes during the five-year period preceding such sale, exchange or other taxable disposition (or the non-U.S. holder's holding period, if shorter). Generally, a corporation is a USRPHC only if the fair market value of its U.S. real property interests equals or exceeds 50% of the sum of the fair market value of its worldwide real property interests plus its other assets used or held for use in a trade or business.

We believe we are not now and we do not anticipate becoming a USRPHC. However, there can be no assurance that we are not now a USRPHC or will not become one in the future. Even if we are or become a USRPHC, for so long as our common stock is "regularly traded," as defined by applicable U.S. Treasury regulations, on an established securities market, sales of our common stock generally will not be subject to tax for non-U.S. holders that have not held more than 5% of our common stock, actually or constructively, during the five-year period preceding such non-U.S. holder's sale, exchange or other taxable disposition of our common stock (or the non-U.S. holder's holding period, if shorter). If we are determined to be a USRPHC and the foregoing exception does not apply, then a purchaser may withhold 15% of the proceeds payable to a non-U.S. holder from a sale of our common stock and the non-U.S. holder generally will be taxed on its net gain derived from the disposition at the graduated U.S. federal income tax rates applicable to U.S. persons.

U.S. Federal Estate Tax

Shares of our common stock that are owned or treated as owned at the time of death by an individual who is not a citizen or resident of the United States, as specifically defined for U.S. federal estate tax purposes, are considered U.S. situs assets and will be included in the individual's gross estate for U.S. federal estate tax purposes. Such shares, therefore, may be subject to U.S. federal estate tax, unless an applicable estate tax or other treaty between the United States and such individual's country of residence provides otherwise.

Information Reporting and Backup Withholding

Generally, we or certain financial middlemen must report annually to the IRS and to each non-U.S. holder the gross amount of dividends and other distributions on our common stock paid to the non-U.S. holder and the amount of tax withheld, if any, with respect to those distributions. Pursuant to applicable income tax treaties or other agreements, the IRS may make these reports available to tax authorities in the non-U.S. holder's country of residence or incorporation.

A non-U.S. holder may be subject to backup withholding with respect to dividends paid on shares of our common stock, unless, generally, the non-U.S. holder certifies under penalties of perjury (usually on IRS Form W-8BEN or W-8BEN-E) that the non-U.S. holder is not a U.S. person or otherwise establishes an exemption. The backup withholding rate is currently 28%. Dividends that are paid to non-U.S. holders subject to the withholding of U.S. federal income tax, as described above under the heading "Distributions on Common Stock" generally will be exempt from U.S. backup withholding.

Additional rules relating to information reporting requirements and backup withholding with respect to payments of the proceeds from the disposition of shares of our common stock are as follows:

- If the proceeds are paid to or through the U.S. office of a broker, the proceeds generally will be subject to backup withholding and information reporting, unless the non-U.S. holder certifies under penalties of perjury (usually on IRS Form W-8BEN or W-8BEN-E) that the non-U.S. holder is not a U.S. person and satisfies certain other requirements or otherwise establishes an exemption.

- If the proceeds are paid to or through a non-U.S. office of a broker that is not a U.S. person and is not a foreign person with certain specified U.S. connections, which we refer to below as a "U.S.-related person," information reporting and backup withholding generally will not apply.

- If the proceeds are paid to or through a non-U.S. office of a broker that is a U.S. person or a U.S.-related person, the proceeds generally will be subject to information reporting (but not to backup withholding), unless the non-U.S. holder certifies under penalties of perjury (usually on IRS Form W-8BEN or W-8BEN-E) that the non-U.S. holder is not a U.S. person. A "U.S.-related person" includes (i) an entity classified as a "controlled foreign corporation" for U.S. federal income tax purposes, (ii) a foreign person, 50% or more of whose gross income from certain periods is effectively connected with a U.S. trade or business, or (iii) a foreign partnership if at any time during its tax year (a) one or more of its partners are U.S. persons who, in the aggregate, hold more than 50% of the income or capital interests of the partnership or (b) the foreign partnership is engaged in a U.S. trade or business.

Backup withholding is not an additional tax. Any amounts withheld from a non-U.S. holder under the backup withholding rules may be allowed as a refund or a credit against the non-U.S. holder's U.S. federal income tax liability, if any, provided that the non-U.S. holder timely furnishes the required information to the IRS. Non-U.S. holders should consult their own tax advisors regarding the application of the information reporting and backup withholding rules to them.

Foreign Account Tax Compliance Act

Sections 1471 to 1474 of the Code (commonly referred to as the Foreign Account Tax Compliance Act, or FATCA) generally impose withholding tax on certain types of payments made to "foreign financial institutions" (as defined in the Code) and other non-U.S. entities unless those institutions and entities meet additional certification, information reporting and other requirements. FATCA generally imposes a 30% withholding tax on dividends on, or gross proceeds from the sale or other disposition of, our common stock paid to a foreign financial institution unless the foreign financial institution enters into an agreement with the U.S. Treasury to, among other things, (i) undertake to identify accounts held by certain U.S. persons (including certain equity and debt holders of such institution) or by U.S.-owned foreign entities, (ii) annually report certain information about such accounts, and (iii) withhold 30% on payments to account holders whose actions prevent it from complying with these reporting and other requirements. In addition, subject to certain exceptions, the legislation imposes a 30% withholding tax on the same types of payments to a "non-financial foreign entity" (as defined in the Code) unless the entity certifies that it does not have any substantial U.S. owners (which generally include any U.S. persons who directly or indirectly own more than 10% of the entity) or furnishes identifying information regarding each such substantial U.S. owner or agrees to report that information to the IRS. These withholding taxes will be imposed on dividends paid on our common stock, and, after December 31, 2018, on gross proceeds from sales or other dispositions of our common stock. Withholding under FATCA generally will not be reduced or limited by bilateral income tax treaties. However, intergovernmental agreements between the U.S. and other countries with respect to the implementation of FATCA and non-U.S. laws, regulations and other authorities enacted or issued with respect to those intergovernmental agreements may modify the FATCA requirements described above. Non-U.S. holders should consult their own tax advisors regarding the possible implications of FATCA on their investment in our common stock and the entities through which they hold our common stock, including, without limitation, the process and deadlines for meeting the applicable requirements to prevent the imposition of the 30% withholding tax under FATCA.

SHARES ELIGIBLE FOR FUTURE SALE

Prior to this offering, there has been no public market for shares of our common stock. We cannot predict the effect, if any, that future sales of shares of common stock, or the availability for future sales of shares of common stock, will have on the market price of shares of our common stock prevailing from time to time. The sale of substantial amounts of shares of our common stock in the public market, or the perception that such sales could occur, could harm the prevailing market price of shares of our common stock.

Currently shares of our common stock are outstanding. Upon the conversion of our preferred stock to common stock prior to the closing of this offering, shares of our common stock will be outstanding, and there will be holders of our common stock.

Upon completion of this offering, we will have a total of shares of our common stock outstanding (or shares of common stock if the underwriters exercise in full their option to purchase additional shares of common stock). Of those shares, shares, including the shares sold in this offering, will be freely tradable without restriction or further registration under the Securities Act by persons other than our "affiliates." Under the Securities Act, an "affiliate" of an issuer is a person who directly or indirectly controls, is controlled by or is under common control with that issuer. In addition, shares of common stock may be granted under the amended and restated 2015 equity incentive plan, as amended and in effect from and after the closing of this offering, or the post-offering Plan.

Our amended and restated certificate of incorporation authorizes us to issue additional shares of common stock and options, rights, warrants and appreciation rights relating to common stock for the consideration and on the terms and conditions established by our board of directors in its sole discretion. In accordance with the Delaware General Corporation Law and the provisions of our amended and restated certificate of incorporation, we may also issue preferred stock that has designations, preferences, rights, powers and duties that are different from, and may be senior to, those applicable to shares of common stock. See "Description of Capital Stock."

Lock-Up Agreements

We, along with our directors, executive officers and all of our other stockholders have agreed with the underwriters that for a period of 180 days (the restricted period), after the date of this prospectus, subject to specified exceptions, we or they will not offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, lend or otherwise transfer or dispose of, directly or indirectly, any shares of common stock or any securities convertible into or exercisable or exchangeable for shares of common stock, or enter into any swap or other arrangement that transfers to another, in whole or in part, any of the economic consequences of ownership of the common stock. All of our outstanding shares are subject to a lock-up agreement. Upon expiration of the "restricted" period, certain of our stockholders will have the right to require us to register their shares under the Securities Act. See "—Registration Rights" below and "Description of Capital Stock—Registration Rights."

After this offering, certain of our employees, including our executive officers and/or directors, may enter into written trading plans that are intended to comply with Rule 10b5-1 under the Securities Exchange Act of 1934, as amended, or the Exchange Act. Sales under these trading plans would not be permitted until the expiration of the lock-up agreements relating to the offering described above.

Registration Rights

Upon closing of this offering, the holders of shares of our common stock will be entitled to rights with respect to the registration of their shares under the Securities Act, subject to the

lock-up agreements described under "—Lock-Up Agreements" above. Registration of these shares under the Securities Act would result in the shares becoming freely tradable without restriction under the Securities Act, except for shares purchased by affiliates, immediately upon the effectiveness of the registration statement of which this prospectus is a part. Any sales of securities by these stockholders could have a material adverse effect on the trading price of our common stock. See "Description of Capital Stock—Registration Rights."

Rule 144

In general, under Rule 144 a person (or persons whose shares are aggregated) who may be deemed our affiliate is entitled to sell within any three-month period a number of restricted securities that does not exceed the greater of 1% of the then outstanding shares of common stock and the average weekly trading volume during the four calendar weeks preceding each such sale, provided that at least six months has elapsed since such shares of common stock were acquired from us or any affiliate of ours and certain manner of sale, notice requirements and requirements as to availability of current public information about us are satisfied. Any person who is deemed to be our affiliate must also comply with such provisions of Rule 144 (other than the six-month holding period requirement) in order to sell shares of common stock which are not restricted securities (such as shares of common stock acquired by affiliates through purchases in the open market following this offering). Upon completion of this offering, shares of our common stock will be "restricted securities" as such term is defined in Rule 144. A person who is not our affiliate, and who has not been our affiliate at any time during the 90 days preceding any sale, is entitled to sell shares of common stock (i) subject only to the requirements as to availability of current public information about us, provided that a period of at least six months has elapsed since the shares of common stock were acquired from us or any affiliate of ours, and (ii) without regard to the requirements as to availability of current public information about us or any other requirement of Rule 144, provided that at least one year has elapsed since the shares of common stock were acquired from us or any affiliate of ours.

Stock Options

As soon as practicable after the completion of this offering, we intend to file a Form S-8 registration statement under the Securities Act to register shares of our common stock subject to options outstanding or reserved for issuance under the post-offering Plan. This registration statement will become effective immediately upon filing, and shares covered by this registration statement will thereupon be eligible for sale in the public markets, subject to vesting restrictions, the lock-up agreements described above and Rule 144 limitations applicable to affiliates. For a more complete discussion of our stock plans, see "Executive and Director Compensation—Employee Benefit and Stock Plans."

UNDERWRITING

Under the terms and subject to the conditions in an underwriting agreement dated the date of this prospectus, the underwriters named below, for whom Morgan Stanley & Co. LLC, Merrill Lynch, Pierce, Fenner & Smith Incorporated and Cowen and Company, LLC are acting as representatives, have severally agreed to purchase, and we have agreed to sell to them, severally, the number of shares indicated below:

Underwriter	Number of Shares
Morgan Stanley & Co. LLC	
Merrill Lynch, Pierce, Fenner & Smith Incorporated	
Cowen and Company, LLC	
Needham & Company, LLC	
Total	

The underwriters and the representatives are collectively referred to as the "underwriters" and the "representatives," respectively. The underwriters are offering the shares of common stock subject to their acceptance of the shares from us and subject to prior sale. The underwriting agreement provides that the obligations of the several underwriters to pay for and accept delivery of the shares of common stock offered by this prospectus are subject to the approval of certain legal matters by their counsel and to certain other conditions. The underwriters are obligated to take and pay for all of the shares of common stock offered by this prospectus if any such shares are taken. However, the underwriters are not required to take or pay for the shares covered by the underwriters' option to purchase additional shares described below.

The underwriters initially propose to offer part of the shares of common stock directly to the public at the offering price listed on the cover page of this prospectus and part to certain dealers. After the initial offering of the shares of common stock, the offering price and other selling terms may from time to time be varied by the representatives.

We have granted to the underwriters an option, exercisable for 30 days from the date of this prospectus, to purchase up to additional shares of common stock at the public offering price listed on the cover page of this prospectus, less underwriting discounts and commissions. To the extent the option is exercised, each underwriter will become obligated, subject to certain conditions, to purchase about the same percentage of the additional shares of common stock as the number listed next to the underwriter's name in the preceding table bears to the total number of shares of common stock listed next to the names of all underwriters in the preceding table.

The following table shows the per share and total public offering price, underwriting discounts and commissions, and proceeds before expenses to us. These amounts are shown assuming both no exercise and full exercise of the underwriters' option to purchase up to an additional shares of common stock.

	Per Share	Total	
		No Exercise	Full Exercise
Public offering price	$	$	$
Underwriting discounts and commissions to be paid by us	$	$	$
Proceeds, before expenses, to us	$	$	$

The estimated offering expenses payable by us, exclusive of the underwriting discounts and commissions, are approximately $. We have agreed to reimburse the underwriters for expenses relating to clearance of this offering with the Financial Industry Regulatory Authority up to $30,000.

The underwriters have informed us that they do not intend sales to discretionary accounts to exceed 5% of the total number of shares of common stock offered by them.

We intend to apply to have our common stock approved for quotation on the NASDAQ Global Market under the trading symbol "RYTM."

We and all directors and officers and the holders of substantially all of our outstanding stock and stock options have agreed that, without the prior written consent of Morgan Stanley & Co. LLC, Merrill Lynch, Pierce, Fenner & Smith Incorporated and Cowen and Company, LLC on behalf of the underwriters, we and they will not, during the period ending 180 days after the date of this prospectus, the restricted period:

- offer, sell, contract to sell, pledge or otherwise dispose of, (or enter into any transaction which is designed to, or might reasonably be expected to, result in the disposition (whether by actual disposition or effective economic disposition due to cash settlement or otherwise), directly or indirectly) any capital stock or any securities convertible into, or exercisable or exchangeable for such capital stock;

- file any registration statement with the SEC (other than a registration statement on Form S-8) relating to the offering of any shares of capital stock or any securities convertible into or exercisable or exchangeable for capital stock; or

- establish or increase a put equivalent position or liquidate or decrease a call equivalent position within the meaning of Section 16 of the Exchange Act and the rules and regulations of the SEC promulgated thereunder with respect to any shares of capital stock or any securities convertible into or exercisable or exchangeable for capital stock;

whether any such transaction described above is to be settled by delivery of common stock or such other securities, in cash or otherwise. In addition, we and each such person agrees that, without the prior written consent of Morgan Stanley & Co. LLC, Merrill Lynch, Pierce, Fenner & Smith Incorporated and Cowen and Company, LLC on behalf of the underwriters, we or such other person will not, during the restricted period, make any demand for, or exercise any right with respect to, the registration of any shares of common stock or any security convertible into or exercisable or exchangeable for common stock.

The restrictions described in the immediately preceding paragraph do not apply to:

- the sale of shares to the underwriters; or

- the issuance by us of shares of common stock upon the exercise of an option or a warrant or the conversion of a security outstanding on the date of this prospectus of which the underwriters have been advised in writing;

- transactions by any person other than us relating to shares of common stock or other securities acquired in open market transactions after the completion of the offering of the shares; provided that no filing under Section 16(a) of the Exchange Act is required or voluntarily made in connection with subsequent sales of the common stock or other securities acquired in such open market transactions; or

- the establishment of a trading plan pursuant to Rule 10b5-1 under the Exchange Act for the transfer of shares of common stock, provided that (i) such plan does not provide for the transfer of common stock during the restricted period and (ii) to the extent a public announcement or filing under the Exchange Act, if any, is required or voluntarily made regarding the establishment of such plan, such announcement or filing shall include a statement to the effect that no transfer of common stock may be made under such plan during the restricted period.

Morgan Stanley & Co. LLC, Merrill Lynch, Pierce, Fenner & Smith Incorporated and Cowen and Company, LLC, in their sole discretion, may release the common stock and other securities subject to the lock-up agreements described above in whole or in part at any time.

In order to facilitate the offering of the common stock, the underwriters may engage in transactions that stabilize, maintain or otherwise affect the price of the common stock. Specifically, the underwriters may sell more shares than they are obligated to purchase under the underwriting agreement, creating a short position. A short sale is covered if the short position is no greater than the number of shares available for purchase by the underwriters under the option. The underwriters can close out a covered short sale by exercising the option or purchasing shares in the open market. In determining the source of shares to close out a covered short sale, the underwriters will consider, among other things, the open market price of shares compared to the price available under the option. The underwriters may also sell shares in excess of the option, creating a naked short position. The underwriters must close out any naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the common stock in the open market after pricing that could adversely affect investors who purchase in this offering. As an additional means of facilitating this offering, the underwriters may bid for, and purchase, shares of common stock in the open market to stabilize the price of the common stock. These activities may raise or maintain the market price of the common stock above independent market levels or prevent or retard a decline in the market price of the common stock. The underwriters are not required to engage in these activities and may end any of these activities at any time.

We and the underwriters have agreed to indemnify each other against certain liabilities, including liabilities under the Securities Act.

A prospectus in electronic format may be made available on websites maintained by one or more underwriters, or selling group members, if any, participating in this offering. The representatives may agree to allocate a number of shares of common stock to underwriters for sale to their online brokerage account holders. Internet distributions will be allocated by the representatives to underwriters that may make Internet distributions on the same basis as other allocations.

The underwriters and their respective affiliates are full service financial institutions engaged in various activities, which may include securities trading, commercial and investment banking, financial advisory, investment management, investment research, principal investment, hedging. financing and brokerage activities. Certain of the underwriters and their respective affiliates have, from time to time, performed, and may in the future perform, various financial advisory and investment banking services for us, for which they received or will receive customary fees and expenses.

In addition, in the ordinary course of their various business activities, the underwriters and their respective affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (including bank loans) for their own account and for the accounts of their customers and may at any time hold long and short positions in such securities and instruments. Such investment and securities activities may involve our securities and instruments. The underwriters and their respective affiliates may also make investment recommendations or publish or express independent research views in respect of such securities or instruments and may at any time hold, or recommend to clients that they acquire, long or short positions in such securities and instruments.

Pricing of the Offering

Prior to this offering, there has been no public market for our common stock. The initial public offering price was determined by negotiations between us and the representatives. Among the factors considered in determining the initial public offering price were our future prospects and those of our industry in general, our sales, earnings and certain other financial and operating information in recent periods, and the price-earnings ratios, price-sales ratios, market prices of securities, and certain financial and operating information of companies engaged in activities similar to ours.

Selling Restrictions

European Economic Area

In relation to each Country of the European Economic Area which has implemented the Prospectus Directive, each, a Relevant Country, an offer to the public of any shares of our common stock may not be made in that Relevant Country, except that an offer to the public in that Relevant Country of any shares of our common stock may be made at any time under the following exemptions under the Prospectus Directive, if they have been implemented in that Relevant Country:

(a) to any legal entity which is a qualified investor as defined in the Prospectus Directive;

(b) to fewer than 100 or, if the Relevant Country has implemented the relevant provision of the 2010 PD Amending Directive, 150, natural or legal persons (other than qualified investors as defined in the Prospectus Directive), as permitted under the Prospectus Directive, subject to obtaining the prior consent of the representatives for any such offer; or

(c) in any other circumstances falling within Article 3(2) of the Prospectus Directive, provided that no such offer of shares of our common stock shall result in a requirement for the publication by us or any underwriter of a prospectus pursuant to Article 3 of the Prospectus Directive.

For the purposes of this provision, the expression an "offer to the public" in relation to any shares of our common stock in any Relevant Country means the communication in any form and by any means of sufficient information on the terms of the offer and any shares of our common stock to be offered so as to enable an investor to decide to purchase any shares of our common stock, as the same may be varied in that Relevant Country by any measure implementing the Prospectus Directive in that Relevant Country, the expression "Prospectus Directive" means Directive 2003/71/EC (and amendments thereto, including the 2010 PD Amending Directive, to the extent implemented in the Relevant Country), and includes any relevant implementing measure in the Relevant Relevant Country, and the expression "2010 PD Amending Directive" means Directive 2010/73/EU.

United Kingdom

Each underwriter has represented and agreed that:

(a) it has only communicated or caused to be communicated and will only communicate or cause to be communicated an invitation or inducement to engage in investment activity (within the meaning of Section 21 of the Financial Services and Markets Act 2000, or FSMA, received by it in connection with the issue or sale of the shares of our common stock in circumstances in which Section 21(1) of the FSMA does not apply to us; and

(b) it has complied and will comply with all applicable provisions of the FSMA with respect to anything done by it in relation to the shares of our common stock in, from or otherwise involving the United Kingdom.

Canada

The shares may be sold only to purchasers purchasing, or deemed to be purchasing, as principal that are accredited investors, as defined in National Instrument 45-106 Prospectus Exemptions or subsection 73.3(1) of the Securities Act (Ontario), and are permitted clients, as defined in National Instrument 31-103 Registration Requirements, Exemptions and Ongoing Registrant Obligations. Any resale of the shares must be made in accordance with an exemption from, or in a transaction not subject to, the prospectus requirements of applicable securities laws.

Securities legislation in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if this prospectus (including any amendment thereto) contains a

misrepresentation, provided that the remedies for rescission or damages are exercised by the purchaser within the time limit prescribed by the securities legislation of the purchaser's province or territory. The purchaser should refer to any applicable provisions of the securities legislation of the purchaser's province or territory for particulars of these rights or consult with a legal advisor.

Pursuant to section 3A.3 (or, in the case of securities issued or guaranteed by the government of a non-Canadian jurisdiction, section 3A.4) of National Instrument 33-105 Underwriting Conflicts (NI 33-105), the underwriters are not required to comply with the disclosure requirements of NI 33-105 regarding underwriter conflicts of interest in connection with this offering.

Notice to Prospective Investors in Switzerland

The shares may not be publicly offered in Switzerland and will not be listed on the SIX Swiss Exchange, or SIX, or on any other stock exchange or regulated trading facility in Switzerland. This document has been prepared without regard to the disclosure standards for issuance prospectuses under art. 652a or art. 1156 of the Swiss Code of Obligations or the disclosure standards for listing prospectuses under art. 27 ff. of the SIX Listing Rules or the listing rules of any other stock exchange or regulated trading facility in Switzerland. Neither this document nor any other offering or marketing material relating to the shares or the offering may be publicly distributed or otherwise made publicly available in Switzerland.

Neither this document nor any other offering or marketing material relating to the offering, the Company or the shares have been or will be filed with or approved by any Swiss regulatory authority. In particular, this document will not be filed with, and the offer of shares will not be supervised by, the Swiss Financial Market Supervisory Authority FINMA (FINMA), and the offer of shares has not been and will not be authorized under the Swiss Federal Act on Collective Investment Schemes, or CISA. The investor protection afforded to acquirers of interests in collective investment schemes under the CISA does not extend to acquirers of shares.

Notice to Prospective Investors in the Dubai International Financial Centre

This prospectus relates to an Exempt Offer in accordance with the Offered Securities Rules of the Dubai Financial Services Authority, or DFSA. This prospectus is intended for distribution only to persons of a type specified in the Offered Securities Rules of the DFSA. It must not be delivered to, or relied on by, any other person. The DFSA has no responsibility for reviewing or verifying any documents in connection with Exempt Offers. The DFSA has not approved this prospectus nor taken steps to verify the information set forth herein and has no responsibility for the prospectus. The shares to which this prospectus relates may be illiquid and/or subject to restrictions on their resale. Prospective purchasers of the shares offered should conduct their own due diligence on the shares. If you do not understand the contents of this prospectus you should consult an authorized financial advisor.

Notice to Prospective Investors in Singapore

This prospectus has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this prospectus and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of Non-CIS Securities may not be circulated or distributed, nor may the Non-CIS Securities be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Singapore other than (i) to an institutional investor under Section 274 of the Securities and Futures Act, Chapter 289 of Singapore, or SFA, (ii) to a relevant person pursuant to Section 275(1), or any person pursuant to Section 275(1A), and in accordance with the conditions specified in Section 275, of the SFA, or (iii) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA.

Where the Non-CIS Securities are subscribed or purchased under Section 275 of the SFA by a relevant person which is:

(a) a corporation (which is not an accredited investor (as defined in Section 4A of the SFA)) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or

(b) a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary of the trust is an individual who is an accredited investor,

securities (as defined in Section 239(1) of the SFA) of that corporation or the beneficiaries' rights and interest (howsoever described) in that trust shall not be transferred within six months after that corporation or that trust has acquired the Non-CIS Securities pursuant to an offer made under Section 275 of the SFA except:

(a) to an institutional investor or to a relevant person defined in Section 275(2) of the SFA, or to any person arising from an offer referred to in Section 275(1A) or Section 276(4)(i)(B) of the SFA;

(b) where no consideration is or will be given for the transfer;

(c) where the transfer is by operation of law;

(d) as specified in Section 276(7) of the SFA; or

(e) as specified in Regulation 32 of the Securities and Futures (Offers of Investments) (Shares and Debentures) Regulations 2005 of Singapore.

Notice to Prospective Investors in Hong Kong

The securities have not been offered or sold and will not be offered or sold in Hong Kong, by means of any document, other than (a) to "professional investors" as defined in the Securities and Futures Ordinance (Cap. 571) of Hong Kong and any rules made under that Ordinance; or (b) in other circumstances which do not result in the document being a "prospectus" as defined in the Companies Ordinance (Cap. 32) of Hong Kong or which do not constitute an offer to the public within the meaning of that Ordinance. No advertisement, invitation or document relating to the securities has been or may be issued or has been or may be in the possession of any person for the purposes of issue, whether in Hong Kong or elsewhere, which is directed at, or the contents of which are likely to be accessed or read by, the public of Hong Kong (except if permitted to do so under the securities laws of Hong Kong) other than with respect to securities which are or are intended to be disposed of only to persons outside Hong Kong or only to "professional investors" as defined in the Securities and Futures Ordinance and any rules made under that Ordinance.

Notice to Prospective Investors in Japan

The securities have not been and will not be registered under the Financial Instruments and Exchange Law of Japan (Law No. 25 of 1948, as amended) and, accordingly, will not be offered or sold, directly or indirectly, in Japan, or for the benefit of any Japanese Person or to others for re-offering or resale, directly or indirectly, in Japan or to any Japanese Person, except in compliance with all applicable laws, regulations and ministerial guidelines promulgated by relevant Japanese governmental or regulatory authorities in effect at the relevant time. For the purposes of this paragraph, "Japanese Person" shall mean any person resident in Japan, including any corporation or other entity organized under the laws of Japan.

Notice to Prospective Investors in Australia

No placement document, prospectus, product disclosure statement or other disclosure document has been lodged with the Australian Securities and Investments Commission, in relation to the offering. This

prospectus does not constitute a prospectus, product disclosure statement or other disclosure document under the Corporations Act 2001, or Corporations Act, and does not purport to include the information required for a prospectus, product disclosure statement or other disclosure document under the Corporations Act.

Any offer in Australia of the shares may only be made to persons, or Exempt Investors, who are "sophisticated investors" (within the meaning of section 708(8) of the Corporations Act), "professional investors" (within the meaning of section 708(11) of the Corporations Act) or otherwise pursuant to one or more exemptions contained in section 708 of the Corporations Act so that it is lawful to offer the shares without disclosure to investors under Chapter 6D of the Corporations Act.

The shares applied for by Exempt Investors in Australia must not be offered for sale in Australia in the period of 12 months after the date of allotment under the offering, except in circumstances where disclosure to investors under Chapter 6D of the Corporations Act would not be required pursuant to an exemption under section 708 of the Corporations Act or otherwise or where the offer is pursuant to a disclosure document which complies with Chapter 6D of the Corporations Act. Any person acquiring shares must observe such Australian on-sale restrictions.

This prospectus contains general information only and does not take account of the investment objectives, financial situation or particular needs of any particular person. It does not contain any securities recommendations or financial product advice. Before making an investment decision, investors need to consider whether the information in this prospectus is appropriate to their needs, objectives and circumstances, and, if necessary, seek expert advice on those matters.

LEGAL MATTERS

The validity of the shares of common stock offered hereby will be passed upon for us by Morgan, Lewis & Bockius LLP, Boston, Massachusetts. Certain legal matters in connection with this offering will be passed upon for the underwriters by Wilmer Cutler Pickering Hale and Dorr LLP, New York, New York.

EXPERTS

The financial statements of Rhythm Pharmaceuticals, Inc. as of December 31, 2015 and 2016, and for the years then ended, included in this prospectus and the registration statement have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their report thereon (which contains an explanatory paragraph describing conditions that raise substantial doubt about the Company's ability to continue as a going concern as described in Note 1 to the financial statements) appearing elsewhere herein, and are included in reliance upon such report given on the authority of such firm as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We have filed with the SEC a registration statement on Form S-1 (including exhibits, schedules, and amendments) under the Securities Act with respect to the shares of common stock offered by this prospectus. This prospectus does not contain all the information set forth in the registration statement. For further information about us and the shares of common stock to be sold in this offering, you should refer to the registration statement. Statements contained in this prospectus relating to the contents of any contract, agreement or other document are not necessarily complete and are qualified in all respects by the complete text of the applicable contract, agreement or other document, a copy of which has been filed as an exhibit to the registration statement. Whenever this prospectus refers to any contract, agreement, or other document, you should refer to the exhibits that are a part of the registration statement for a copy of the contract, agreement, or document.

You may read and copy all or any portion of the registration statement or any other information we file at the SEC's public reference room at 100 F Street, N.E., Room 1580, Washington, D.C. 20549. You can request copies of these documents, upon payment of a duplicating fee, by writing to the SEC. Please call the SEC at 1-800-SEC-0330 for further information about the operation of the public reference rooms. Our SEC filings, including the registration statement, are also available to you on the SEC's Website (*http://www.sec.gov*).

Upon completion of this offering, we will become subject to the information and periodic reporting requirements of the Exchange Act. Under the Exchange Act, we will file annual, quarterly and current reports, as well as proxy statements and other information with the SEC. These periodic reports, proxy statements, and other information will be available for inspection and copying at the SEC's Public Reference Room and the website of the SEC referred to above.

RHYTHM PHARMACEUTICALS, INC.
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REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

The Board of Directors and Shareholders of
Rhythm Pharmaceuticals, Inc.

We have audited the accompanying balance sheets of Rhythm Pharmaceuticals, Inc. as of December 31, 2015 and 2016, and the related statements of operations and comprehensive loss, convertible preferred stock and stockholders' equity (deficit) and cash flows for each of the years then ended. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. We were not engaged to perform an audit of the Company's internal control over financial reporting. Our audits included consideration of internal control over financial reporting as a basis for designing audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion. An audit also includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the financial position of Rhythm Pharmaceuticals, Inc. at December 31, 2015 and 2016, and the results of its operations and its cash flows for the years then ended in conformity with U.S. generally accepted accounting principles.

The accompanying financial statements have been prepared assuming that the Company will continue as a going concern. As discussed in Note 1 to the financial statements, the Company has recurring losses from operations and has a net capital deficiency that raise substantial doubt about its ability to continue as a going concern. Management's plans in regard to this matter are also described in Note 1. The financial statements do not include any adjustments that may result from the outcome of this uncertainty.

/s/ Ernst & Young LLP

Boston, Massachusetts
May 23, 2017

RHYTHM PHARMACEUTICALS, INC.

BALANCE SHEETS

(in thousands, except share and per share data)

	December 31,		June 30,	Pro Forma June 30,
	2015	2016	2017	2017
			(unaudited)	
Assets				
Current assets:				
Cash and cash equivalents	$ 34,869	$ 6,540	$ 8,723	$ 29,198
Short-term investments	—	3,997	9,017	9,017
Prepaid expenses and other current assets	623	638	722	722
Total current assets	35,492	11,175	18,462	38,937
Property, plant and equipment, net	17	930	822	822
Deferred issuance costs	1,481	9	895	895
Due from Rhythm Holding Company, LLC	60	—	—	—
Restricted cash	225	225	225	225
Total assets	$ 37,275	$ 12,339	$ 20,404	$ 40,879
Liabilities, convertible preferred stock and stockholders' equity (deficit)				
Current liabilities:				
Accounts payable	$ 1,428	$ 1,895	$ 1,293	$ 1,293
Deferred grant income	249	—	—	—
Due to related party	635	105	—	—
Deferred rent	—	76	80	80
Accrued expenses and other current liabilities	2,962	2,655	3,470	3,470
Total current liabilities	5,274	4,731	4,843	4,843
Long-term liabilities:				
Series A investor instrument	—	—	410	—
Deferred rent	—	311	270	270
Total liabilities	5,274	5,042	5,523	5,113
Commitments and contingencies (Note 9)				
Series A Convertible Preferred Stock, $1.00 par value: 80,950,000 shares authorized; 40,000,000 shares issued and outstanding at December 31, 2015 and 2016, 60,475,001 shares issued and outstanding at June 30, 2017, no shares issued and outstanding at June 30, 2017 (pro forma) (aggregate liquidation preferences of $44,129 and $66,977 at December 31, 2016 and June 30, 2017, respectively)	40,000	40,000	60,147	—
Stockholders' equity (deficit):				
Common stock, $0.001 par value: 195,700,000 shares authorized; 93,500,000 shares issued and outstanding December 31, 2015 and 2016 and June 30, 2017; 174,449,999 shares issued and outstanding at June 30, 2017 (pro forma)	93	93	93	174
Additional paid-in capital	42,579	43,747	44,346	125,297
Accumulated deficit	(50,671)	(76,543)	(89,705)	(89,705)
Total stockholders' equity (deficit)	(7,999)	(32,703)	(45,266)	35,766
Total liabilities, convertible preferred stock and stockholders' equity	$ 37,275	$ 12,339	$ 20,404	$ 40,879

The accompanying notes are an integral part of these financial statements

RHYTHM PHARMACEUTICALS, INC.

STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS

(in thousands, except share and per share data)

	Year Ended December 31 2015	Year Ended December 31, 2016	Six Months Ended June 30,	
			2016	2017
			(unaudited)	
Operating expenses:				
Research and development	$ 7,148	$ 19,594	$ 8,544	$ 10,270
General and administrative	3,425	6,311	2,585	2,873
Total operating expenses	10,573	25,905	11,129	13,143
Loss from operations	(10,573)	(25,905)	(11,129)	(13,143)
Other income (expense):				
Revaluation of Series A Investor Right/Obligation and Series A Investor Instrument	(500)	—	—	(82)
Interest income, net	—	33	14	63
Total other income (expense):	(500)	33	14	(19)
Net loss and comprehensive loss	$ (11,073)	$ (25,872)	$ (11,115)	$ (13,162)
Net loss attributable to common stockholders	$ (12,000)	$ (29,074)	$ (12,711)	$ (15,534)
Net loss attributable to common stockholders per common share, basic and diluted (Note 2)	$ (0.13)	$ (0.31)	$ (0.14)	$ (0.17)
Weighted average common shares outstanding, basic and diluted	93,500,000	93,500,000	93,500,000	93,500,000
Pro forma net loss attributable to common stockholders per common share, basic and diluted (unaudited)		$ (0.19)		$ (0.09)
Pro forma weighted average common shares outstanding, basic and diluted (unaudited)		133,500,000		153,409,393

The accompanying notes are an integral part of these financial statements

RHYTHM PHARMACEUTICALS, INC.

STATEMENTS OF CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY (DEFICIT)

(in thousands, except share and per share data)

	Series A Convertible Preferred Stock		Common Stock		Series A-1 Junior Preferred Stock		Additional Paid-In Capital	Accumulated Deficit	Total Stockholders' Equity (Deficit)
	Shares	Amount	Shares	Amount	Shares	Amount			
Balance at December 31, 2014	—	—	93,500,000	$ 93	—	—	39,147	(39,598)	(358)
Equity contribution	—	—	—	—	—	—	2,094	—	2,094
Modification of warrant in connection with a license agreement	—	—	—	—	—	—	923	—	923
Stock compensation expense	—	—	—	—	—	—	298	—	298
Dividend to Rhythm Holding Company LLC (associated with common stock options granted to employees of Motus Therapeutics, Inc.)	—	—	—	—	—	—	2,695	—	2,695
Dividend to Rhythm Holding Company LLC (associated with common stock options granted to employees of Motus Therapeutics, Inc.)	—	—	—	—	—	—	(2,695)	—	(2,695)
Reclassification of Series A Investor Right/Obligation liability upon Series A second tranche closing	—	883	—	—	—	—	117	—	117
Issuance of Series A Convertible Preferred Stock	40,000,000	39,117	—	—	—	—	—	—	—
Net loss	—	—	—	—	—	—	—	(11,073)	(11,073)
Balance at December 31, 2015	40,000,000	40,000	93,500,000	93	—	—	42,579	(50,671)	(7,999)
Stock compensation expense	—	—	—	—	—	—	1,168	—	1,168
Net loss	—	—	—	—	—	—	—	(25,872)	(25,872)
Balance at December 31, 2016	40,000,000	40,000	93,500,000	93	—	—	43,747	(76,543)	(32,703)
Stock compensation expense	—	—	—	—	—	—	698	—	698
Change in unrealized loss on marketable securities	—	—	—	—	—	—	(1)	—	(1)
Net loss	—	—	—	—	—	—		(13,162)	(13,162)
Issuance of Series A Convertible Preferred Stock	20,475,001	20,147	—	—	—	—	(98)	—	(98)
Balance at June 30, 2017 (unaudited)	60,475,001	60,147	93,500,000	93	—	—	44,346	(89,705)	(45,266)
Settlement of Series A investor instrument	—	410	—	—	—	—	—	—	—
Issuance of Series A Convertible Preferred Stock	20,474,998	20,475	—	—	—	—	—	—	—
Exchange of common stock held by LLC entity for Series A-1 Junior Preferred Stock (Note 12)	—	—	(78,666,209)	(79)	78,666,209	79	—	—	—
Conversion of Series A Convertible Preferred Stock and Series A-1 Junior Preferred Stock into common stock on a one-to-one basis	(80,949,999)	(81,032)	159,616,208	160	(78,666,209)	(79)	80,951	—	81,032
Pro-forma balance at June 30, 2017 (unaudited)	—	—	174,449,999	$ 174	—	—	125,297	(89,705)	35,766

The accompanying notes are an integral part of these financial statements

RHYTHM PHARMACEUTICALS, INC.

STATEMENTS OF CASH FLOWS

(in thousands, except share and per share data)

	Year Ended December 31, 2015	Year Ended December 31, 2016	Six Months Ended June 30, 2016	Six Months Ended June 30, 2017
			(unaudited)	
Operating activities				
Net loss	$ (11,073)	$ (25,872)	$ (11,115)	$ (13,162)
Adjustments to reconcile net loss to cash used in operating activities:				
Stock-based compensation expense	298	1,168	559	698
Depreciation and amortization	—	144	33	108
Non-cash rent expense	—	11	47	(37)
Modification of warrant in connection with license agreement	923	—	—	—
Mark to market revaluation of Series A Investor Right/Obligation and Series A Investor Instrument	500	—	—	82
Changes in operating assets and liabilities:				
Prepaid expenses and other current assets	(581)	41	(957)	(68)
Deferred issuance costs	(1,481)	1,472	(344)	(886)
Tenant improvement allowance	—	376	376	—
Restricted cash	(225)	—	—	—
Accounts payable	893	467	882	(602)
Deferred grant income	249	(249)	(249)	—
Due to Motus Therapeutics, Inc.	635	(635)	(133)	—
Due (from) to Rhythm Holding Company, LLC	(60)	165	60	(105)
Accrued expenses and other current liabilities	2,945	(307)	(1,756)	814
Net cash used in operating activities	(6,977)	(23,219)	(12,597)	(13,158)
Investing activities				
Purchases of short-term investments	—	(15,222)	(7,080)	(13,021)
Maturities of short-term investments	—	11,169	1,780	7,985
Purchases of property, plant and equipment	(17)	(1,057)	(986)	—
Net cash used in investing activities	(17)	(5,110)	(6,286)	(5,036)
Financing activities				
Net proceeds from issuance of Series A Convertible Preferred Stock	39,617	—	—	20,377
Equity contribution	2,094	—	—	—
Net cash provided by financing activities	41,711	—	—	20,377
Net increase (decrease) in cash and cash equivalents	34,717	(28,329)	(18,883)	2,183
Cash and cash equivalents at beginning of period	152	34,869	34,869	6,540
Cash and cash equivalents at end of period	$ 34,869	$ 6,540	$ 15,986	$ 8,723

The accompanying notes are an integral part of these financial statements

Rhythm Pharmaceuticals, Inc.

Notes to Financial Statements

(including data applicable to unaudited periods)
(Information as of June 30, 2017 and for the
six months ended June 30, 2016 and 2017 is unaudited)

(In thousands, except share and per share information)

1. Nature of Business

Rhythm Pharmaceuticals, Inc. (the "Company"), is a biopharmaceutical company focused on the development and commercialization of peptide therapeutics for the treatment of genetic deficiencies that result in life-threatening metabolic disorders. The Company's lead product candidate is setmelanotide (RM-493), which is a potent, first-in-class, melanocortin-4, or MC4, receptor agonist for the treatment of rare genetic disorders of obesity caused by MC4 pathway deficiencies. The Company is currently evaluating setmelanotide for the treatment of six genetic disorders of obesity: pro-opiomelanocortin, or POMC, leptin receptor, or LepR, Bardet-Biedl syndrome, Alström syndrome, POMC heterozygous, and POMC epigenetic disorders.

Corporate Reorganization

The Company is a Delaware corporation organized in February 2013 under the name Rhythm Metabolic, Inc. Prior to the Company's organization and the Corporate Reorganization referred to below, the Company was part of Rhythm Pharmaceuticals, Inc. (the "Predecessor Company"), a Delaware corporation which was organized in November 2008 and which commenced active operations in 2010.

In March 2013, the Predecessor Company underwent a corporate reorganization, (the "Corporate Reorganization"), pursuant to which all of the outstanding equity securities of the Predecessor Company were exchanged for units of Rhythm Holding Company, LLC, a newly-organized limited liability company (the "LLC entity"). After the consummation of this exchange and as part of the Corporate Reorganization, the Predecessor Company contributed setmelanotide and the MC4R agonist program to the Company and distributed to the LLC entity all of the then issued and outstanding shares of the Company's stock. The result of the Corporate Reorganization was that the Company and the Predecessor Company became wholly-owned subsidiaries of the LLC entity and the two product candidates and related programs that were originally held by the Predecessor Company were separated, with relamorelin and the ghrelin agonist program being retained by the Predecessor Company and setmelanotide and the MC4R agonist program being held by the Company. The Predecessor Company, after consummation of the Corporate Reorganization, is referred to within these Notes to Financial Statements as the Relamorelin Company and/or Motus.

On October 13, 2015, the Relamorelin Company changed its name to Motus Therapeutics, Inc ("Motus") and the Company changed its name to Rhythm Pharmaceuticals, Inc. On December 15, 2016, Motus was sold to a large pharmaceutical company. On August 21, 2017, the LLC entity distributed to its members all of its shares of the Company (see Note 12 for further discussion).

Liquidity

The Company has incurred operating losses and negative cash flows from operations since inception, incurred a net loss of $25,872 and $13,162 during the year ended December 31, 2016 and the six months ended June 30, 2017, respectively, and has an accumulated deficit of $89,705 as of June 30, 2017. The Company has primarily funded these losses through capital contributions received from the LLC entity and the sale of preferred stock to outside investors. To date, the Company has no product revenue and

Rhythm Pharmaceuticals, Inc.

Notes to Financial Statements (Continued)

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1. Nature of Business (Continued)

management expects operating losses to continue for the foreseeable future. The Company has devoted substantially all of its resources to its drug development efforts, comprising research and development, manufacturing, conducting clinical trials for its product candidates, protecting its intellectual property and general and administrative functions relating to these operations. The future success of the Company is dependent on its ability to develop its product candidates and ultimately upon its ability to attain profitable operations. At June 30, 2017, the Company had $17,740 of cash and cash equivalents and short-term investments on hand. In January 2017, the Company closed the first tranche on the sale of preferred stock resulting in net proceeds of $20,377. The second tranche of $20,475 closed in August 2017 (see Note 12 for further discussion).

The Company is subject to a number of risks, including the need for substantial additional capital for clinical research and product development. Based upon the Company's $17,740 in existing cash, cash equivalents and short-term investments as of June 30, 2017, the Company does not have sufficient existing cash, cash equivalents and short-term investments to support operations for at least the next year following the date that the financial statements are issued.

The conditions in the preceding paragraph raise substantial doubt about the Company's ability to continue as a going concern within one year after the date that the financial statements are issued. Management's plans to alleviate the conditions that raise substantial doubt regarding the Company's ability to continue as a going concern include pursuing one or more of the following steps to raise additional funding and/or reduce expenditures:

- Raise funding through the possible sales of the Company's common or preferred stock, including public or private equity financings.
- Seek a partner to advance development of setmelanotide for the potential treatment of one or more genetic disorders of obesity.
- Defer or terminate planned clinical trials.

There can be no assurance, however, that the Company will receive cash proceeds from any of these potential resources or reduce its operating expenses. Furthermore, to the extent cash proceeds are received or expenses are reduced, there can be no assurance that those proceeds or reductions in expenses would be sufficient to support the Company's operations for at least the next year following the date that the financial statements are issued. Management has concluded that the likelihood that its plans to obtain sufficient funding from one or more of these sources will be successful or its plans to reduce its operating expenses, while reasonably possible, is less than probable. Accordingly, management has concluded that substantial doubt exists regarding the Company's ability to continue as a going concern.

If the Company is unable to raise capital when needed or on attractive terms, or if it is unable to procure partnership arrangements to advance its programs, or if it is unable to reduce its operating expenses, the Company would be forced to delay, reduce or eliminate its research and development programs and any future commercialization efforts.

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Notes to Financial Statements (Continued)

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1. Nature of Business (Continued)

The accompanying financial statements have been prepared on a going concern basis, which contemplates the realization of assets and satisfaction of liabilities in the ordinary course of business. The financial statements do not include any adjustments relating to the recoverability and classification of recorded asset amounts or the amounts and classification of liabilities that might result from the outcome of the uncertainties described above.

2. Summary of Significant Accounting Policies

Basis of Presentation

The Company's financial statements have been prepared in conformity with accounting principles generally accepted in the United States ("GAAP"). Any reference in these notes to applicable guidance is meant to refer to the authoritative United States generally accepted accounting principles as found in the Accounting Standards Codification ("ASC") and Accounting Standards Updates ("ASU") of the Financial Accounting Standards Board ("FASB").

The Company has historically existed and functioned as part of the consolidated businesses of the Predecessor Company. As noted above, the Predecessor Company's setmelanotide and the MC4R agonist program were transferred to the Company as part of the Corporate Reorganization on March 21, 2013. These financial statements include the results of operations of setmelanotide and the MC4R agonist program from its inception. As part of the Corporate Reorganization, the Company also entered into a formal payroll services intercompany agreement with the Relamorelin Company. On November 16, 2016, the employees of the Relamorelin Company that were providing services to the Company, terminated their employment contracts with the Relamorelin Company and entered into new employment agreements with the Company. On December 15, 2016, the Relamorelin Company closed on its sale to a large pharmaceutical company. At June 30, 2017, the Company had ten employees directly employed by the Company. During 2015 and 2016, costs have been allocated to the Company for the purposes of preparing the financial statements based on a specific identification basis or, when specific identification is not practicable, a proportional cost allocation method which allocates expenses based upon the percentage of employee time and research and development effort expended on the Company's business as compared to total employee time and research and development effort of the combined Motus and Rhythm. The proportional use basis adopted to allocate shared costs is in accordance with the guidance of SEC Staff Accounting Bulletin ("SAB") Topic 1B, *Allocation Of Expenses And Related Disclosure In Financial Statements Of Subsidiaries, Divisions Or Lesser Business Components Of Another Entity*. Management has determined that the method of allocating costs to the Company is reasonable. Cost allocation was no longer required subsequent to the 2016 sale of the Relamorelin Company.

Management believes that the statements of operations include a reasonable allocation of costs and expenses incurred by the Relamorelin Company, which benefited the Company. However, such amounts may not be indicative of the actual level of costs and expenses that would have been incurred by the Company if it had operated as an independent company or of the costs and expenses expected to be incurred in the future. Management has not presented an estimate of what the expenses of the Company

Rhythm Pharmaceuticals, Inc.

Notes to Financial Statements (Continued)

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2. Summary of Significant Accounting Policies (Continued)

would have been on a standalone basis as it was not practicable to make a reasonable estimate. As such, the financial information herein may not necessarily reflect the financial position, results of operations and cash flows of the Company expected in the future or what it would have been had it been an independent company during the periods presented.

As described above, Relamorelin Company employee costs are allocated to the Company based on a proportional use method. For those employees who became employees of the Company on November 16, 2016, their full employment cost was $3,155 and $2,727 for the years ended December 31, 2015 and 2016, respectively.

On August 3, 2015, the Company's board of directors approved a 93,500-for-1 forward stock split of the Company's issued and outstanding shares of common stock. All share and per share amounts in the financial statements have been retrospectively adjusted for all periods presented to give effect of the forward stock split.

Use of Estimates

The preparation of financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent liabilities at the date of the financial statements and the reported amounts of revenue and expenses during the reporting period. The Company bases its estimates on historical experience and other market-specific or other relevant assumptions that it believes to be reasonable under the circumstances. This process may result in actual results differing materially from those estimated amounts used in the preparation of the financial statements if these results differ from historical experience, or other assumptions do not turn out to be substantially accurate, even if such assumptions are reasonable when made. Significant estimates relied upon in preparing these financial statements include the allocation of costs from the Relamorelin Company in accordance with SAB Topic 1B, accrued expenses, stock-based compensation expense, the valuation allowance on the Company's deferred tax assets, and the fair value of the Series A Investor Right/Obligations and the Series A Investor Call Options. See Note 4.

Unaudited Interim Presentation

The accompanying interim balance sheet as of June 30, 2017, the statements of operations and comprehensive loss and cash flows for the periods ended June 30, 2016 and 2017 and the statement of convertible preferred stock and stockholders' equity (deficit) for the six months ended June 30, 2017 and the related footnote disclosures are unaudited. These unaudited interim financial statements have been prepared in accordance with GAAP. In management's opinion, the unaudited interim financial statements have been prepared on the same basis as the audited financial statements and include all adjustments, which include only normal recurring adjustments necessary for the fair presentation of the interim financial statements. The results for the six months ended June 30, 2017 are not necessarily indicative of the results expected for the full fiscal year.

Rhythm Pharmaceuticals, Inc.

Notes to Financial Statements (Continued)

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2. Summary of Significant Accounting Policies (Continued)

Unaudited Pro Forma Financial Information

The unaudited pro forma balance sheet and statement of convertible preferred stock and stockholders' equity (deficit) as of June 30, 2017 reflect the issuance of 20,474,998 shares of Series A Convertible Preferred Stock and the exchange of 78,666,209 shares of Common Stock for an equal number of Series A-1 Junior Preferred Stock on August 21, 2017 and the conversion of all the outstanding shares of Series A Convertible Preferred Stock and Series A-1 Junior Preferred Stock into shares of Common Stock upon the closing of an initial public offering.

Unaudited pro forma net loss per share attributable to common stockholders for the year-ended December 31, 2015 and 2016 and the six months ended June 30, 2016 and 2017, is computed using the weighted-average number of common shares outstanding after giving effect to the conversion of all Preferred Stock into shares of the Common Stock as if such conversion had occurred at the beginning of the period presented, or the date of original issuance, if later. Accordingly, the pro forma basic and diluted net loss per share attributable to common stockholders does not include the effects of the cumulative Preferred Stock dividends.

Off-Balance Sheet Risk and Concentrations of Credit Risk

Financial instruments, which potentially subject the Company to significant concentration of credit risk, consist primarily of cash and cash equivalents and short-term investments, which are maintained at two federally insured financial institutions. The deposits held at these two institutions are in excess of federally insured limits. The Company has not experienced any losses in such accounts and management believes that the Company is not exposed to significant credit risk due to the financial position of the depository institutions in which those deposits are held. The Company has no off-balance sheet risk, such as foreign exchange contracts, option contracts, or other foreign hedging arrangements.

Segment Information

Operating segments are defined as components of an entity about which separate discrete information is available for evaluation by the chief operating decision maker, or decision-making group, in deciding how to allocate resources and in assessing performance. The Company views its operations and manages its business in one operating segment operating exclusively in the United States.

Cash and Cash Equivalents

The Company considers all highly liquid investments with original or remaining maturity from the date of purchase of three months or less to be cash equivalents. Cash and cash equivalents includes bank demand deposits, U.S. treasury bills and money market funds that invest primarily in U.S. government treasuries.

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Notes to Financial Statements (Continued)

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2. Summary of Significant Accounting Policies (Continued)

Short-term Investments

Short-term investments consist of investments with original maturities greater than 90 days, as of the date of purchase. The Company has classified its investments with maturities beyond one year as short term, based on their highly liquid nature and because such marketable securities represent the investment of cash that is available for current operations. The Company considers its investment portfolio available-for-sale. Accordingly, these investments are recorded at fair value, which is based on quoted market prices. Unrealized gains and losses are reported as a component of accumulated other comprehensive income (loss) in stockholders' equity (deficit). Realized gains and losses and declines in value judged to be other than temporary are included as a component of other income (expense), net based on the specific identification method. When determining whether a decline in value is other than temporary, the Company considers various factors, including whether the Company has the intent to sell the security, and whether it is more likely than not that the Company will be required to sell the security prior to recovery of its amortized cost basis. Fair value is determined based on quoted market prices.

Restricted Cash

Restricted cash consists of a security deposit in the form of a letter of credit placed in a separate restricted bank account as required under the terms of the Company's new lease arrangement for its corporate office in Boston, Massachusetts.

Deferred Issuance Costs

Deferred issuance costs, which consist of direct incremental legal and accounting fees relating to the potential initial public offering ("IPO"), are capitalized. The deferred issuance costs will be offset against IPO proceeds upon the consummation of the offering. In the event the offering is terminated, deferred issuance costs will be expensed and included in non-current assets.

The Company had capitalized $1,825 of deferred issuance costs related to prior registration statements confidentially submitted to the Securities and Exchange Commission in 2015 and 2016. In the fourth quarter of 2016, the Company wrote off these deferred issuance costs to general and administrative expenses because the offering was postponed significantly in excess of 90 days. As a result, the costs were not deemed realizable as the Company expects to incur similar costs in connection with its current planned IPO. The Company incurred $9 and $895 of deferred issuance costs as of December 31, 2016 and June 30, 2017, respectively, which is included in non-current assets.

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Notes to Financial Statements (Continued)

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2. Summary of Significant Accounting Policies (Continued)

Prepaid Expenses and Other Current Assets

Prepaid expenses and other current assets consist primarily of costs incurred in advance of services being received, including services related to clinical trial programs.

	December 31, 2015	December 31, 2016	June 30, 2017
Prepaid research and development costs	$ 595	$ 422	$ 550
Other current assets	28	216	172
Prepaid expenses and other current assets	$ 623	$ 638	$ 722

Property, Plant and Equipment

Property, Plant and Equipment consists of the following:

	Useful Life	December 31, 2015	December 31, 2016	June 30, 2017
Leasehold improvements	*	$ 17	$ 891	$ 891
Office equipment	5 years	—	70	70
Computers and software	3 years	—	19	19
Furniture and fixtures	5 years	—	94	94
		17	1,074	1,074
Less accumulated depreciation and amortization		—	(144)	(252)
Property, Plant and Equipment, net		$ 17	$ 930	$ 822

* Shorter of asset life or lease term.

Leasehold improvements made during the year ended December 31, 2015 represent costs related to the Company's newly-leased office space in Boston, Massachusetts. The assets were transferred into service in 2016 and are being amortized over the shorter of the lease term or their expected useful life.

2015 Series A Investor Right/Obligation, 2015 Series A Investor Call Option and 2017 Series A Investor Instrument

The Company classified its 2015 Series A Investor Right/Obligation, its 2015 Series A Investor Call Option and its 2017 Series A Investor Instrument (see Note 4) as liabilities as they are free-standing financial instruments. The 2015 Series A Investor Right/Obligation, the 2015 Series A Investor Call Option and 2017 Series A Investor Instrument were recorded at fair value upon the issuance of Series A Convertible Preferred Stock in August 2015 and January 2017, respectively, and subsequently remeasured to fair value. Changes in fair value of these financial instruments are recognized as a component of other income (expense), net in the Statement of Operations and Comprehensive Loss. The 2015 Series A

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2. Summary of Significant Accounting Policies (Continued)

Investor Right/Obligation was exercised and the 2015 Series A Investor Call Option expired on December 1, 2015 upon the 2015 Series A Second Tranche Closing.

The Company used the Black-Scholes option-pricing model, which incorporates assumptions and estimates, to value the 2015 and 2017 Series A Investor Call Options (see Note 4). The Company assessed these assumptions and estimates on a quarterly basis as additional information impacting the assumptions was obtained. Estimates and assumptions impacting the fair value measurement include the fair value per share of the underlying Series A Convertible Preferred Stock, the expected term of the Series A Investor Call Options, risk-free interest rate, expected dividend yield and expected volatility of the price of the underlying preferred stock. The Company determined the fair value per share of the underlying preferred stock by taking into consideration the most recent sale of its convertible preferred stock and the investors' right to invest in a subsequent tranche. The Company's history as a private company means that it lacks company-specific historical and implied volatility information of its stock. Therefore, it estimates its expected stock volatility based on the historical volatility of publicly traded peer companies for a term comparable to the estimated term of the Series A Investor Call Options. The risk-free interest rate is determined by reference to the U.S. Treasury yield curve for time periods approximately equal to the estimated term of the Series A Investor Call Options. A dividend yield of zero is assumed.

The Company estimated the fair value of the 2015 and 2017 Series A Investor Right/Obligations as the probability-weighted present value of the expected benefit of the investment (see Notes 4 and 5).

Government Grants

The Company obtained an Orphan Products Development grant entitled "Phase 2 study of the melanocortin 4 receptor agonist RM-493 for the treatment of Prader-Willi syndrome" in 36 patients. The grant was awarded by the Public Health Service ("PHS") Food and Drug Administration. The PHS grant is for a total of $999 and is effective July 2015 through June 2018 for reimbursement of expenses relating to the Phase 2 Prader-Willi Study.

The Company recognizes government grants upon the determination that it will comply with the conditions attached to the grant arrangement and the grant will be received. Government grants are recognized in the statements of operations on a systematic basis over the periods in which the Company recognizes the related costs for which the government grant is intended to compensate. Government grants for research and development efforts are deducted in reporting the related expense in the statement of operations. Government grant income received during the year ended December 31, 2015 and 2016 and the six months ended June 30, 2016 and 2017 of $147, $642, $249 and zero, respectively, is included as a deduction to research and development expense in the statements of operations. Deferred grant income on the balance sheet as of December 31, 2015 and 2016 and June 30, 2017 was $249, zero and zero, respectively.

Rhythm Pharmaceuticals, Inc.

Notes to Financial Statements (Continued)

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2. Summary of Significant Accounting Policies (Continued)

Research and Development Expenses

Costs incurred in the research and development of the Company's products are expensed to operations as incurred. Research and development expenses consist of costs incurred in performing research and development activities, including salaries and benefits, facilities costs, overhead costs, contract services and other outside costs, both directly incurred and allocated from the Relamorelin Company. The value of goods and services received from contract research organizations or contract manufacturing organizations in the reporting period are estimated based on the level of services performed and progress in the period for which the Company has not yet received an invoice from the supplier.

Nonrefundable advance payments for goods or services to be received in the future for use in research and development activities are recorded as prepaid expenses, and expensed as the related goods are delivered or the services are performed.

Income Taxes

The Company is taxed as a C corporation for federal income tax purposes. Income taxes for the Company are recorded in accordance with FASB ASC Topic 740, *Income Taxes* ("ASC 740"), which provides for deferred taxes using an asset and liability approach. Income taxes have been calculated on a separate tax return basis. Certain of the Company's activities and costs have been included in the tax returns filed by the Relamorelin Company and the LLC entity. Prior to the Corporate Reorganization, the Company's operations were included in the tax returns filed by the Predecessor Company. The Company has filed tax returns on its own behalf since the Corporate Reorganization. Deferred tax assets and liabilities are recognized for the future tax consequences attributable to differences between the financial statement carrying amounts of existing assets and liabilities and their respective tax bases using enacted tax rates in effect for the year in which the differences are expected to affect taxable income. Tax benefits are recognized when it is more likely than not that a tax position will be sustained during an audit. Deferred tax assets are reduced by a valuation allowance if current evidence indicates that it is considered more likely than not that these benefits will not be realized.

Net Loss Per Share Attributable to Common Shareholders

Basic net loss per share attributable to common stockholders is calculated by dividing net loss attributable to common stockholders by the weighted average shares outstanding during the period, without consideration for Common Stock equivalents. Net loss attributable to common stockholders is calculated by adjusting the net loss of the Company for cumulative preferred stock dividends. During periods of income, the Company allocates participating securities a proportional share of income determined by dividing total weighted average participating securities by the sum of the total weighted average common shares and participating securities (the "two class method"). The Company's convertible preferred stock participates in any dividends declared by the Company and are therefore considered to be participating securities. Participating securities have the effect of diluting both basic and diluted earnings per share during periods of income. During periods of loss, the Company allocates no loss to participating

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2. Summary of Significant Accounting Policies (Continued)

securities because they have no contractual obligation to share in the losses of the Company. Diluted net loss per share attributable to common stockholders is calculated by adjusting weighted average shares outstanding for the dilutive effect of Common Stock equivalents outstanding for the period, determined using the treasury-stock and if-converted methods. For purposes of the diluted net loss per share attributable to common stockholders calculation, convertible preferred stock and stock options are considered to be Common Stock equivalents but have been excluded from the calculation of diluted net loss per share attributable to common stockholders, as their effect would be anti-dilutive for all periods presented. Therefore, basic and diluted net loss per share were the same for all periods presented.

As the years ended December 31, 2015 and 2016 and the six months ended June 30, 2016 and 2017 resulted in net losses, there is no income allocation required under the two-class method or dilution attributed to pro forma weighted average shares outstanding in the calculation of pro forma diluted loss per share attributable to common stockholders.

Basic and diluted earnings per share is calculated as follows:

	Year Ended December 31,		Six Months Ended June 30,	
	2015	2016	2016	2017
Numerator:				
Net loss	$ (11,073)	$ (25,872)	$ (11,115)	$ (13,162)
Cumulative dividends on convertible preferred shares	(927)	(3,202)	(1,596)	(2,372)
Loss attributable to common shares—basic and diluted	$ (12,000)	$ (29,074)	$ (12,711)	$ (15,534)
Denominator:				
Weighted-average number of common shares—basic and diluted	93,500,000	93,500,000	93,500,000	93,500,000
Loss per common share—basic and diluted	$ (0.13)	$ (0.31)	$ (0.14)	$ (0.17)

Rhythm Pharmaceuticals, Inc.

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2. Summary of Significant Accounting Policies (Continued)

Pro forma earnings per share is computed as follows:

	Year Ended December 31, 2016	Six Months Ended June 30, 2017
Numerator:		
Net loss attributable to common shares—basic and diluted	$ (25,872)	$ (13,162)
Add: Cumulative dividends on convertible preferred shares	—	—
Net loss attributable to common stockholders—basic and diluted	$ (25,872)	$ (13,162)
Denominator:		
Weighted average common shares outstanding—basic and diluted	93,500,000	93,500,000
Add: Assumed conversion of convertible preferred stock to common stock	40,000,000	59,909,393
Pro forma weighted-average shares outstanding	133,500,000	153,409,393
Pro forma net loss per share—basic and diluted	$ (0.19)	$ (0.09)

Patent Costs

Costs to secure and defend patents are expensed as incurred and are classified as general and administrative expenses. Patent costs were $280 and $231 for the years ended December 31, 2015 and 2016 and $137 and $117 for the six months ended June 30, 2016 and 2017, respectively.

Application of New or Revised Accounting Standards

From time to time, new accounting pronouncements are issued by the FASB and adopted by the Company as of the specified effective date. Unless otherwise discussed, the Company believes that the impact of recently issued standards that are not yet effective will not have a material impact on its financial position or results of operations upon adoption.

In April 2012, the Jump-Start Our Business Startups Act (the "JOBS Act") was signed into law. The JOBS Act contains provisions that, among other things, reduce certain reporting requirements for an "emerging growth company." As an emerging growth company, the Company elected to not take advantage of the extended transition period afforded by the JOBS Act for the implementation of new or revised accounting standards, and as a result, will comply with new or revised accounting standards on the relevant dates on which adoption of such standards is required for non-emerging growth companies.

Rhythm Pharmaceuticals, Inc.

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2. Summary of Significant Accounting Policies (Continued)

In August 2014, the FASB issued ASU No. 2014-15, Presentation of Financial Statements—Going Concern ("ASU No. 2014-15"). The new guidance addresses management's responsibility to evaluate whether there is substantial doubt about an entity's ability to continue as a going concern and to provide related footnote disclosures. Management's evaluation should be based on relevant conditions and events that are known and reasonably knowable at the date that the financial statements are issued. This standard is effective for the annual period ending after December 15, 2016 and for the annual periods and interim periods thereafter. The Company adopted ASU 2014-15 for the year ended December 31, 2016. Refer to Note 1, Nature of Business—Liquidity for further discussion.

In November 2015, the FASB issued Accounting Standards Update No. 2015-17, *Income Taxes (Topic 740)* ("ASU 2015-17"). ASU 2015-17 requires deferred tax liabilities and assets to be classified as noncurrent in a classified statement of financial position, instead of separating deferred income tax liabilities and assets into current and noncurrent amounts. The amendments under ASU 2015-17 apply to all entities that present a classified statement of financial position and are effective, for public entities, for financial statements issued for annual periods beginning after December 15, 2016, and interim periods within those annual periods, with early adoption permitted for all entities as of the beginning of an interim or annual reporting period. The Company elected to early adopt ASU 2015-17 effective December 31, 2016. Adoption of this ASU resulted in a retrospective reclassification but did not have an impact on the Company's Balance Sheets as of December 31, 2015 and 2016.

In February 2016, the FASB issued ASU 2016-02, Leases (Topic 842). ASU 2016-02 requires lessees to recognize lease assets and lease liabilities for those leases classified as operating leases under previous GAAP. A lessee should recognize in the statement of financial position a liability to make lease payments (the lease liability) and a right-of-use asset representing its right to use the underlying asset for the lease term. For leases with a term of 12 months or less, a lessee is permitted to make an accounting policy election by class of underlying asset not to recognize lease assets and lease liabilities. The recognition, measurement, and presentation of expenses and cash flows arising from a lease by a lessee have not significantly changed from previous GAAP. There continues to be a differentiation between finance leases and operating leases. ASU 2016-02 is effective for fiscal years beginning after December 15, 2018, and interim periods within those fiscal years, and early adoption is permitted. The Company is currently in the process of evaluating the impact of adoption of ASU No. 2016-02 on its financial position and results of operations.

In March 2016, the FASB issued ASU 2016-09, *Improvements to Employee Share-Based Payment Accounting (Topic 718)* that changes the accounting for certain aspects of share-based payments to employees. The guidance requires the recognition of the income tax effects of awards in the income statement when the awards vest or are settled, thus eliminating additional paid in capital pools. The guidance also allows for the employer to repurchase more of an employee's shares for tax withholding purposes without triggering liability accounting. In addition, the guidance allows for a policy election to account for forfeitures as they occur rather than on an estimated basis. The guidance is effective for annual periods beginning after December 15, 2016, and interim periods within those annual periods with early adoption permitted. Accordingly, the standard is effective for the Company on January 1, 2018. The

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2. Summary of Significant Accounting Policies (Continued)

Company adopted the standard as of January 1, 2017. The adoption did not have a material impact on the Company's financial position, results of operations or cash flows.

In November 2016, the FASB issued ASU No. 2016-18, Statement of Cash Flows (Topic 230): Restricted Cash ("ASU 2016-18") that changes the presentation of restricted cash and cash equivalents on the statement of cash flows. Restricted cash and restricted cash equivalents will be included with cash and cash equivalents when reconciling the beginning-of-period and end-of-period total amounts shown on the statement of cash flows. This amendment is effective for fiscal years beginning after December 15, 2017, including interim periods within those fiscal years. Early adoption is permitted, including adoption in an interim period. The Company is currently evaluating the impact of this new pronouncement on its statements of cash flows.

In May 2017, the FASB issued ASU 2017-09, Compensation-Stock Compensation (Topic 718): Scope of Modification Accounting, ('ASU 2017-09'). ASU 2017-09 provides clarity and reduces both (1) diversity in practice and (2) cost and complexity when applying the guidance in Topic 718, to a change to the terms or conditions of a share-based payment award. The amendments in ASU 2017-09 should be applied prospectively to an award modified on or after the adoption date. This ASU is effective for fiscal years, and interim periods within those years, beginning after December 15, 2017. The adoption of this ASU is not expected to have a material impact on the Company's financial position or results of operations.

In July 2017, the FASB issued ASU 2017-11, Earnings Per Share (Topic 260), Distinguishing Liabilities from Equity (Topic 480) and Derivatives and Hedging (Topic 815): I. Accounting for Certain Financial Instruments with Down Round Features; II. Replacement of the Indefinite Deferral for Mandatorily Redeemable Financial Instruments of Certain Nonpublic Entities and Certain Mandatorily Redeemable Noncontrolling Interests with a Scope Exception, ('ASU 2017-11'). Part I of this update addresses the complexity of accounting for certain financial instruments with down round features. Down round features are features of certain equity-linked instruments (or embedded features) that result in the strike price being reduced on the basis of the pricing of future equity offerings. Current accounting guidance creates cost and complexity for entities that issue financial instruments (such as warrants and convertible instruments) with down round features that require fair value measurement of the entire instrument or conversion option. Part II of this update addresses the difficulty of navigating Topic 480, Distinguishing Liabilities from Equity, because of the existence of extensive pending content in the FASB Accounting Standards Codification. This pending content is the result of the indefinite deferral of accounting requirements about mandatorily redeemable financial instruments of certain nonpublic entities and certain mandatorily redeemable noncontrolling interests. The amendments in Part II of this update do not have an accounting effect. This ASU is effective for fiscal years, and interim periods within those years, beginning after December 15, 2018. The Company is currently assessing the potential impact of adopting ASU 2017-11 on its financial statements and related disclosures.

Subsequent Events

The Company considers events or transactions that occur after the balance sheet date but prior to the issuance of the financial statements to provide additional evidence for certain estimates or to identify

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2. Summary of Significant Accounting Policies (Continued)

matters that require additional disclosure. Subsequent events have been evaluated as required. See Note 12.

3. Accrued Expenses

Accrued expenses consisted of the following:

	December 31, 2015	December 31, 2016	June 30 2017
Research and development costs	$ 998	$ 2,049	$ 2,456
Professional fees	1,920	182	612
Payroll related	—	344	355
Other	44	80	47
Accrued expenses	$ 2,962	$ 2,655	$ 3,470

4. Preferred Stock

In August 2015, pursuant to the Series A Preferred Stock Purchase Agreement, by and among the Company and certain purchasers, and as part of an initial tranche closing, the Company issued 25,000,000 shares of Series A Convertible Preferred Stock, par value $0.001 per share, at a purchase price of $1.00 per share, resulting in net proceeds of $24,976 to the Company (the "August 2015 Initial Tranche Closing"). The Series A Preferred Stock Purchase Agreement provided for the delayed issuance of up to an additional 15,000,000 shares of Series A Convertible Preferred Stock as part of a Second Tranche Closing. The delayed issuance was to be automatically settled upon the achievement of a specific milestone, resulting in the issuance of shares of Series A Convertible Preferred Stock (the "2015 Series A Investor Right/Obligation"). The 2015 Series A Investor Call Option would become exercisable in the event that a Second Tranche Closing was not been consummated. Both the 2015 Series A Investor Right/Obligation and the 2015 Series A Investor Call Option were evaluated and determined to be free standing instruments and were being accounted as liabilities (see Note 2). In December 2015, the specific milestones were met and 15,000,000 shares of Series A Convertible Preferred Stock were issued at a purchase price of $1.00 per share for net proceeds of $14,641. The 2015 Series A Investor Call Option expired unexercised at that time.

In January 2017, pursuant to the Series A Preferred Stock Purchase Agreement, by and among the Company and certain purchasers, and as part of an initial tranche closing, the Company issued 20,475,001 shares of Series A Convertible Preferred Stock, par value $0.001 per share, at a purchase price of $1.00 per share, resulting in net proceeds of $20,377 to the Company (the "January 2017 Initial Tranche Closing"). The Series A Preferred Stock Purchase Agreement provided for the delayed issuance by the Company of up to an additional 20,474,998 shares of Series A Convertible Preferred Stock as part of a second tranche closing at a purchase price of $1.00 per share (the "2017 Series A Investor Right/Obligation"). The second tranche is contingent upon: (1) the Company's cash, cash equivalents and short-term investments balance, net of accounts payable and accrued liabilities, falling below $5.0 million and (2) the Company's

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4. Preferred Stock (Continued)

satisfaction of contractual and customary representations and warranties. Unless otherwise mutually agreed upon in writing, the rights and obligations underlying the second tranche (if not previously executed) will terminate on the first to occur of the following dates: (1) the date (the "Roadshow Acceleration Date") on which the Company files with the SEC the last pre-effective amendment to the Registration Statement prior to the start of the Company's roadshow in connection with the IPO, provided, that such termination shall be contingent upon the consummation of the IPO pursuant to the same Registration Statement that was on file with the SEC on the Roadshow Acceleration Date, without withdrawal thereof or filing of a subsequent Registration Statement in replacement thereof; and (2) the date of the consummation of a Deemed Liquidation Event (as defined below). To the extent the closing of the second tranche has not already taken place, the investors in the first tranche also have a call right on the shares underlying the second tranche whereby such shares can be purchased for the same price as the second tranche (the "2017 Series A Investor Call Option"). The 2017 Series A Investor Call Option terminates upon the Roadshow Acceleration Date. The 2017 Series A Investor Right/Obligation and the 2017 Series A Investor Call Option have been evaluated and determined to be a free standing instrument, the 2017 Series A Investor Instrument. The 2017 Series A Investor Instrument is being accounted for as a liability (see Note 2). In August 2017, the Series A Investors waived the $5.0 million cash balance requirement of the Series A Investor Right/Obligation and closed the second tranche of the series A preferred stock financing (see Note 12 for further discussion).

Upon the closing of an initial public offering with a minimum price per share and gross proceeds of at least $1.00 and $50.0 million, respectively, the Series A Convertible Preferred Stock will automatically convert into shares of Common Stock on a one-for-one basis.

The holders of the Series A Convertible Preferred Stock have the following rights and preferences:

Voting Rights

The holders of Series A Convertible Preferred Stock are entitled to vote, together with the holders of Common Stock, on all matters submitted to stockholders for a vote. Each preferred stockholder is entitled to the number of votes equal to the number of shares of Common Stock into which each preferred share is convertible at the time of such vote. In addition, pursuant to the Company's charter, the holders of record of the outstanding shares of Series A Convertible Preferred Stock are entitled to elect one director to serve as the Series A Preferred Director on the board of directors of the Company.

Dividends

The holders of Series A Convertible Preferred Stock are entitled to receive dividends in preference to any dividend on Common Stock at the rate of 8.0% per year of the original issue price. Dividends shall accrue annually, whether or not declared, and shall be cumulative. The Company may not declare, pay or set aside any dividends on shares of any other class or series of capital stock of the Company unless the holders of Series A Convertible Preferred Stock then outstanding shall first receive, or simultaneously receive, dividends on each outstanding share of Series A Convertible Preferred Stock. Through December 31, 2016 and June 30, 2017, no dividends had been declared or paid by the Company. Accrued dividends, whether or not declared, shall also be payable upon any liquidation event. At December 31,

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4. Preferred Stock (Continued)

2016 and June 30, 2017, cumulative preference dividends amounted to $4,129, or $0.10 per share and $6,502, or $0.11 per share, respectively.

Liquidation

In the event of any liquidation, dissolution or winding-up of the Company or a Deemed Liquidation Event (as defined below), the holders of Series A Convertible Preferred Stock then outstanding shall be entitled to be paid out of the assets of the Company available for distribution to stockholders, and before any payment shall be made to holders of Common Stock, an amount per share equal to greater of (i) the original issue price per share, plus any accrued but unpaid dividends thereon, whether or not declared, plus any declared but unpaid dividends thereon, if any, or (ii) such amount per share as would have been payable had all shares of Series A Convertible Preferred Stock been converted to Common Stock prior to such liquidation. If upon such event, the assets of the Company available for distribution are insufficient to permit payment in full to the holders of Series A Convertible Preferred Stock, the proceeds will be ratably distributed among the holders of Series A Convertible Preferred Stock in proportion to the respective amounts that they would have received if they were paid in full. After payments have been made in full to the holders of Series A Convertible Preferred Stock, the remaining assets of the Company available for distribution will be distributed among the holders of Series A Convertible Preferred Stock and the holders of Common Stock as if the shares of Series A Convertible Preferred Stock were converted to Common Stock immediately prior to the liquidation event.

A merger, acquisition, sale of voting control or other transaction of the Company in which the stockholders of the Company do not own a majority of the outstanding shares of the surviving company shall be considered a Deemed Liquidation Event. A sale, exclusive license, transfer or other disposition of all or substantially all of the assets of the Company shall also be considered a Deemed Liquidation Event. Each share of Series A Convertible Preferred Stock may be redeemed at the option of the holder upon the occurrence of a deemed liquidation event. As of December 31, 2015 and 2016 and June 30, 2017, the liquidation preference of the outstanding shares of Series A Convertible Preferred Stock was approximately $40,927, $44,129 and $66,977, respectively.

Conversion

Each share of Series A Convertible Preferred Stock is convertible into common stock at the option of the stockholder at any time after the date of issuance. In addition, each share of Series A Convertible Preferred Stock will be automatically converted into shares of common stock, at the applicable conversion ratio then in effect, upon the earlier of (i) a qualified public offering with gross proceeds of at least $50,000 and a price of not less than $1.00 per share, subject to appropriate adjustment for any stock dividend, stock split, combination or other similar recapitalization, and (ii) the date specified by vote or written consent of the holders of at least two-thirds of the then outstanding shares of series A preferred stock. The shares of Series A Convertible Preferred Stock will be converted to common stock, at par value, with the remainder recorded to additional paid-in capital.

The conversion ratio of the Series A Convertible Preferred Stock is determined by dividing the original issue price per share by the conversion price of $1.00 per share, subject to appropriate adjustment

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4. Preferred Stock (Continued)

in the event of any stock dividend, stock split, combination or recapitalization affecting the Series A Convertible Preferred Stock. As of December 31, 2016 and June 30, 2017, the outstanding shares of Series A Convertible Preferred Stock were convertible into 40,000,000 and 60,475,001 shares of common stock, respectively.

5. Fair Value of Financial Assets and Liability

As of December 31, 2015 and 2016 and June 30, 2017, the carrying amount of cash and cash equivalents and short-term investments was $34,869, $10,537 and $17,740 respectively, which approximates fair value. Cash and cash equivalents and short-term investments includes investments in money market funds that invest in U.S. government securities that are valued using quoted market prices. Accordingly, money market funds and government funds are categorized as Level 1 and had a total balance of $11,972, $7,984 and $13,316 as of December 31, 2015 and 2016 and June 30, 2017, respectively.

For the years ended December 31, 2015 and 2016, the Company had no financial liabilities outstanding measured at fair value. The Company recognized a financial liability during 2015 related to its 2015 Series A Investor Right/Obligation and 2015 Series A Investor Call Option that was exercised or expired, respectively, in December 2015. The liability was based on significant inputs not observable in the market, which represents a Level 3 measurement within the fair value hierarchy. A financial liability was recognized during the six months ending June 30, 2017 related to the 2017 Series A Investor Instrument. The liability was valued based on significant inputs not observable in the market, which represents a Level 3 measurement within the fair value hierarchy.

The following tables present information about the Company's financial assets and liabilities measured at fair value on a recurring basis and indicate the level of the fair value hierarchy utilized to determine such fair values:

	Fair value Measurements as of June 30, 2017 Using:			
	Level 1	Level 2	Level 3	Total
Assets:				
Cash Equivalents:				
Government Funds	$ —	$ —	$ —	$ —
Money Market Funds	4,299	—	—	4,299
Marketable Securities:				
Government Funds	9,017	—	—	9,017
Total	$ 13,316	$ —	$ —	$ 13,316
Liabilities:				
2017 Series A Investor Instrument	$ —	$ —	$ 410	$ 410
Total	$ —	$ —	$ 410	$ 410

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5. Fair Value of Financial Assets and Liability (Continued)

	Fair value Measurements as of December 31, 2016 Using:			
	Level 1	Level 2	Level 3	Total
Assets:				
Cash Equivalents:				
Government Funds	$ 2,000	$ —	$ —	$ 2,000
Money Market Funds	1,987	—	—	1,987
Marketable Securities:				
Government Funds	3,997	—	—	3,997
Total	$ 7,984	$ —	$ —	$ 7,984

	Fair Value Measurements as of December 31, 2015 Using:			
	Level 1	Level 2	Level 3	Total
Assets:				
Cash Equivalents:				
Government Funds	$ 4,508	$ —	$ —	$ 4,508
Money Market Funds	7,464	—	—	7,464
Liabilities:				
Series A Investor Right/Obligation and Series A Investor Call Option	$ —	$ —	$ —	$ —
Total	$ 11,972	$ —	$ —	$ 11,972

Marketable Securities

The following tables summarize the Company's marketable securities:

	June 30, 2017			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Assets				
Government Funds (due within 1 year)	$ 9,020	$ —	$ (3)	$ 9,017
	$ 9,020	$ —	$ (3)	$ 9,017

	December 31, 2016			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Assets				
Government Funds (due within 1 year)	$ 3,997	$ —	$ —	$ 3,997
	$ 3,997	$ —	$ —	$ 3,997

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5. Fair Value of Financial Assets and Liability (Continued)

Below is a roll forward of the fair value of financial liabilities for the year ended December 31, 2015:

	2015 Series A Investor Right/Obligation And 2015 Series A Investor Call Option
Fair value at December 31, 2014	$ —
Fair value upon the August 2015 Initial Closing	$ 500
Change in fair value through the date of settlement	500
Reclassification of liability upon December 2015 Second Tranche closing	(1,000)
Fair value at December 31, 2015	$ —

The following assumptions and inputs were used in determining the fair value of the 2015 Series A Investor Call Option valued using the Black- Scholes option pricing model:

	August 2015 Initial Tranche Closing
Series A Convertible Preferred Stock Exercise Price	$1.00
Series A Convertible Preferred Stock Fair Value	$0.81
Expected term	2 months
Expected volatility	24.0%
Expected interest rate	0.08%
Expected dividend yield	—

The 2015 Series A Investor Call Option expired upon the Second Tranche Closing in December 2015.

The Company estimated the fair value of the 2015 Series A Investor Right/Obligation as the probability-weighted present value of the expected benefit of the investment. The expected benefit is the difference between the expected future value of shares issued upon the second tranche closing and the investment price for the second tranche closing. The expected future value as of the August 2015 Initial Tranche Closing was estimated through a backsolve calculation which assumes a 70 percent probability of closing, a discount rate of 0.08% and a second tranche closing date of November 30, 2015.

The Company performed a contemporaneous valuation of the 2015 Series A Investor Right/Obligation to invest in the second tranche of our series A preferred stock financing. This valuation coincided with the 2015 Series A Second Tranche Closing on December 1, 2015. The Company valued the 2015 Series A Investor Right/Obligation as the benefit associated with the second tranche investment. The benefit is a function of the difference between the fair value of the series A shares and the 2015 Series A Investor Right/Obligation exercise price on the date of closing and the number of shares acquired. The Company estimated the fair value of the 2015 Series A Investor Right/Obligation as the probability weighted average of two scenarios: an IPO and a remain-private scenario.

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5. Fair Value of Financial Assets and Liability (Continued)

Below is a roll forward of the fair value of the 2017 Series A Investor Instrument for the six months ended June 30, 2017:

	2017 Series A Investor Instrument
Fair value at December 31, 2016	$ —
Fair value upon the January 2017 Initial Closing, net	328
Change in fair value	82
Fair value at June 30, 2017, net	$ 410

The fair value of the Series A Investor Instrument is the sum of the probability-weighted fair value of the 2017 Investor Right/Obligation and the 2017 Series A Call Option.

The following assumptions and inputs were used in determining the fair value of the 2017 Series A Investor Call Option valued using the Black- Scholes option pricing model:

	June 30, 2017
Series A Convertible Preferred Stock Exercise Price	$1.00
Series A Convertible Preferred Stock Fair Value	$1.30
Expected term	3.5 months
Expected volatility	72.0%
Expected interest rate	1.03%
Expected dividend yield	—

The Company estimated the fair value of the 2017 Series A Investor Right/Obligation as the probability-weighted present value of the expected benefit of the investment. The expected benefit is the difference between the expected future value of shares issued upon the second tranche closing and the investment price for the second tranche closing. The expected future value is estimated as a weighted average of IPO and remain private scenarios, and the future value is converted to a present value assuming a closing date of August 15, 2017 and a nominal, risk-free discount rate.

6. Common Stock

In March 2013, the Company issued 93,500,000 shares of common stock at a purchase price of $0.001 per share. As of December 31, 2015 and 2016 and June 30, 2017, the LLC entity owned all of these shares.

In August 2015, the Company's board of directors approved a 93,500-for-one forward stock split of the Company's issued and outstanding shares of common stock. All shares and per share amounts in the financial statements have been retrospectively adjusted for all periods presented to give effect of the forward stock split. The Company filed an amended and restated certificate of incorporation with the Secretary of State of the State of Delaware to increase its authorized number of shares of common stock to 150,000,000 shares of common stock, $0.001 par value per share, 93,500,000 shares of which were issued and outstanding as of June 30, 2017.

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6. Common Stock (Continued)

In January 2017, the Company filed a second amended and restated certificate of incorporation with the Secretary of State of the State of Delaware to increase its authorized number of shares of common stock to 195,700,000 shares of common stock, $0.001 par value per share. The Company has reserved 21,250,000 shares of common stock for issuance to officers, directors, employees and consultants of the Company pursuant to the 2015 Stock Incentive Plan (the "Plan") duly adopted by the Company's board of directors and approved by the Company's stockholders. Of such reserved shares of common stock, as of June 30, 2017 no shares have been issued pursuant to restricted stock purchase agreements, 13,143,019 options to purchase shares of common stock have been granted, and 8,106,981 shares of common stock remain available for issuance to officers, directors, employees and consultants pursuant to the Plan.

In August 2017, the Company filed a third amended and restated certificate of incorporation with the Secretary of State of the State of Delaware to increase its authorized number of shares of common stock to 274,366,209 shares of common stock, $0.001 par value per share.

7. Stock-based Compensation

2015 Stock Incentive Plan

2015 Plan Overview

In August 2015, the Company's board of directors approved the 2015 equity incentive plan, as amended and in effect prior to the closing of this offering, or the Plan, which provides for the grant of incentive and non-qualified stock options and restricted stock awards to employees, consultants, advisors and directors, as determined by the board of directors. The Company reserved 21,250,000 shares of common stock to be issued under the Plan. Shares of common stock issued upon exercise of stock options are generally issued from new shares of the Company. The Plan provides that the exercise price of incentive stock options cannot be less than 100% of the fair market value of the common stock on the date of the award for participants who own less than 10% of the total combined voting power of stock of the Company, and not less than 110% for participants who own more than 10% of the Company's voting power. Options and restricted stock granted under the Plan will vest over periods as determined by the Company's board of directors. For options granted to date, the exercise price equaled the fair value of the common stock as determined by the board of directors on the date of grant.

The Company estimates the fair value of stock-based awards to employees and non-employees using the Black-Scholes option-pricing model, which requires the input of highly subjective assumptions, including (a) the expected volatility of the underlying common stock, (b) the expected term of the award, (c) the risk-free interest rate, and (d) expected dividends. Due to the lack of a public market for the trading of its common stock and a lack of company-specific historical and implied volatility data, the Company based its estimate of expected volatility on the historical volatility of a group of companies in the pharmaceutical and biotechnology industries in a similar stage of development as the Company that are publicly traded. For these analyses, the Company selected companies with comparable characteristics to its own including enterprise value, risk profiles and with historical share price information sufficient to meet the expected life of the stock-based awards. The Company computes the historical volatility data using the

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7. Stock-based Compensation (Continued)

daily closing prices for the selected companies' shares during the equivalent period of the calculated expected term of its stock-based awards. The Company will continue to apply this process until a sufficient amount of historical information regarding the volatility of its own stock price becomes available. The Company estimated the expected life of its employee stock options using the "simplified" method, whereby, the expected life equals the average of the vesting term and the original contractual term of the option. The risk-free interest rates for periods within the expected life of the option are based on the U.S. Treasury yield curve in effect during the period the options were granted.

The Company is also required to estimate forfeitures at the time of grant, and revise those estimates in subsequent periods if actual forfeitures differ from estimates. The Company used historical data to estimate pre-vesting option forfeitures and record stock-based compensation expense only for those awards that are expected to vest. To the extent that actual forfeitures differ from its estimates, the difference is recorded as a cumulative adjustment in the period the estimates were revised. Stock-based compensation expense recognized in the financial statements is based on awards that are ultimately expected to vest. Upon adopting ASU 2016-09 on January 1, 2017, the Company elected to account for forfeitures as they occur.

The grant date fair value of awards subject to service-based vesting, net of estimated forfeitures, is recognized ratably over the requisite service period, which is generally the vesting period of the respective awards. The Company's stock option awards typically vest over a service period that ranges from three to four years and includes awards with one year cliff vesting followed by ratable monthly vesting thereafter and ratable monthly vesting beginning on the grant date.

The unvested portion of stock options granted to non-employees are subject to remeasurement at subsequent reporting periods.

2017 Activity

During the six months ended June 30, 2017, the Company granted 4,432,500 common stock option awards to certain directors, employees and non-employees.

The fair value of share options granted during the six months ended June 30, 2017 was estimated using the Black-Scholes option pricing model with the following weighted-average assumptions:

	Six Months Ended June 30, 2017
Risk-free interest rate	2.00%
Expected term (in years)	6.03
Expected volatility	66.28%
Expected dividend yield	—

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7. Stock-based Compensation (Continued)

2016 Activity

During the year ended December 31, 2016, the Company granted 1,506,000 common stock option awards to certain of its employees and non-employees.

The fair value of share options granted to employees during the year ended December 31, 2016 was estimated using the Black-Scholes option pricing model with the following weighted-average assumptions:

	Year ended December 31, 2016
Risk-free interest rate	1.39%
Expected term (in years)	6.25
Expected volatility	74.20%
Expected dividend yield	—

The fair value of share options granted to non-employees during the year ended December 31, 2016 was estimated using the Black-Scholes option pricing model with the following weighted-average assumptions:

	Year ended December 31, 2016
Risk-free interest rate	1.58%
Expected term (in years)	10.0
Expected volatility	71.18%
Expected dividend yield	—

2015 Activity

During 2015, the Company granted 8,254,519 common stock option awards to certain of its employees and non-employees. Of the awards granted, 6,011,844 were to Motus employees providing service to the Company through a service arrangement (See Note 2). As Motus and the Company are under the common control of the LLC entity, the awards are treated as a dividend to the LLC entity for the Company's standalone financial reporting in accordance with ASC 718, Compensation—Stock Compensation. The grant date fair value of $2,695 for the grants was established using a Black-Scholes model with assumptions consistent with ASC 505-50, Equity-Based Payments to Non-employees and was recorded as a dividend with a corresponding credit to Additional Paid-in Capital. As Motus is recognizing these grants to its employees as compensation expense on a fair value basis in accordance with ASC 815, Derivatives and Hedging, the Company is recognizing its proportionate share of the compensation expense recognized by Motus consistent with its accounting policy described in Note 2.

On November 16, 2016, the Motus employees terminated their employment contracts with Motus and entered into new employment agreements with the Company. The fair value of the remaining unvested

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7. Stock-based Compensation (Continued)

awards for these employees will be expensed in accordance with ASC 718, Compensation—Stock Compensation over their remaining vesting period.

The fair value of share options granted to employees and directors during the year ended December 31, 2015 was estimated using the Black-Scholes option pricing model with the following weighted-average assumptions:

	Year Ended December 31, 2015
Risk-free interest rate	1.84%
Expected term (in years)	5.93
Expected volatility	66.5%
Expected dividend yield	—

The fair value of share options granted to non-employees during the year ended December 31, 2015 was estimated using the Black-Scholes option pricing model with the following weighted-average assumptions:

	Year Ended December 31, 2015
Risk-free interest rate	2.25%
Expected term (in years)	10.0
Expected volatility	75.7%
Expected dividend yield	—

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7. Stock-based Compensation (Continued)

A summary of the Company's common stock option activity for the year ended December 31, 2016 and six months ended June 30, 2017 is as follows:

	Number of Units	Weighted-Average Grant Date Fair Value Per Unit	Weighted Average Exercise Price	Weighted-Average Remaining Contractual Term
Outstanding as of December 31, 2015	8,254,519	$ 0.41	$ 0.55	9.90
Granted	1,506,000	0.50	0.74	—
Exercised	—	—	—	—
Cancelled	—	—	—	—
Outstanding as of December 31, 2016	9,760,519	0.43	0.58	9.02
Granted	4,432,500	0.41	0.67	—
Exercised	—	—	—	—
Cancelled	(1,050,000)	(0.50)	(0.75)	—
Outstanding as of June 30, 2017	13,143,019	$ 0.41	$ 0.60	8.87
Options vested and expected to vest as of December 31, 2016	9,760,519	$ 0.43	$ 0.58	9.02
Options vested and expected to vest as of June 30, 2017	12,643,019	$ 0.41	$ 0.59	8.84
Options exercisable at December 31, 2016	2,843,684	$ 0.42	$ 0.55	8.90
Options exercisable at June 30, 2017	4,157,686	$ 0.42	$ 0.57	8.52

Under the Plan, the Company recorded stock-based compensation of $192 and $993 during the year ended December 31, 2015 and 2016, respectively, that consists of stock-based compensation expense for stock options granted to employees and Company directors of $39 and $277, respectively and stock options granted to non-employees and employees of the Motus entity that are allocated to the Company of $153 and $716, respectively.

Stock compensation expense incurred under the Plan was $473 and $627 during the six months ended June 30, 2016 and 2017, respectively, consisting of stock-based compensation expense for awards granted to employees and our directors of $100 and $581, respectively, and non-employees and, for the six months ended June 30, 2016, employees of the Relamorelin Company that were allocated to us of $373 and $46, respectively. As of December 31, 2016 and June 30, 2017, the Company has unrecognized compensation cost of $2,826 and $3,622, respectively, related to non-vested employee, non-employee and director awards that is expected to be recognized over a weighted-average period of 2.78 years and 2.65 years, respectively.

Rhythm Pharmaceuticals, Inc.

Notes to Financial Statements (Continued)

(including data applicable to unaudited periods)
(Information as of June 30, 2017 and for the six months ended June 30, 2016 and 2017 is unaudited)

(In thousands, except share and per share information)

7. Stock-based Compensation (Continued)

The following table summarizes the classification of the Company's stock-based compensation expenses related to the Plan recognized in the Company's statements of operations and comprehensive loss.

	Year Ended December 31,		Six Months Ended June 30,	
	2015	2016	2016	2017
Research and development	$ 68	$ 343	$ 152	$ 190
General and administrative	124	650	321	437
Total	$ 192	$ 993	$ 473	$ 627

LLC Incentive Plan

The Company was allocated stock compensation expense from the LLC entity's plan using the same proportional use basis for other shared costs (see Note 2). The following table summarizes the classification of the Company's stock-based compensation expenses related to the costs allocated from the LLC's Plan recognized in the Company's statements of operations and comprehensive loss.

	Year Ended December 31,		Six Months Ended June 30,	
	2015	2016	2016	2017
Research and development	$ 76	$ 163	$ 78	$ 71
General and administrative	30	12	8	—
Total	$ 106	$ 175	$ 86	$ 71

The remainder of this Note discloses the stock-based compensation activity of the Predecessor Company and the LLC entity.

Original Plan

The Predecessor Company had one stock based compensation plan—the 2010 equity incentive plan, as amended (the "Original Plan"). The Original Plan previously provided for the grant of incentive and non-qualified stock options and restricted stock grants to employees, consultants, advisors and directors, as determined by the board of directors of the Predecessor Company.

As a result of the Corporate Reorganization, all outstanding option grants under the Original Plan were cancelled. Each holder of a stock option that was cancelled was issued a restricted common unit of the LLC entity in its place on a one-for-one basis. Restricted common unit vesting agreements were contracted between the LLC entity and the restricted common unit holder granting the holder the same

Rhythm Pharmaceuticals, Inc.

Notes to Financial Statements (Continued)

(including data applicable to unaudited periods)
(Information as of June 30, 2017 and for the
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(In thousands, except share and per share information)

7. Stock-based Compensation (Continued)

vesting terms as originally granted in the respective option agreement. Any unvested portion of the stock option at the Corporate Reorganization would continue to vest under those original time frames and conditions. Exercise prices were eliminated as they are not applicable to common unit instruments, and all equity incentive grants after the Corporate Reorganization were of restricted common units.

The holder of a restricted common unit is entitled to one vote per unit. After the payment of all preferential amounts to the holders of the convertible preferred units, the holder of a restricted common unit is entitled to his pro rata share of the remaining consideration, if any, based on the number of restricted common units held by the holder.

Restricted Common Units

Upon the Corporate Reorganization, all 615,685 common stock options of the Predecessor Company under the Original Plan outstanding as of March 21, 2013 were exchanged on a one-for-one basis for 615,685 restricted common units of the LLC entity. Vesting continued on the same schedule as originally granted per the respective option agreement. At the time of the exchange, the LLC entity determined the fair value of a restricted common unit to be $1.21 per unit, equivalent to the fair value of a common unit. The fair value of stock options immediately prior to the Corporate Reorganization was determined using a Black-Scholes option pricing model and ranged in value from $0.48 to $0.64. The exchange was accounted for by the LLC entity as a modification in accordance with ASC 718, with the incremental fair value determined to be $255, of which $99 was recognized immediately upon the Corporate Reorganization for the portion related to the vested awards, and the remaining $156 will be recognized over the remaining service period of the restricted common units, net of estimated forfeitures. No common stock options were issued by the Relamorelin Company under the Original Plan subsequent to the Corporate Reorganization.

All restricted common units granted subsequent to the Corporate Reorganization were valued at the fair value of the LLC entity's common unit on the date of grant and will be expensed over their respective service period. Forfeitures are required to be estimated at the time of grant and revised, if necessary, in subsequent periods if actual forfeitures differ from those estimates. The term "forfeitures" is distinct from "cancellations" and represents only the unvested portion of the surrendered unit. Ultimately, the actual expense recognized over the vesting period will only be for those options that vest.

Rhythm Pharmaceuticals, Inc.

Notes to Financial Statements (Continued)

(including data applicable to unaudited periods)
(Information as of June 30, 2017 and for the six months ended June 30, 2016 and 2017 is unaudited)

(In thousands, except share and per share information)

7. Stock-based Compensation (Continued)

A summary of the LLC entity's restricted common unit activity for the year ended December 31, 2016 and the six months ended June 30, 2017 is as follows:

	Number of Units	Weighted-Average Grant Date Fair Value Per Unit
Outstanding unvested as of December 31, 2015	145,413	$ 3.59
Granted	—	—
Vested	(50,796)	4.10
Cancelled	—	—
Outstanding unvested as of December 31, 2016	94,617	$ 3.31
Granted	—	—
Vested	(14,124)	5.06
Cancelled	—	—
Outstanding unvested as of June 30, 2017	80,493	$ 3.01

The LLC entity recorded total stock-based compensation expense for restricted common units granted to employees, directors and non-employees of $337 and $221 during the years ended December 31, 2015 and 2016, respectively and $108 and $71 for the six months ended June 30, 2016 and 2017, respectively. The total fair value of restricted common units vested during the years ended December 31, 2015 and 2016 and six months ended June 30, 2017 was $309, $208 and $71, respectively. As of December 31, 2016 and June 30, 2017, we have unrecognized compensation expense related to the unvested portion of these awards of $314 and $242, respectively, and we expect to recognize this amount over a weighted-average period of approximately 1.8 years and 1.31 years, respectively.

Restricted Common Unit Grants to Non-Employees

During the years ended December 31, 2015, subsequent to the Corporate Reorganization, the LLC entity granted restricted common units to non-employee consultants. The LLC entity valued these restricted common units based on their fair value on the date of grant, determined to be the fair value of a common unit.

The unvested restricted common units held by consultants have been and will be remeasured using the LLC entity's estimate of fair value at each reporting period through the remaining vesting period. As of December 31, 2016, the restricted common units held by consultants have been vested. Stock-based compensation expense of $47 and $57 was recorded for the years ended December 31, 2015 and 2016, respectively, relating to non-employee unit awards.

Rhythm Pharmaceuticals, Inc.

Notes to Financial Statements (Continued)

(including data applicable to unaudited periods)
(Information as of June 30, 2017 and for the six months ended June 30, 2016 and 2017 is unaudited)

(In thousands, except share and per share information)

8. Significant Agreements

License Agreements

The Predecessor Company entered into a license agreement on February 26, 2010 with Ipsen Pharma, S.A.S. ("Ipsen") that granted full worldwide right for two programs that include the clinical candidates setmelanotide, which is in Phase 2 clinical trials, and relamorelin, which has completed a Phase 2 clinical trial. As a result of the Corporate Reorganization described in Note 1, the Ipsen license was converted to separate license agreements for the setmelanotide program held by the Company and the relamorelin program held by the Relamorelin Company, respectively. Under the terms of the setmelanotide Ipsen license agreement, assuming that setmelanotide is successfully developed, receives regulatory approval and is commercialized, Ipsen may receive aggregate payments of up to $40,000 upon the achievement of certain development and commercial milestones and royalties on future product sales in the mid-single digits. Substantially all of such aggregate payments of up to $40,000 are for milestones that may be achieved no earlier than first commercial sale of setmelanotide. In the event that the Company executes a sublicense agreement, it shall make payments to Ipsen, depending on the date of such sublicense agreement, ranging from 10% to 20% of all revenues actually received under such sublicense agreement.

In connection with this license agreement, the LLC entity issued two warrants in March 2010 to an affiliate of Ipsen to purchase a total of 489,500 common units. These warrants were vested in full in 2010 and 2011, respectively. In July 2015, the warrant agreement was amended to extend the expiration date to July 31, 2015 as the original warrant agreement expired in March 2015. In July 2015, an affiliate of Ipsen elected to exercise these warrants in full for a total of 489,500 common units of the LLC entity. In July 2015, upon exercise, warrant expense of $923 was allocated to the Company relating to the modification of these warrants and is included within research and development expense.

In January 2016, the Company entered into a licensing agreement with Camurus AB, or Camurus, for the use of Camurus' drug delivery technology. The contract includes a non-refundable and non-creditable signing fee of $500, which was paid during January 2016. The Camurus Agreement also includes up to $7,750 in one-time, non-refundable development milestones achievable upon certain regulatory successes. The Company is also required to pay to Camurus royalties, mid to mid-high single digit, on a product-by-product and country-by-country basis of annual net sales, until the later of (i) 10 years after the date of first commercial sale of such product in such country; or (ii) the expiration of the last to expire valid claim of all licensed patent rights in such country covering such product. The Company is also required to pay one-time, non-refundable, non-creditable sales milestones upon the achievement of certain sales levels for such product and cannot be in excess of $57,000.

In March 2017, the Company achieved the first milestone event associated with this license agreement. The Company completed the first manufactured batch using the Camurus drug delivery technology and filed an investigational new drug application with the FDA. The fee associated with this milestone was $250.

Rhythm Pharmaceuticals, Inc.

Notes to Financial Statements (Continued)

(including data applicable to unaudited periods)
(Information as of June 30, 2017 and for the six months ended June 30, 2016 and 2017 is unaudited)

(In thousands, except share and per share information)

9. Commitments and Contingencies

The Company is not a party to the lease for the facility it previously shared with the Relamorelin Company. In November 2015, the Company entered into a Lease Agreement for an office facility at 500 Boylston Street, Boston, Massachusetts. The lease term commenced in May 2016 and has a term of 5 years with a five -year renewal option to extend the lease. Rent expense for the years ended December 31, 2015 and 2016 and the six months ended June 30, 2017 was zero, $179 and $107, respectively.

Future minimum payments under the operating lease agreements as of December 31, 2016, are as follows:

2017	$ 291
2018	298
2019	305
2020	311
2021	131
Total	$ 1,336

10. Related-Party Transactions

The Company shared costs with the Relamorelin Company, its affiliate, including payroll, facilities, information technology and other research and development and general and administrative overhead costs. Additionally, the Relamorelin Company had paid certain Company expenses directly on behalf of the Company. Shared costs incurred by the Relamorelin Company and Company expenses paid by the Relamorelin Company on behalf of the Company are allocated from the Relamorelin Company to the Company as described in Note 1 and Note 2. These net costs totaled $2,149 and $1,570 for the years ended December 31, 2015 and 2016, respectively. From August 1, 2015 to December 31, 2015, Company expenses paid by the Relamorelin Company on behalf of the Company amounted to $1,416 of which $781 were repaid by the Company and $635 were recorded as a liability within Due to related party on the balance sheet as of December 31, 2015. Prior to August 1, 2015, these amounts were recorded by the Company within Additional Paid-in Capital as capital contributions from the LLC entity as such amounts are not repayable from the Company to the Relamorelin Company or the LLC entity. Prior to August 1, 2015, these capital contributions were recorded as financing activities in the statements of cash flows. Beginning on August 1, 2015 the liabilities due to Relamorelin Company were recorded as operating activities in the statements of cash flows, as they are fully repayable and relate to the Company's operating costs. Cash transfers to the Company from the LLC entity totaled $1,595 for the years ended December 31, 2015. There were no cash transfers in the period from August 1, 2015 to December 31, 2016. These amounts have been recorded by the Company within Additional Paid-in Capital as capital contributions from the LLC entity as such amounts are not repayable from the Company to the Relamorelin Company or the LLC entity. As of December 31, 2015, these capital contributions totaled $42,462. The Relamorelin Company was sold to a large pharmaceutical company on December 15, 2016.

Rhythm Pharmaceuticals, Inc.

Notes to Financial Statements (Continued)

(including data applicable to unaudited periods)
(Information as of June 30, 2017 and for the
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(In thousands, except share and per share information)

10. Related-Party Transactions (Continued)

The Company made payments on behalf of the LLC entity totaling $60 related to third party services to an unaffiliated vendor. Those costs are capitalized as a receivable due from the LLC entity to the Company at December 31, 2015 on the balance sheet. There were no such payments by the Company during 2016. The LLC made payments on behalf of the Company totaling $105 related to allocated 2016 employee bonuses. Those costs are recorded as a payable due to the LLC entity from the Company at December 31, 2016 on the balance sheet.

Expenses paid directly by the Company to consultants considered to be related parties amounted to $153, $619, $202 and $586 for the year ended December 31, 2015 and 2016 and the six months ended June 30, 2016 and 2017, respectively. Outstanding payments due to these related parties as of December 31, 2015 and 2016 and June 30, 2017 were $13, $50 and $89, respectively and were included within Accounts payable on the balance sheet. Expenses paid by the Relamorelin Company to these related parties amounted to $1,357, $966, $449 and zero for the year ended December 31, 2015 and 2016 and the six months ended June 30, 2016 and 2017, respectively. Outstanding payments due by the Relamorelin Company on the Company's behalf to these related parties as of December 31, 2015 and 2016 were $58 and zero, respectively.

Employees of certain holders of series A and series B convertible preferred units of the LLC entity, have been retained as consultants supporting development activities of the Company and the Relamorelin Company for which the holders are paid cash compensation pursuant to consulting arrangements. Compensation payments related to these consultants totaled $125, $78, $37 and $44 for the years ended December 31, 2015 and 2016 and the six months ended June 30, 2016 and 2017, respectively.

11. Income Tax

In the Company's financial statements, income taxes, including deferred tax balances, have been calculated on a separate tax return basis. Certain of the Company's activities and costs have been included in the tax returns filed by the Relamorelin Company and the LLC entity. Prior to the Corporate Reorganization, the Company's operations were included in the tax returns filed by the Predecessor Company. The Company has filed tax returns on its own behalf since the Corporate Reorganization.

For the years ended December 31, 2015 and 2016, the Company did not have a current or deferred income tax expense or benefit as the entity has incurred losses since inception and has provided a full valuation allowance against its deferred tax assets.

Rhythm Pharmaceuticals, Inc.

Notes to Financial Statements (Continued)

(including data applicable to unaudited periods)
(Information as of June 30, 2017 and for the six months ended June 30, 2016 and 2017 is unaudited)

(In thousands, except share and per share information)

11. Income Tax (Continued)

A reconciliation of the income tax benefit at the federal statutory tax rate to the Company's effective income tax rate follows:

	Year Ended December 31,	
	2015	2016
Statutory tax rate	34.00%	34.00%
State tax, net of federal benefit	4.33%	2.63%
Research and development credit	0.85%	1.34%
Orphan drug credit	1.91%	2.15%
Non deductible deferred issuance costs	—%	(2.40)%
Other	(2.23)%	(1.32)%
Non deductible warrant expense	(2.82)%	—%
Change in valuation allowance	(36.04)%	(36.40)%
Effective tax rate	0.00%	0.00%

The principal components of the Company's deferred tax assets are as follows:

	As of December 31,	
	2015	2016
Deferred tax assets:		
Net operating loss carryforwards	$ 9,481	$ 17,248
Research and development credits	895	1,214
Orphan drug credit	322	1,164
Capitalized license fee	357	600
Other	16	262
Total gross deferred tax assets	11,071	20,488
Valuation allowance	(11,071)	(20,488)
Net deferred tax assets	$ —	$ —

ASC 740 requires a valuation allowance to reduce the deferred tax assets reported if, based on the weight of available evidence, it is more likely than not that some portion or all of the deferred tax assets will not be realized. After consideration of all the evidence, both positive and negative, the Company has recorded a full valuation allowance against its deferred tax assets at December 31, 2015 and 2016, because the Company's management has determined that is it more likely than not that these assets will not be realized. The increase in the valuation allowance of $4,012 in 2015 and $9,417 in 2016 primarily relates to the net loss incurred by the Company during each period.

As of December 31, 2016, the Company had federal and state net operating loss carryforwards of approximately $46,934 and $24,432, respectively, which are available to reduce future taxable income. The net operating loss carryforwards expire at various times beginning in 2033 for federal and state purposes.

Rhythm Pharmaceuticals, Inc.

Notes to Financial Statements (Continued)

(including data applicable to unaudited periods)
(Information as of June 30, 2017 and for the six months ended June 30, 2016 and 2017 is unaudited)

(In thousands, except share and per share information)

11. Income Tax (Continued)

As of December 31, 2016, the Company had federal and state research tax credits of approximately $971 and $369, respectively, which may be used to offset future tax liabilities. Additionally, as of December 31, 2016, the Company had a federal orphan drug credit related to qualifying research of $1,164. These tax credit carryforwards will begin to expire at various times beginning in 2033 for federal purposes and 2028 for state purposes.

The net operating loss and tax credit carryforwards are subject to review and possible adjustment by the Internal Revenue Service and state tax authorities. Net operating loss and tax credit carryforwards may become subject to an annual limitation in the event of certain cumulative changes in the ownership interest of significant stockholders over a three-year period in excess of 50%, as defined under Sections 382 and 383 of the Internal Revenue Code, respectively, as well as similar state provisions and other provisions within the Internal Revenue Code. This could limit the amount of tax attributes that can be utilized annually to offset future taxable income or tax liabilities. The amount of the annual limitation is determined based on the value of the Company immediately prior to the ownership change. Subsequent ownership changes may further affect the limitation in future years.

The Company has not recorded any reserves for uncertain tax positions as of December 31, 2015 and 2016 and June 30, 2017. The Company has not, as yet, conducted a study of research and development credit carryforwards. This study may result in an adjustment to the Company's research and development credit carryforwards; however, until a study is completed and any adjustment is known, no amounts are being presented as an uncertain tax position. A full valuation allowance has been provided against the Company's research and development credits and, if an adjustment is required, this adjustment would be offset by an adjustment to the valuation allowance. Thus, there would be no impact to the balance sheets or statements of operations and comprehensive loss if an adjustment were required.

Interest and penalty charges, if any, related to unrecognized tax benefits will be classified as income tax expense in the accompanying statements of operations and comprehensive loss. As of December 31, 2015 and 2016 and June 30, 2017, the Company had no accrued interest or penalties related to uncertain tax positions.

The Company is subject to examination by the U.S. federal, state and local income tax authorities for tax years 2013 forward. The Company is not currently under examination by the Internal Revenue Service or any other jurisdictions for any tax years.

12. Subsequent Events

The Company completed an evaluation of all subsequent events after the audited balance sheet date as of December 31, 2016 through May 23, 2017, the date the financial statements were available to be issued, to ensure that this filing includes appropriate disclosure of events both recognized in the financial statements as of December 31, 2016, and events which occurred subsequently but were not recognized in the financial statements.

Rhythm Pharmaceuticals, Inc.

Notes to Financial Statements (Continued)

(including data applicable to unaudited periods)
(Information as of June 30, 2017 and for the
six months ended June 30, 2016 and 2017 is unaudited)

(In thousands, except share and per share information)

12. Subsequent Events (Continued)

The Company has completed an evaluation of all subsequent events after the unaudited balance sheet date of June 30, 2017 through August 23, 2017, the date the financial statements were available to be issued, to ensure that this filing includes appropriate disclosure of events both recognized in the financial statements as of June 30, 2017, and events which occurred subsequently, but were not recognized in the financial statements.

On August 18, 2017 the Series A Investors waived the $5.0 million cash balance requirement of the Series A Investor Right/Obligation and closed on the second tranche of the January 2017 Series A Preferred Stock financing. The Company issued 20,474,998 shares of Series A Convertible Preferred Stock, par value $0.001 per share, at a purchase price of $1.00 per share, resulting in gross proceeds of $20,475 to the Company.

On August 21, 2017, the LLC entity exchanged 78,666,209 of its shares of the Company's common stock for an equal number of shares of the Company's series A-1 junior preferred stock and the LLC entity distributed all of its shares of the Company's series A-1 junior preferred stock to the holders of its preferred units and the remaining 14,833,791 shares of its common stock to the holders of its common units. Following this Distribution, the LLC entity no longer owns any of the Company's shares. The series A-1 junior preferred stock is not redeemable and does not have a stated dividend or liquidation preference. These shares will convert to common stock on a one-to-one basis upon the earlier of (i) a qualified public offering with gross proceeds of at least $50,000 and a price of not less than $1.00 per share, subject to appropriate adjustment for any stock dividend, stock split, combination or other similar recapitalization, and (ii) the date specified by vote or written consent of the holders of the requisite holders of series A preferred stock and series A-1 preferred stock.

On August 21, 2017, the Company filed a third amended and restated certificate of incorporation with the Secretary of State of the State of Delaware to increase its authorized number of shares of common stock to 274,336,209 shares of common stock, $0.001 par value per share.

* * * * * *

Shares

Common Stock

PRELIMINARY PROSPECTUS

MORGAN STANLEY *BofA MERRILL LYNCH* *COWEN*

NEEDHAM & COMPANY

Until , all dealers that effect transactions in these securities, whether or not participating in this offering, may be required to deliver a prospectus. This is in addition to the dealers' obligation to deliver a prospectus when acting as underwriters and with respect to their unsold allotments or subscriptions.

, 2017

PART II
INFORMATION NOT REQUIRED IN PROSPECTUS

Item 13. Other Expenses of Issuance and Distribution.

The following table sets forth the fees and expenses in connection with the issuance and distribution of the securities being registered (excluding the underwriting discount). Except for the SEC registration fee and the FINRA filing fee, all amounts are estimates.

	Amount Paid or to be Paid
SEC registration fee	$ 13,328.50
FINRA filing fee	*
NASDAQ listing fee	*
Legal fees and expenses	*
Accounting fees and expenses	*
Printing expenses	*
Transfer and registrar fee	*
Miscellaneous	*
Total	*

* To be provided by Amendment

Item 14. Indemnification of Directors and Officers.

Section 145 of the Delaware General Corporation Law authorizes a corporation's board of directors to grant, and authorizes a court to award, indemnity to officers, directors, and other corporate agents.

As permitted by Delaware law, our amended and restated certificate of incorporation provides that, to the fullest extent permitted by Delaware law, no director will be personally liable to us or our stockholders for monetary damages for breach of fiduciary duty as a director. Pursuant to Delaware law such protection would be not available for liability:

- for any breach of a duty of loyalty to us or our stockholders;
- for acts or omissions not in good faith or that involve intentional misconduct or a knowing violation of law;
- for any transaction from which the director derived an improper benefit; or
- for an act or omission for which the liability of a director is expressly provided by an applicable statute, including unlawful payments of dividends or unlawful stock repurchases or redemptions as provided in Section 174 of the Delaware General Corporation Law.

Our amended and restated certificate of incorporation also provides that if Delaware law is amended after the approval by our stockholders of the amended and restated certificate of incorporation to authorize corporate action further eliminating or limiting the personal liability of directors, then the liability of our directors will be eliminated or limited to the fullest extent permitted by Delaware law.

Our amended and restated bylaws further provide that we must indemnify our directors and officers to the fullest extent permitted by Delaware law. Our amended and restated bylaws also authorize us to indemnify any of our employees or agents and permit us to secure insurance on behalf of any officer, director, employee or agent for any liability arising out of his or her action in that capacity, whether or not Delaware law would otherwise permit indemnification.

In addition, our amended and restated bylaws also provide that we are required to advance expenses to our directors and officers as incurred in connection with legal proceedings against them for which they may be indemnified and that the rights conferred in the amended and restated bylaws are not exclusive.

We intend to enter into indemnification agreements with each of our directors and executive officers. These agreements, among other things, would require us to indemnify each director and officer to the fullest extent permitted by Delaware law, the amended and restated certificate of incorporation and amended and restated bylaws, for expenses such as, among other things, attorneys' fees, judgments, fines, and settlement amounts incurred by the director or executive officer in any action or proceeding, including any action by or in our right, arising out of the person's services as our director or executive officer or as the director or executive officer of any subsidiary of ours or any other company or enterprise to which the person provides services at our request. Upon consummation of the offering, we intend to obtain and maintain directors' and officers' liability insurance.

The SEC has taken the position that personal liability of directors for violation of the federal securities laws cannot be limited and that indemnification by us for any such violation is unenforceable. The limitation of liability and indemnification provisions in our amended and restated certificate of incorporation and amended and restated bylaws may discourage stockholders from bringing a lawsuit against our directors and officers for breach of their fiduciary duty. They may also reduce the likelihood of derivative litigation against our directors and officers, even though an action, if successful, might benefit us and other stockholders. Further, a stockholder's investment may be adversely affected to the extent that we pay the costs of settlement and damage awards against directors and officers as required by these indemnification provisions.

Item 15. Recent Sales of Unregistered Securities

Set forth below is information regarding securities we have issued within the past three years that were not registered under the Securities Act:

On August 3, 2015, December 1, 2015, January 6, 2017 and August 18, 2017 we issued 25,000,000 shares, 15,000,000, 20,475,001 and 20,474,998 shares, respectively, of series A preferred stock, $0.001 par value per share, to a number of accredited investors for $1.00 per share. These shares were issued in reliance on Regulation D, Rule 506 and/or Rule 4(2) under the Securities Act.

From January 1, 2014 through August 31, 2017, we granted options under the Plan to purchase an aggregate of 19,154,019 shares of our common stock to employees, consultants and directors, having exercise prices ranging from $0.50 to $0.82 per share. During this period, 200,000 of these stock options were exercised and 1,050,000 were forfeited.

The offers and sales of the securities described in the foregoing paragraph were exempt from registration under Rule 701 promulgated under the Securities Act in that the transactions were under compensatory benefit plans and contracts relating to compensation as provided under Rule 701. The recipients of such securities were our employees, directors or consultants and received the securities under the Plan. Appropriate legends were affixed to the securities issued in these transactions.

Item 16. Exhibits and Financial Statement Schedules.

(a) Exhibits

The exhibits to the registration statement are listed in the Exhibit Index attached hereto and incorporated by reference herein.

(b) Financial Statement Schedules

All financial statement schedules have been omitted because they are not required or because the required information is given in the financial statements or notes to those statements.

Item 17. Undertakings.

The undersigned Registrant hereby undertakes to provide to the underwriters at the closing specified in the underwriting agreement certificates in such denominations and registered in such names as required by the underwriters to permit prompt delivery to each purchaser.

Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers and controlling persons of the Registrant pursuant to the foregoing provisions, or otherwise, the Registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the Registrant of expenses incurred or paid by a director, officer or controlling person of the Registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the Registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Act and will be governed by the final adjudication of such issue.

The undersigned Registrant hereby undertakes that:

(1) For purposes of determining any liability under the Securities Act, the information omitted from the form of prospectus filed as part of this registration statement in reliance upon Rule 430A and contained in a form of prospectus filed by the Registrant pursuant to Rule 424(b)(1) or (4) or 497(h) under the Securities Act shall be deemed to be part of this registration statement as of the time it was declared effective.

(2) For the purpose of determining any liability under the Securities Act, each post-effective amendment that contains a form of prospectus shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof.

EXHIBIT INDEX

Number	Description
1.1*	Form of Underwriting Agreement.
3.1	Third Amended and Restated Certificate of Incorporation of the Registrant.
3.2	Bylaws of the Registrant.
3.3*	Form of Amended and Restated Certificate of Incorporation of the Registrant to become effective upon the closing of this offering.
3.4*	Form of Amended and Restated Bylaws of the Registrant to become effective upon the closing of this offering.
4.1*	Form of Common Stock Certificate of the Registrant.
4.2	Amended and Restated Investors' Rights Agreement, dated August 21, 2017, by and among the Registrant and the investors set forth therein.
5.1*	Opinion of Morgan, Lewis & Bockius LLP.
10.1†*	Form of Indemnification Agreement by and between the Registrant and its directors and officers.
10.2†*	Amended and Restated 2015 Equity Incentive Plan and Forms of Option Agreements and Notice of Exercise.
10.3†	Offer Letter, dated November 16, 2016, by and between the Registrant and Bart Henderson.
10.4†	Offer Letter, dated November 16, 2016, by and between the Registrant and Keith M. Gottesdiener.
10.5†	Offer Letter, dated November 16, 2016, by and between the Registrant and Fred T. Fiedorek.
10.6‡	License Agreement, dated March 21, 2013, by and between the Registrant (f/k/a Rhythm Metabolic, Inc.) and Ipsen Pharma S.A.S.
10.7‡	Development and Manufacturing Services Agreement, dated July 17, 2013, by and between the Registrant (f/k/a Rhythm Metabolic, Inc.) and Peptisyntha Inc. (n/k/a Corden Pharma International).
10.8‡	License Agreement dated January 4, 2016, by and between the Registrant and Camurus AB
10.9	Amended and Restated Payroll Services Agreement, dated March 21, 2013, by and between the Registrant (f/k/a Rhythm Metabolic, Inc.) and Rhythm Pharmaceuticals, Inc.
10.10†*	Rhythm Pharmaceuticals, Inc. 2017 Employee Stock Purchase Plan.
10.11	Lease, dated November 25, 2015, by and between 500 Boylston & 222 Berkeley Owner (DE) LLC and the Registrant.
10.12	Consulting Agreement, dated June 12, 2017, by and between the Registrant and Bart Henderson.
10.13*†	Offer Letter, dated , 2017, by and between the Registrant and Keith M. Gottesdiener.
10.14*†	Offer Letter, dated , 2017, by and between the Registrant and Fred T. Fiedorek.

Number	Description
10.15	Development and Manufacturing Services Agreement, dated as of December 21, 2016, by and between Registrant and Recipharm Monts S.A.S.
10.16†	Offer Letter, dated July 17, 2017, by and between the Registrant and Hunter Smith.
10.17†	Offer Letter, dated July 5, 2017, by and between the Registrant and Nithya Desikan.
10.18*†	Offer Letter, dated , 2017, by and between the Registrant and Hunter Smith.
10.19*†	Offer Letter, dated , 2017, by and between the Registrant and Nithya Desikan.
10.20†	Summary of Non-Employee Director Compensation Policy.
23.1	Consent of Ernst & Young LLP, Independent Registered Public Accounting Firm.
23.2*	Consent of Morgan, Lewis & Bockius LLP. Reference is made to Exhibit 5.1.
24.1	Power of Attorney. Reference is made to the signature page hereto.

* To be filed by amendment.

† Indicates management contract or compensatory plan.

‡ Indicates confidential treatment has been requested with respect to specific portions of this exhibit. Omitted portions have been filed with the Securities and Exchange Commission pursuant to Rule 406 of the Securities Act.

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, as amended, the Registrant has duly caused this Registration Statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the city of Boston, Commonwealth of Massachusetts on September 5, 2017.

RHYTHM PHARMACEUTICALS, INC.

By: /s/ KEITH M. GOTTESDIENER

Keith M. Gottesdiener
Chief Executive Officer, President and Director

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Keith M. Gottesdiener and Hunter Smith his true and lawful attorney-in-fact and agent with full power of substitution, for him and in his name, place and stead, in any and all capacities, to sign any and all amendments (including post-effective amendments) to this registration statement, and to sign any registration statement for the same offerings covered by the registration statement that is to be effective upon filing pursuant to Rule 462(b) promulgated under the Securities Act, and all post-effective amendments thereto, and to file the same, with all exhibits thereto and all documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorney-in-fact and agent, full power and authority to do and perform each and every act and thing requisite and necessary to be done in and about the premises, as fully to all intents and purposes as he might or could do in person, hereby ratifying and confirming that all said attorneys-in-fact and agents or any of them, or his or their substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Act, this Registration Statement has been signed by the following persons in the capacities and on the dates indicated.

Name	Title	Date
/s/ KEITH M. GOTTESDIENER Keith M. Gottesdiener	Chief Executive Officer, President and Director (Principal Executive Officer)	September 5, 2017
/s/ HUNTER SMITH Hunter Smith	Chief Financial Officer and Treasurer (Principal Financial and Accounting Officer)	September 5, 2017
/s/ JOHN J. HULBURT John J. Hulburt	Controller	September 5, 2017
/s/ NEIL EXTER Neil Exter	Director	September 5, 2017
/s/ TODD FOLEY Todd Foley	Director	September 5, 2017

Name	Title	Date
/s/ CHRISTOPHE R. JEAN Christophe R. Jean	Director	September 5, 2017
/s/ ED MATHERS Ed Mathers	Director	September 5, 2017
/s/ JONATHAN T. SILVERSTEIN Jonathan T. Silverstein	Director	September 5, 2017
/s/ DAVID W. J. MCGIRR David W. J. McGirr	Director	September 5, 2017
/s/ DAVID P. MEEKER David P. Meeker	Director, Chairman of the Board	September 5, 2017

RHYTHM PHARMACEUTICALS, INC.

THIRD AMENDED AND RESTATED
CERTIFICATE OF INCORPORATION

THIRD AMENDED AND RESTATED
CERTIFICATE OF INCORPORATION
OF
RHYTHM PHARMACEUTICALS, INC.

(Pursuant to Sections 242 and 245 of the
General Corporation Law of the State of Delaware)

Rhythm Pharmaceuticals, Inc., a corporation organized and existing under and by virtue of the provisions of the General Corporation Law of the State of Delaware (the "**General Corporation Law**"),

DOES HEREBY CERTIFY:

1. That the name of this corporation is Rhythm Pharmaceuticals, Inc., that this corporation was formerly known as Rhythm Metabolic, Inc. and that this corporation was originally incorporated pursuant to the General Corporation Law on February 26, 2013.

2. That the Board of Directors duly adopted resolutions proposing to amend and restate the Certificate of Incorporation of this corporation, declaring said amendment and restatement to be advisable and in the best interests of this corporation and its stockholders, and authorizing the appropriate officers of this corporation to solicit the consent of the stockholders therefor, which resolution setting forth the proposed amendment and restatement is as follows:

RESOLVED, that the Certificate of Incorporation of this corporation be amended and restated in its entirety to read as follows:

FIRST: The name of this corporation is **RHYTHM PHARMACEUTICALS, INC.** (the "**Corporation**").

SECOND: The address of the registered office of the Corporation in the State of Delaware is 2711 Centerville Road, Suite 400, in the City of Wilmington, County of New Castle, Delaware 19808. The name of its registered agent at such address is Corporation Service Company.

THIRD: The nature of the business or purposes to be conducted or promoted is to engage in any lawful act or activity for which corporations may be organized under the General Corporation Law.

FOURTH: The total number of shares of all classes of stock that the Corporation shall have authority to issue is (i) 274,366,209 shares of common stock, $0.001 par value per share ("**Common Stock**"), and (ii) 159,616,209 shares of preferred stock, $0.001 par value per share.

FIFTH: The following is a statement of the designations and the powers, privileges and rights, and the qualifications, limitations or restrictions thereof in respect of each class of capital stock of the Corporation.

A. COMMON STOCK

1. General. The voting, dividend and liquidation rights of the holders of the Common Stock are subject to and qualified by the rights, powers and preferences of the holders of the Preferred Stock (as defined in the first paragraph of Part B of this Article Fifth) set forth herein.

2. Increase or Decrease in Authorized Number. The number of authorized shares of Common Stock may be increased or decreased (but not below the number of shares thereof then outstanding) by (in addition to any vote of the holders of capital stock of the Corporation that may be required by the terms of this Certificate of Incorporation) the affirmative vote of the holders of shares of capital stock of the Corporation representing a majority of the votes represented by all outstanding shares of capital stock of the Corporation entitled to vote, irrespective of the provisions of Section 242(b)(2) of the General Corporation Law.

3. Voting. Except as otherwise required by law, and subject to the voting rights provided to the holders of Preferred Stock, the holders of Common Stock shall have full voting rights and powers to vote on all matters submitted to stockholders of the Corporation for vote, consent or approval, and each holder of Common Stock shall be entitled to one vote for each share of Common Stock held of record by such holder.

4. Dividend, Liquidation and Other Rights. Each share of Common Stock issued and outstanding shall be identical in all respects with each other such share, and no dividends shall be paid on any shares of Common Stock unless the same dividend is paid on all shares of Common Stock outstanding at the time of such payment. Except for and subject to those rights expressly granted to the holders of Preferred Stock and except as may be provided by the General Corporation Law, the holders of Common Stock shall have all other rights of stockholders, including, without limitation, (a) the right to receive dividends, when and as declared by the Board of Directors of the Corporation (the "**Board**"), out of assets lawfully available therefor, and (b) in the event of any distribution of assets upon a liquidation or otherwise, the right to receive ratably and equally all the assets and funds of the Corporation remaining after the payment to the holders of the Preferred Stock or of any other class or series of stock ranking senior to the Common Stock upon liquidation of the specific preferential amounts which they are entitled to receive upon such liquidation.

B. PREFERRED STOCK

The Corporation hereby designates (x) 80,950,000 shares of preferred stock of the Corporation as Series A Preferred Stock, $0.001 par value per share (the "**Series A Preferred Stock**"), with the rights, preferences, powers, privileges and restrictions, qualifications and limitations set forth below in this Certificate of Incorporation, and (y) 78,666,209 shares of preferred stock of the Corporation as Series A-1 Junior Preferred Stock, $0.001 par value per share (the "**Series A-1 Junior Preferred Stock**"), with the rights, preferences, powers, privileges and restrictions, qualifications and limitations set forth below in this Certificate of Incorporation. The term "**Preferred Stock**," as used in this Certificate of Incorporation, shall mean, as the context may require or permit, either or both of the Series A Preferred Stock and the Series A-1 Junior Preferred Stock. Unless otherwise indicated, references to "sections" or "subsections" in this Part B of this Article Fifth refer to sections and subsections of Part B of this Article Fifth.

1. Dividends.

1.1. From and after the date of the issuance of any share of Series A Preferred Stock, cash dividends at the rate per annum of $0.08 per share (subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization (collectively, "**Recapitalizations**") with respect to the Series A Preferred Stock) shall accrue on each such outstanding share of Series A Preferred Stock (the "**Series A Accruing Dividends**"). Series A Accruing Dividends shall accrue quarterly in arrears on the last day of each calendar quarter, whether or not declared, and shall be cumulative; provided, however, that except as set forth in Subsection 1.2 and Section 2, the Corporation shall be under no obligation to pay such Series A Accruing Dividends unless and until, and such Series A Accruing Dividends shall be payable only when, as, and if, declared by a majority vote of the Board.

1.2. Except as set forth in Section 2 and except for dividends on shares of Common Stock payable in shares of Common Stock to which the provisions of Section 4.6 are applicable, the Corporation shall not declare, pay or set aside any dividends on shares of any class or series of capital stock of the Corporation (other than Series A Preferred Stock) unless (in addition to obtaining any consents required elsewhere in this Certificate of Incorporation) the holders of Series A Preferred Stock then outstanding shall first receive, or simultaneously receive, a dividend on each outstanding share of Series A Preferred Stock in an amount at least equal to the sum of (i) the amount of the aggregate Series A Accruing Dividends then accrued on such share of Series A Preferred Stock and not previously paid and (ii) (A) in the case of a dividend on Common Stock, Series A-1 Junior Preferred Stock or any other class or series of capital stock (other than Series A Preferred Stock) that is convertible into Common Stock, that dividend per share of Series A Preferred Stock as would equal the product of (1) the dividend payable on each share of Common Stock, Series A-1 Junior Preferred Stock or such other class or series of capital stock determined, if applicable, as if all shares of Series A-1 Junior Preferred Stock or such other class or series of capital stock had been converted into Common Stock and (2) the number of shares of Common Stock issuable upon conversion of a share of Series A Preferred Stock, in each case calculated on the record date for determination of holders entitled to receive such dividend or (B) in the case of a dividend on any class or series of capital stock that is not convertible into Common Stock, at a rate per share of Series A Preferred Stock determined by (1) dividing the amount of the dividend payable on each share of such class or series of capital stock by the original issuance price of such class or series of capital stock (subject to appropriate adjustment in the event of any Recapitalization with respect to such class or series of capital stock) and (2) multiplying such fraction by an amount equal to the Series A Original Issue Price (as defined in Subsection 1.3 below) of the Series A Preferred Stock; provided that if the Corporation declares, pays or sets aside, on the same date, a dividend on shares of more than one class or series of capital stock, the dividend payable to the holders of Series A Preferred Stock pursuant to this Section 1 shall be calculated based upon the dividend on the class or series of capital stock that would result in the highest dividend per share of Series A Preferred Stock.

1.3. The term "**Series A Original Issue Price**" shall mean $1.00 per share of Series A Preferred Stock, subject to appropriate adjustment in the event of any Recapitalization with respect to the Series A Preferred Stock that is effected at any time after the Series A-1 Original Issue Date (as defined in Subsection 4.4.1). The term "**Series A-1 Original Issue Price**" shall mean $0.75 per share of Series A-1 Junior Preferred Stock, subject to appropriate

adjustment in the event of any Recapitalization with respect to the Series A-1 Junior Preferred Stock that is effected at any time after the Series A-1 Original Issue Date. The term "**Original Issue Price**" shall mean, as the context may require or permit, either or both of the Series A Original Issue Price and Series A-1 Original Issue Price.

2. Liquidation, Dissolution or Winding Up; Certain Mergers, Consolidations and Asset Sales.

2.1 Preferential Payments to Holders of Series A Preferred Stock. In the event of any voluntary or involuntary liquidation, dissolution or winding up of the Corporation or Deemed Liquidation Event (a "**Liquidation**"), the holders of shares of Series A Preferred Stock then outstanding shall be entitled to be paid out of the assets of the Corporation available for distribution to its stockholders before any payment shall be made to the holders of Common Stock or Series A-1 Junior Preferred Stock by reason of their ownership thereof, an amount per share equal to the greater of (i) the Series A Original Issue Price, plus any Series A Accruing Dividends accrued but unpaid thereon, whether or not declared, together with any other dividends declared but unpaid thereon or (ii) such amount per share as would have been payable had all shares of Series A Preferred Stock been converted into Common Stock pursuant to Section 4 immediately prior to such Liquidation (the amount payable pursuant to this sentence is hereinafter referred to as the "**Series A Liquidation Amount**"). If upon any such Liquidation, the assets of the Corporation available for distribution to its stockholders shall be insufficient to pay the holders of each outstanding share of Series A Preferred Stock the full amount of the Series A Liquidation Amount, the holders of shares of Series A Preferred Stock shall share ratably in any distribution of the assets available for distribution in proportion to the respective amounts which would otherwise be payable in respect of the shares of Series A Preferred Stock held by them upon such distribution if all amounts payable on or with respect to such shares were paid in full.

2.2 Payments to Holders of Series A-1 Junior Preferred Stock and Common Stock. In the event of any Liquidation, after the payment of all preferential amounts required to be paid to the holders of shares of Series A Preferred Stock, the remaining assets of the Corporation available for distribution to its stockholders, if any, shall be distributed among the holders of shares of Series A-1 Junior Preferred Stock and the holders of shares of Common Stock, pro rata based on the number of shares of Common Stock held by each such holder, treating for this purpose all shares of Series A-1 Junior

Preferred Stock as if they had been converted to Common Stock pursuant to the terms of the Certificate of Incorporation immediately prior to such Liquidation.

2.3 Deemed Liquidation Events.

2.3.1 Definition. Each of the following events shall be considered a "**Deemed Liquidation Event**" unless the holders of a majority of the outstanding shares of Series A Preferred Stock, voting exclusively as a separate class (the "**Requisite Series A Holders**"), elect otherwise by written notice sent to the Corporation at least two (2) business days prior to the effective date of any such event:

(a) the acquisition of the Corporation by another entity by means of any reorganization, merger or consolidation (but excluding any reorganization,

merger or consolidation effected exclusively for the purpose of changing the domicile of the Corporation), or any acquisition, transaction or series of related transactions in which

(i) the Corporation is a constituent party or

(ii) a subsidiary of the Corporation is a constituent party and the Corporation issues shares of its capital stock pursuant to such acquisition or transaction or series of related transactions,

and the holders of the shares of capital stock of the Corporation outstanding immediately prior to such acquisition, transaction or series of related transactions will, immediately after such acquisition, transaction or series of related transactions (by virtue of securities issued in such acquisition, transaction or series of related transactions), not continue to represent, or are converted into or exchanged for shares of capital stock that do not represent, immediately following such acquisition, transaction or series of related transactions, at least a majority, by voting power, of the capital stock of (1) the surviving or resulting corporation or (2) if the surviving or resulting corporation is a wholly owned subsidiary of another corporation immediately following such acquisition, transaction or series of related transactions, the parent corporation of such surviving or resulting corporation; provided, however, that any transaction or series of transactions principally for bona fide equity financing purposes in which cash is received by the Corporation or indebtedness of the Corporation is cancelled or converted (or a combination thereof) shall not be deemed to be a Liquidation;

(b) the sale, lease, transfer, exclusive license or other disposition, in a single transaction or series of related transactions, by the Corporation or any subsidiary of the Corporation of all or substantially all the assets of the Corporation and its subsidiaries taken as a whole or the sale or disposition (whether by merger, consolidation or otherwise) of one or more subsidiaries of the Corporation if substantially all of the assets of the Corporation and its subsidiaries taken as a whole are held by such subsidiary or subsidiaries, except where such sale, lease, transfer, exclusive license or other disposition is to a wholly owned subsidiary of the Corporation.

2.3.2 Effecting a Deemed Liquidation Event.

(a) The Corporation shall not have the power to effect or be a party to any Deemed Liquidation Event referred to in Subsection 2.3.1(a)(i) unless the definitive agreement, including any plan of merger or consolidation for such transaction (the "**Merger Agreement**") provides that the consideration payable to the stockholders of the Corporation shall be allocated among the holders of capital stock of the Corporation in accordance with Subsections 2.1 and 2.2.

(b) In the event of a Deemed Liquidation Event referred to in Subsection 2.3.1(a)(ii) or 2.3.1(b), if the Corporation does not effect a dissolution of the Corporation under the General Corporation Law within 90 days after such Deemed Liquidation Event, then (i) the Corporation shall send a written notice to each holder of Series A Preferred Stock no later than the 90th day after the Deemed Liquidation Event advising such holders of their right (and the requirements to be met to secure such right) pursuant to the terms of the

following clause (ii) to require the redemption of such shares of Series A Preferred Stock, and (ii) if the Requisite Series A Holders so request in a written instrument delivered to the Corporation not later than 120 days after such Deemed Liquidation Event, the Corporation shall use the consideration received by the Corporation for such Deemed Liquidation Event (net of any retained liabilities associated with the assets sold or technology licensed, as determined in good faith by the Board**),** together with any other assets of the Corporation available for distribution to its stockholders, all to the extent permitted by Delaware law governing distributions to stockholders (the "**Available Proceeds**"), on the 150th day after such Deemed Liquidation Event, to redeem all outstanding shares of Series A Preferred Stock at a price per share equal to the Series A Liquidation Amount. If the Available Proceeds are not sufficient to redeem all of each holder's outstanding shares of Series A Preferred Stock, the Corporation shall redeem a pro rata portion of each holder's outstanding shares of Series A Preferred Stock to the fullest extent of such Available Proceeds, based on the respective amounts which would otherwise be payable in respect of the outstanding shares of Series A Preferred Stock to be redeemed if the Available Proceeds were sufficient to redeem all such outstanding shares of Series A Preferred Stock, and shall redeem the remaining shares of Series A Preferred Stock to have been redeemed as soon as the Corporation has funds legally available therefor.

(c) Upon redemption of the Series A Preferred Stock pursuant to Subsection 2.3.2(b), each holder of shares of Series A Preferred Stock shall surrender the certificate or certificates representing all of such holder's shares of Series A Preferred Stock to be redeemed (or, if such registered holder alleges that such certificate has been lost, stolen or destroyed, a lost certificate affidavit and agreement reasonably acceptable to the Corporation to indemnify the Corporation against any claim that may be made against the Corporation on account of the alleged loss, theft or destruction of such certificate) to the Corporation, in the manner and at the place designated in the written notice sent by the Corporation pursuant to Subsection 2.3.2(b), and thereupon the redemption price for such shares shall be payable to the order of the person whose name appears on such certificate or certificates as the owner thereof. In the event less than all of the shares of Series A Preferred Stock represented by a certificate are redeemed, a new certificate, instrument or book entry representing the unredeemed shares of Series A Preferred Stock shall promptly be issued to such holder. If the redemption price payable with respect to any shares of Series A Preferred Stock redeemed pursuant to Subsection 2.3.2(b) is paid or tendered for payment or deposited with an independent

payment agent so as to be available therefor in a timely manner, then, notwithstanding that the certificates evidencing any of such shares of Series A Preferred Stock so redeemed shall not have been surrendered, dividends with respect to such shares of Series A Preferred Stock shall cease to accrue after such redemption and all rights with respect to such shares shall forthwith after such redemption terminate, except only the right of the holders to receive the redemption price without interest upon surrender of any such certificate or certificates therefor (or, if applicable, a lost certificate affidavit and agreement reasonably acceptable to the Corporation).

(d) Prior to the distribution or redemption provided for in this Subsection 2.3.2, the Corporation shall not expend or dissipate the consideration received for such Deemed Liquidation Event, except to discharge expenses incurred in connection with such Deemed Liquidation Event.

2.3.3 Amount Deemed Paid or Distributed. If the amount deemed paid or distributed under this Subsection 2.3 is made in property other than in cash, the value of such distribution shall be the fair market value of such property, determined as follows:

(a) For securities not subject to investment letters or other similar restrictions on free marketability,

(i) if traded on a securities exchange, the value shall be deemed to be the average of the closing prices of the securities on such exchange or market over the thirty (30) day period ending three (3) days prior to the closing of such Deemed Liquidation Event;

(ii) if actively traded over-the-counter, the value shall be deemed to be the average of the closing bid prices over the thirty (30) day period ending three (3) days prior to the closing of such Deemed Liquidation Event; or

(iii) if there is no active public market, the value shall be the fair market value thereof, as determined in good faith by the Board.

(b) The method of valuation of securities subject to investment letters or other similar restrictions on free marketability (other than restrictions arising solely by virtue of a stockholder's status as an affiliate or former affiliate) shall take into account an appropriate discount (as determined in good faith by the Board) from the market value as determined pursuant to clause (a) above so as to reflect the approximate fair market value thereof.

2.3.4 Allocation of Escrow and Contingent Consideration. In the event of a Deemed Liquidation Event pursuant to Subsection 2.3.1(a)(i), if any portion of the consideration payable to the stockholders of the Corporation is placed into escrow, retained as holdback or is payable to the stockholders of the Corporation only upon satisfaction of contingencies (the "**Additional Consideration**"), the Corporation shall cause the Merger Agreement to provide that (a) the portion of such consideration that is not Additional Consideration (such portion, the "**Initial Consideration**") shall be allocated among the holders of capital stock of the Corporation in accordance with Subsections 2.1 and 2.2 as if the Initial Consideration were the only consideration payable in connection with such Deemed Liquidation Event and (b) any Additional Consideration which becomes payable to the stockholders of the Corporation upon satisfaction of such contingencies shall be allocated among the holders of capital stock of the Corporation in accordance with Subsections 2.1 and 2.2, treating the previous payment of the Initial Consideration (and any prior payment of Additional Consideration) as part of the same transaction with such distribution of Additional Consideration. For the purposes of this Subsection 2.3.4, consideration placed into escrow or retained as holdback to be available

for satisfaction of indemnification or similar obligations in connection with such Deemed Liquidation Event shall be deemed to be Additional Consideration.

2.3.5 No Impairment or Circumvention. Notwithstanding anything to the contrary in this Certificate of Incorporation, the Corporation shall not through any reorganization, transfer of assets, merger, dissolution, redemption, issue or sale of securities, declaration or payment of any dividend or distribution or any other voluntary action: (i) avoid or seek to avoid the observance or performance of any of the terms to be observed or performed hereunder by the Corporation in respect of the payment of the Series A Liquidation Amount; or (ii) circumvent the rights of the holders of the Series A Preferred Stock to receive the Series A Liquidation Amount.

3. Voting.

3.1 General. On any matter presented to the stockholders of the Corporation for their action or consideration at any meeting of stockholders of the Corporation (or by written consent of stockholders in lieu of meeting), each holder of outstanding shares of Preferred Stock shall be entitled, with respect to each share of Preferred Stock, to cast the number of votes equal to the number of whole shares of Common Stock into which such share of Preferred Stock held by such holder is convertible as of the record date for determining stockholders entitled to vote on such matter. Except as provided by law or by the other provisions of this Certificate of Incorporation, holders of Preferred Stock shall vote together with the holders of Common Stock as a single class.

3.2 Election of Directors. The holders of record of the outstanding shares of Series A Preferred Stock, exclusively and as a separate class, shall be entitled to elect one (1) director of the Corporation (the "**Series A Preferred Director**") at or pursuant to each meeting or consent of the Corporation's stockholders for the election of directors. The Series A Preferred Director may be removed without cause by, and only by, the affirmative vote of the Requisite Series A Holders, given either at a special meeting of such stockholders duly called for that purpose or pursuant to a written consent of stockholders. If the holders of shares of Series A Preferred Stock fail to elect the director they are entitled to elect, voting exclusively and as a separate class, pursuant to the foregoing provisions of this Subsection 3.2, then such directorship not so filled shall remain vacant until such time as the holders of Series A Preferred Stock elect a person to fill such directorship by vote or written consent in lieu of a meeting; and no such directorship may be filled by stockholders of the Corporation other than by the holders of Series A Preferred Stock, voting exclusively and as a separate class on an as-converted to Common Stock basis. The holders of record of the shares of Series A Preferred Stock, Series A-1 Junior Preferred Stock, Common Stock and of any and all other classes or

series of voting stock, exclusively and voting together as a single class on an as-converted to Common Stock basis, shall be entitled to elect the balance of the total number of directors of the Corporation. At any meeting held for the purpose of electing a director, the presence in person or by proxy of the holders of a majority of the outstanding shares of the class(es) or series, on an as-converted to Common Stock basis, entitled to elect such director shall constitute a quorum for the purpose of electing such director. Except as otherwise provided in this Subsection 3.2, a vacancy in any directorship filled by the holders of any class(es) or series shall be filled only by vote or written consent in lieu of a meeting of the holders of such class(es) or series or by any remaining director or directors elected by the holders of such class(es) or series pursuant to this Subsection 3.2. For purposes of this Certificate of Incorporation, the term "**Investor Directors**" shall mean,

collectively, those members of the Board that have been designated by, or that are serving on the Board because of the rights of, certain of the holders of capital stock of the Corporation to designate directors pursuant to that certain Amended and Restated Voting Agreement, dated on or about the Series A-1 Original Issue Date, by and among the Corporation, the holders of Preferred Stock and certain other stockholders of the Corporation that are parties thereto, as amended and in effect from time to time (the "**Voting Agreement**"). The term "**Investor Director**" shall mean any one of the Investor Directors.

3.3 Protective Provisions.

3.3.1 The Corporation shall not, either directly or indirectly by amendment, merger, consolidation or otherwise, do any of the following without (in addition to any other vote required by law or this Certificate of Incorporation) the written consent or affirmative vote of the Requisite Holders (as defined in Subsection 3.3.3 below), in each case given in writing or by vote at a meeting, and any such act or transaction entered into without such consent or vote shall be null and void *ab initio*, and of no force or effect:

(a) liquidate, dissolve or wind-up all or substantially all of the business and affairs of the Corporation or any of its subsidiaries, cease to conduct all or any substantial part of the business of the Corporation or any of its subsidiaries, or consent to any of the foregoing, or enter into an agreement to do any of the foregoing or permit any of its subsidiaries to enter into an agreement to do any of the foregoing;

(b) effect any merger or consolidation involving the Corporation or any of its subsidiaries, or effect any Deemed Liquidation Event, or consent to any of the foregoing or enter into an agreement to do any of the foregoing or permit any of its subsidiaries to enter into an agreement to do any of the foregoing;

(c) sell, transfer, lease, grant an exclusive license with respect to, or otherwise dispose of, any material asset or business of the Corporation or any of its subsidiaries, or cause or permit any of its subsidiaries to do or enter into an agreement to do any of the foregoing;

(d) increase or decrease the authorized number of shares of Common Stock or Preferred Stock of the Corporation;

(e) extend, or permit any subsidiary to extend, any credit or guarantee in respect of any loan or grant of credit in excess of $500,000 individually or $1,000,000 in the aggregate;

(f) dispose of any fixed assets or intellectual property having a fair market value of greater than $500,000;

(g) create, authorize or designate, whether by reclassification or otherwise, of a new class or series of capital stock of the Corporation or any of its subsidiaries or of securities convertible into or exercisable or exchangeable for any such new class or series of capital stock of the Corporation or any of its subsidiaries;

(h) create, authorize or issue any debt security, or incur any new indebtedness for borrowed money, or permit any subsidiary to authorize or issue any debt security or to incur any new indebtedness for borrowed money, in excess of $500,000 individually or $1,000,000 in the aggregate;

(i) purchase or redeem (or permit any subsidiary to purchase or redeem) or pay or declare any dividend or make any distribution on, any shares of capital stock of the Corporation other than (1) dividends or other distributions payable on the Common Stock solely in the form of additional shares of Common Stock, (2) dividends or distributions paid or declared by any subsidiary on shares of capital stock of such subsidiary held by the Corporation, (3) repurchases of stock from former employees, officers, directors, consultants or other persons who performed services for the Corporation or any subsidiary in connection with the cessation of such employment or service at a price no greater than the lower of the original purchase price thereof and the then-current fair market value thereof, and (4) repurchases by any subsidiary of any stock of such subsidiary held by the Corporation;

(j) increase or decrease the authorized number of members of the Board;

(k) acquire all or substantially all of the business or assets of any other entity, including by way of exclusive license, or permit any of the subsidiaries of the Corporation to do any of the foregoing;

(l) adopt or approve any new equity incentive plan of the Corporation or adopt or approve any amendment or modification to any existing equity incentive plan of the Corporation, except for the adoption or approval of any such new equity incentive plan of the Corporation or any such amendment or modification to any existing equity incentive plan of the Corporation approved by the Board, provided that such approval by the Board includes the affirmative vote or approval of at least a majority of the Investor Directors;

(m) change in any material respect the line of business of the Corporation or any of its subsidiaries;

(n) create, or hold capital stock in, any subsidiary that is not wholly owned (either directly or through one or more other subsidiaries) by the Corporation, or sell, transfer or otherwise dispose of any capital stock of any direct or indirect subsidiary of the Corporation, or permit any direct or indirect subsidiary to sell, lease, transfer, exclusively license or otherwise dispose (in a single transaction or series of related transactions) of all or substantially all of the assets of such subsidiary;

(o) enter into any transaction, or permit any of its subsidiaries to enter into any transaction, with any of the Corporation's founders, officers or directors or with any of the officers, managers or employees of Rhythm Holding Company, LLC ("**Parent**"), except for (1) any transaction in the ordinary course of business of the Corporation or any of its subsidiaries and (2) any transaction approved by a majority of those members of the Board that are disinterested with respect to such transaction; or

(p) amend, alter, waive or repeal any provision of this Certificate of Incorporation or Bylaws of the Corporation if such amendment, alteration, waiver or repeal adversely affects the rights, preferences or privileges of any series of Preferred Stock.

3.3.2 The Corporation shall not, either directly or indirectly by amendment, merger, consolidation or otherwise, do any of the following without (in addition to any other vote required by law or this Certificate of Incorporation) the written consent or affirmative vote of the holders of at least sixty percent (60%) of the then outstanding shares of Series A Preferred Stock, in each case given in writing or by vote at a meeting, and any such act or transaction entered into without such consent or vote shall be null and void *ab initio*, and of no force or effect:

(a) amend, alter, waive or repeal any provision of this Certificate of Incorporation or Bylaws of the Corporation if such amendment, alteration, waiver or repeal would adversely affect the preferences, privileges, rights or powers of the Series A Preferred Stock (regardless of whether the preferences, privileges, rights or powers of any other class or series of capital stock of the Corporation are correspondingly affected);

(b) reclassify, alter or amend any existing security of the Corporation that is pari passu with the Series A Preferred Stock in respect of the distribution of assets on the liquidation, dissolution or winding up of the Corporation, the payment of dividends, redemption rights or voting rights, if such reclassification, alteration or amendment would render such other security senior to the Series A Preferred Stock in respect of any such right, preference, or privilege, or reclassify, alter or amend any existing security of the Corporation that is junior to the Series A Preferred Stock in respect of the distribution of assets on the liquidation, dissolution or winding up of the Corporation, the payment of dividends, redemption rights or voting rights, if such reclassification, alteration or amendment would render such other security senior to or pari passu with the Series A Preferred Stock in respect of any such right, preference or privilege; or

(c) increase or decrease the number of authorized shares of Series A Preferred Stock.

3.3.3 For purposes of this Certificate of Incorporation, the term "**Requisite Holders**" shall mean the holders of a majority of all shares of Preferred Stock and Common Stock outstanding then held by all holders of Preferred Stock and Common Stock, voting together as a single class on an as-converted to Common Stock basis, and for this purpose, disregarding and treating as if they were not issued or outstanding any shares of Common Stock then outstanding that are held by officers, managers, employees, consultants or advisors of the Corporation or Parent or by transferees of any such officers, managers, employees, consultants or advisors.

4. Optional Conversion.

The holders of Preferred Stock shall have conversion rights as follows (the "**Conversion Rights**"):

4.1 Right to Convert.

4.1.1 Conversion Ratio. Each outstanding share of Preferred Stock shall be convertible, at the option of the holder thereof, at any time and from time to time, and without the payment of additional consideration by the holder thereof, into such number of fully paid and nonassessable shares of Common Stock as is determined by (i) in the case of the Series A Preferred Stock, dividing the Series A Original Issue Price by the Series A Conversion Price (as defined below) in effect at the Conversion Time (as defined in Subsection 4.3.1 below) and (ii) in the case of the Series A-1 Junior Preferred Stock, dividing the Series A-1 Original Issue Price by the Series A-1 Conversion Price (as defined below) in effect at the Conversion Time. The "**Series A Conversion Price**" shall initially be equal to $1.00; and the "**Series A-1 Conversion Price**" shall initially be equal to $0.75. The Series A Conversion Price and the Series A-1 Conversion Price are collectively referred to as the "**Conversion Prices**" and each individually as a "**Conversion Price**". The Conversion Price of each series of Preferred Stock, and the rate at which shares of each series of Preferred Stock may be converted into shares of Common Stock, shall be subject to adjustment as provided below in this Section 4.

4.1.2 Termination of Conversion Rights. In the event of a Liquidation, the Conversion Rights shall terminate at the close of business on the last full day preceding the date fixed for the payment of any such amounts distributable on such event to the holders of Preferred Stock.

4.2 Fractional Shares. No fractional shares of Common Stock shall be issued upon conversion of any shares of Preferred Stock. In lieu of any fractional shares to which the holder would otherwise be entitled, the Corporation shall pay cash equal to such fraction multiplied by the fair market value of a share of Common Stock as determined in good faith by the Board. Whether or not fractional shares would be issuable upon such conversion shall be determined on the basis of the total number of shares of the particular series of Preferred Stock the holder is at the time converting into Common Stock and the aggregate number of shares of Common Stock issuable upon such conversion.

4.3 Mechanics of Conversion.

4.3.1 Notice of Conversion. In order for a holder of Preferred Stock to voluntarily convert shares of Preferred Stock into shares of Common Stock, such holder shall (a) provide written notice to the Corporation's transfer agent at the office of the transfer agent for the Preferred Stock (or at the principal office of the Corporation if the Corporation serves as its own transfer agent) that such holder elects to convert all or any number of such holder's shares of Preferred Stock and, if applicable, any event on which such conversion is contingent and (b), if such holder's shares are certificated, surrender the certificate or certificates for such shares of Preferred Stock (or, if such registered holder alleges that such certificate has been lost, stolen or destroyed, a lost certificate affidavit and agreement reasonably acceptable to the Corporation to indemnify the Corporation against any claim that may be made against the Corporation on account of the alleged loss, theft or destruction of such certificate), at the office of the transfer agent for the Preferred Stock (or at the principal office of the Corporation if the Corporation serves as its own transfer agent). Such notice shall state such holder's name or the names of

the nominees in which such holder wishes the shares of Common Stock to be issued. If required by the Corporation, certificates surrendered for conversion shall be endorsed or accompanied by a written instrument or instruments of transfer, in form satisfactory to the Corporation, duly executed by the registered holder or his, her or its attorney duly authorized in writing. The close of business on the date of receipt by the transfer agent (or by the Corporation if the Corporation

serves as its own transfer agent) of such notice and, if applicable, certificates (or lost certificate affidavit and agreement), or with respect to any conversion conditioned upon the consummation of any Liquidation, the close of business on the date of such Liquidation, shall be the time of conversion (the "**Conversion Time**"), and the shares of Common Stock issuable upon conversion of the specified shares shall be deemed to be outstanding of record as of such date. The Corporation shall, as soon as practicable after the Conversion Time, (i) issue and deliver to such holder of Preferred Stock, or to his, her or its nominees, a certificate or certificates for the number of full shares of Common Stock issuable upon such conversion in accordance with the provisions hereof and a certificate for the number (if any) of the shares of Preferred Stock represented by the surrendered certificate that were not converted into Common Stock, (ii) pay in cash such amount as provided in Subsection 4.2 in lieu of any fraction of a share of Common Stock otherwise issuable upon such conversion and (iii) pay all declared but unpaid dividends on the shares of Preferred Stock converted.

4.3.2 Reservation of Shares. The Corporation shall at all times when Preferred Stock shall be outstanding, reserve and keep available out of its authorized but unissued capital stock, for the purpose of effecting the conversion of such Preferred Stock, such number of its duly authorized shares of Common Stock as shall from time to time be sufficient to effect the conversion of all outstanding Preferred Stock; and if at any time the number of authorized but unissued shares of Common Stock shall not be sufficient to effect the conversion of all then outstanding shares of Preferred Stock, the Corporation shall take such corporate action as may be necessary to increase its authorized but unissued shares of Common Stock to such number of shares as shall be sufficient for such purposes, including, without limitation, engaging in best efforts to obtain the requisite stockholder approval of any necessary amendment to this Certificate of Incorporation. Before taking any action which would cause an adjustment reducing the Conversion Price of any series of Preferred Stock below the then par value of the shares of Common Stock issuable upon conversion of such series of Preferred Stock, the Corporation will take any corporate action which may, in the opinion of its counsel, be necessary in order that the Corporation may validly and legally issue fully paid and nonassessable shares of Common Stock at such adjusted Conversion Price.

4.3.3 Effect of Conversion. All shares of Preferred Stock which shall have been surrendered for conversion as herein provided shall no longer be deemed to be outstanding and all rights with respect to such shares shall immediately cease and terminate at the Conversion Time, except only the right of the holders thereof to receive shares of Common Stock in exchange therefor, to receive payment in lieu of any fraction of a share otherwise issuable upon such conversion as provided in Subsection 4.2 and to receive payment of any dividends declared but unpaid thereon. The shares of any series of Preferred Stock so converted shall be retired and cancelled and may not be reissued as shares of such series of Preferred Stock, and the Corporation may thereafter take such appropriate action (without the need for stockholder action) as may be necessary to reduce the authorized number of shares of such series of Preferred Stock accordingly.

4.3.4 No Further Adjustment. Upon any such conversion, no adjustment to the Conversion Price of the applicable series of Preferred Stock shall be made for any declared but unpaid dividends on the shares of such applicable series of Preferred Stock surrendered for conversion or on the Common Stock delivered upon conversion.

4.3.5 Taxes. The Corporation shall pay any and all issue and other similar taxes that may be payable in respect of any issuance or delivery of shares of Common Stock upon conversion of shares of Preferred Stock pursuant to this Section 4. The Corporation shall not, however, be required to pay any tax which may be payable in respect of any transfer involved in the issuance and delivery of shares of Common Stock in a name other than that in which the shares of Preferred Stock so converted were registered, and no such issuance or delivery shall be made unless and until the person or entity requesting such issuance has paid to the Corporation the amount of any such tax or has established, to the satisfaction of the Corporation, that such tax has been paid.

4.4 Adjustments to Series A Conversion Price for Diluting Issues.

4.4.1 Special Definitions. For purposes of this Article Fifth, the following definitions shall apply:

(a) "**Option**" shall mean rights, options or warrants to subscribe for, purchase or otherwise acquire Common Stock or Convertible Securities.

(b) "**Series A-1 Original Issue Date**" shall mean the date on which the first share of Series A-1 Junior Preferred Stock was issued.

(c) "**Exchange Agreement**" shall mean that certain Exchange Agreement, dated on or about the Series A-1 Original Issue Date, by and among the Corporation and Parent, as amended and in effect from time to time.

(d) "**Convertible Securities**" shall mean any evidences of indebtedness, shares or other securities directly or indirectly convertible into or exchangeable for Common Stock, but excluding Options.

(e) "**Additional Shares of Common Stock**" shall mean all shares of Common Stock issued (or, pursuant to Subsection 4.4.3 below, deemed to be issued) by the Corporation after the Series A-1 Original Issue Date, other than (1) the following shares of Common Stock and (2) shares of Common Stock deemed issued pursuant to the following Options and Convertible Securities (clauses (1) and (2), collectively, "**Exempted Securities**"):

(i) shares of Common Stock, Options or Convertible Securities issued as a dividend or distribution on any series of Preferred Stock, provided that, in the case of any such dividend or distribution on shares of

Series A-1 Junior Preferred Stock, the Corporation complies with all of the applicable provisions of Subsection 1.2 hereof;

(ii) shares of Common Stock, Options or Convertible Securities issued by reason of a dividend, stock split, split-up or other distribution on shares of Common Stock that is covered by Subsection 4.5, 4.6, 4.7 or 4.8;

(iii) shares of Common Stock or Options issued to employees or directors of, or consultants or advisors to, the Corporation or any of its subsidiaries pursuant to a plan, agreement or arrangement approved by the Board, including the affirmative approval, consent or vote of a majority of the Investor Directors;

(iv) shares of Common Stock or Convertible Securities actually issued upon the exercise of Options or shares of Common Stock actually issued upon the conversion or exchange of Convertible Securities (including, without limitation, any series of Preferred Stock), in each case provided such issuance is pursuant to the terms of such Option or Convertible Security (including, without limitation, such series of Preferred Stock);

(v) shares of Common Stock issued by the Corporation in connection with the Corporation's initial public offering;

(vi) any and all shares of Series A-1 Junior Preferred Stock issued or issuable pursuant to the Exchange Agreement (as defined in this Subsection 4.4.1);

(vii) shares of Common Stock, Options or Convertible Securities issued to banks, equipment lessors or other financial institutions, or to real property lessors, pursuant to a debt financing, equipment leasing or real property leasing transaction approved by the Board, including the affirmative approval, consent or vote of a majority of the Investor Directors;

(viii) shares of Common Stock, Options or Convertible Securities issued to suppliers or third party service providers in connection with the provision of goods or services pursuant to transactions approved by the Board, including the affirmative approval, consent or vote of a majority of the Investor Directors;

(ix) shares of Common Stock, Options or Convertible Securities issued pursuant to the acquisition of another corporation by the Corporation by merger, purchase of substantially all of the assets or other reorganization or to a joint venture agreement, provided that such issuances are approved by the

Board, including the affirmative approval, consent or vote of a majority of the Investor Directors; or

(x) shares of Common Stock, Options or Convertible Securities issued in connection with sponsored research, collaboration, technology license, development, marketing or other similar agreements or strategic partnerships approved by the Board, including the affirmative approval, consent or vote of a majority of the Investor Directors.

4.4.2 No Adjustment of Series A Conversion Price. No adjustment in the Series A Conversion Price shall be made as the result of the issuance or deemed issuance of Additional Shares of Common Stock if the Corporation receives written notice from the Requisite Series A Holders agreeing that no such adjustment shall be made as the result of the issuance or deemed issuance of such Additional Shares of Common Stock.

4.4.3 Deemed Issue of Additional Shares of Common Stock.

(a) If the Corporation at any time or from time to time after the Series A-1 Original Issue Date shall issue any Options or Convertible Securities (excluding Options or Convertible Securities which are themselves Exempted Securities) or shall fix a record date for the determination of holders of any class of securities entitled to receive any such Options or Convertible Securities, then the maximum number of shares of Common Stock (as set forth in the instrument relating thereto, assuming the satisfaction of any conditions to exercisability, convertibility or exchangeability but without regard to any provision contained therein for a subsequent adjustment of such number) issuable upon the exercise of such Options or, in the case of Convertible Securities and Options therefor, the conversion or exchange of such Convertible Securities, shall be deemed to be Additional Shares of Common Stock issued as of the time of such issue or, in case such a record date shall have been fixed, as of the close of business on such record date.

(b) If the terms of any Option or Convertible Security, the issuance of which resulted in an adjustment to the Series A Conversion Price pursuant to the terms of Subsection 4.4.4, are revised as a result of an amendment to such terms or any other adjustment pursuant to the provisions of such Option or Convertible Security (but excluding automatic adjustments to such terms pursuant to anti-dilution or similar provisions of such Option or Convertible Security) to provide for either (1) any increase or decrease in the number of shares of Common Stock issuable upon the exercise, conversion and/or exchange of any such Option or Convertible Security or (2) any increase or decrease in the consideration payable to the Corporation upon such exercise, conversion and/or exchange, then, effective upon such increase or decrease becoming effective, the Series A Conversion Price computed upon the original issue of such Option or Convertible Security (or upon the occurrence of a record date with respect thereto) shall be readjusted to the Series A Conversion Price as would have obtained had such revised terms been in effect upon the original date of issuance of such Option or Convertible Security. Notwithstanding the foregoing, no readjustment pursuant to this clause (b) shall have the effect of increasing the Series A Conversion Price subject to such readjustment to an amount which exceeds the lower of (i) the Series A Conversion Price in effect immediately prior to the original adjustment made as a result of the issuance of such Option or Convertible Security, or

(ii) the Series A Conversion Price that would have resulted from any issuances of Additional Shares of Common Stock (other than deemed issuances of Additional Shares of Common Stock as a result of the issuance of such Option or Convertible Security) between the original adjustment date and such readjustment date.

(c) If the terms of any Option or Convertible Security (excluding Options or Convertible Securities which are themselves Exempted Securities), the issuance of which did not result in an adjustment to the Series A Conversion Price pursuant to the terms of Subsection 4.4.4 (either because the consideration per share (determined pursuant to Subsection 4.4.5) of the Additional Shares of Common Stock subject thereto was equal to or greater than the Series A Conversion Price then in effect, or because such Option or Convertible Security was issued before Series A-1 Original Issue Date), are revised after the Series A-1 Original Issue Date as a result of an amendment to such terms or any other adjustment pursuant to the provisions of such Option or Convertible Security (but excluding automatic adjustments to such terms pursuant to anti-dilution or similar provisions of such Option or Convertible Security) to provide for either (1) any increase in the number of shares of Common Stock issuable upon the exercise, conversion or exchange of any such Option or Convertible Security or (2) any decrease in the consideration payable to the Corporation upon such exercise, conversion or exchange, then such Option or Convertible Security, as so amended or adjusted, and the Additional Shares of Common Stock subject thereto (determined in the manner provided in Subsection 4.4.3(a)) shall be deemed to have been issued effective upon such increase or decrease becoming effective.

(d) Upon the expiration or termination of any unexercised Option or unconverted or unexchanged Convertible Security (or portion thereof) which resulted (either upon its original issuance or upon a revision of its terms) in an adjustment to the Series A Conversion Price pursuant to the terms of Subsection 4.4.4, such Series A Conversion Price shall be readjusted to the Series A Conversion Price as would have obtained had such Option or Convertible Security (or portion thereof) never been issued.

(e) If the number of shares of Common Stock issuable upon the exercise, conversion and/or exchange of any Option or Convertible Security, or the consideration payable to the Corporation upon such exercise, conversion and/or exchange, is calculable at the time such Option or Convertible Security is issued or amended but is subject to adjustment based upon subsequent events, any adjustment to the Series A Conversion Price provided for in this Subsection 4.4.3 shall be effected at the time of such issuance or amendment based on such number of shares or amount of consideration without regard to any provisions for subsequent adjustments (and any subsequent adjustments shall be treated as provided in clauses (b) and (c) of this Subsection 4.4.3). If the number of shares of Common Stock issuable upon the exercise, conversion and/or exchange of any Option or Convertible Security, or the consideration payable to the Corporation upon such exercise, conversion and/or exchange, cannot be calculated at all at the time such Option or Convertible Security is issued or amended, any adjustment to the Series A Conversion Price that would result under the terms of this Subsection 4.4.3 at the time of such issuance or amendment shall instead be effected at the time such number of shares and/or amount of consideration is first calculable (even if subject to subsequent adjustments), assuming for purposes of calculating such adjustment to the Series A Conversion Price that such issuance or amendment took place at the time such calculation can first be made.

4.4.4 Adjustment of the Series A Conversion Price Upon Issuance of Additional Shares of Common Stock. In the event the Corporation shall at any time after the Series A-1 Original Issue Date issue Additional Shares of Common Stock (including Additional Shares of Common Stock deemed to be issued pursuant to Subsection 4.4.3), without consideration or for a consideration per share less than the Series A Conversion Price in effect immediately prior to such issue, then the Series A Conversion Price shall be reduced, concurrently with such issue, to a price (calculated to the nearest one-hundredth of a cent) determined in accordance with the following formula:

$$CP_2 = CP_1 * (A + B) \div (A + C).$$

For purposes of the foregoing formula, the following definitions shall apply:

(a) "CP_2" shall mean the Series A Conversion Price in effect immediately after such issue of Additional Shares of Common Stock

(b) "CP_1" shall mean the Series A Conversion Price in effect immediately prior to such issue of Additional Shares of Common Stock;

(c) "A" shall mean the number of shares of Common Stock outstanding immediately prior to such issue of Additional Shares of Common Stock (treating for this purpose as outstanding all shares of Common Stock issuable upon exercise of Options outstanding immediately prior to such issue or upon conversion or exchange of Convertible Securities (including the Preferred Stock) outstanding (assuming exercise of any outstanding Options therefor) immediately prior to such issue);

(d) "B" shall mean the number of shares of Common Stock that would have been issued if such Additional Shares of Common Stock had been issued at a price per share equal to CP_1 (determined by dividing the aggregate consideration received by the Corporation in respect of such issue by CP_1); and

(e) "C" shall mean the number of such Additional Shares of Common Stock issued in such transaction.

4.4.5 Determination of Consideration. For purposes of this Subsection 4.4, the consideration received by the Corporation for the issue of any Additional Shares of Common Stock shall be computed as follows:

(a) Cash and Property: Such consideration shall:

(i) insofar as it consists of cash, be computed at the aggregate amount of cash received by the Corporation, excluding amounts paid or payable for accrued interest;

(ii) insofar as it consists of property other than cash, be computed at the fair market value thereof at the time of such issue, as determined in good faith by

the Board, including the Series A Preferred Director and a majority of the other Investor Directors; and

(iii) in the event Additional Shares of Common Stock are issued together with other shares or securities or other assets of the Corporation for consideration which covers both, be the proportion of such consideration so received, computed as provided in clauses (i) and (ii) above, as determined in good faith by the Board, including the Series A Preferred Director and a majority of the other Investor Directors.

(b) Options and Convertible Securities. The consideration per share received by the Corporation for Additional Shares of Common Stock deemed to have been issued pursuant to Subsection 4.4.3, relating to Options and Convertible Securities, shall be determined by dividing:

(i) the total amount, if any, received or receivable by the Corporation as consideration for the issue of such Options or Convertible Securities, plus the minimum aggregate amount of additional consideration (as set forth in the instruments relating thereto, without regard to any provision contained therein for a subsequent adjustment of such consideration) payable to the Corporation upon the exercise of such Options or the conversion or exchange of such Convertible Securities, or in the case of Options for Convertible Securities, the exercise of such Options for Convertible Securities and the conversion or exchange of such Convertible Securities, by

(ii) the maximum number of shares of Common Stock (as set forth in the instruments relating thereto, without regard to any provision contained therein for a subsequent adjustment of such number) issuable upon the exercise of such Options or the conversion or exchange of such Convertible Securities, or in the case of Options for Convertible Securities, the exercise of such Options for Convertible Securities and the conversion or exchange of such Convertible Securities.

4.4.6 Multiple Closing Dates. In the event the Corporation shall issue on more than one date Additional Shares of Common Stock that are a part of one transaction or a series of related transactions and that would result in an adjustment to the Series A Conversion Price pursuant to the terms of Subsection 4.4.4, and such issuance dates occur within a period of no more than 90 days from the first such issuance to the final such issuance, then, upon the final

such issuance, the Series A Conversion Price shall be readjusted to give effect to all such issuances as if they occurred on the date of the first such issuance (and without giving effect to any additional adjustments as a result of any such subsequent issuances within such period).

4.5 Adjustment for Stock Splits and Combinations. If the Corporation shall at any time or from time to time after the Series A-1 Original Issue Date effect a subdivision of the outstanding Common Stock, the Conversion Price of each series of Preferred Stock in effect immediately before that subdivision shall be proportionately decreased so that the number of shares of Common Stock issuable on conversion of each share of such series of Preferred Stock shall be increased in proportion to such increase in the aggregate number of shares of Common Stock outstanding. If the Corporation shall at any time or from time to time after the Series A-1 Original Issue Date combine the outstanding shares of Common Stock, the Conversion Price of each series of Preferred Stock in effect immediately before the combination shall be proportionately increased so that the number of shares of Common Stock issuable on conversion of each share of such series of Preferred Stock shall be decreased in proportion to such decrease in the aggregate number of shares of Common Stock outstanding. Any adjustment under this subsection shall become effective at the close of business on the date the subdivision or combination becomes effective.

4.6 Adjustment for Certain Dividends and Distributions. In the event the Corporation at any time or from time to time after the Series A-1 Original Issue Date shall make or issue, or fix a record date for the determination of holders of Common Stock entitled to receive, a dividend or other distribution payable on the Common Stock in additional shares of Common Stock, then and in each such event the Conversion Price of each series of Preferred Stock in effect immediately before such event shall be decreased as of the time of such issuance or, in the event such a record date shall have been fixed, as of the close of business on such record date, by multiplying such Conversion Price then in effect by a fraction:

(1) the numerator of which shall be the total number of shares of Common Stock issued and outstanding immediately prior to the time of such issuance or the close of business on such record date, and

(2) the denominator of which shall be the total number of shares of Common Stock issued and outstanding immediately prior to the time of such issuance or the close of business on such record date plus the number of shares of Common Stock issuable in payment of such dividend or distribution.

Notwithstanding the foregoing, (a) if such record date shall have been fixed and such dividend is not fully paid or if such distribution is not fully made on the date fixed therefor, the Conversion Price of each series of Preferred Stock shall be recomputed accordingly as of the close of business on such record date and thereafter such Conversion Price shall be adjusted pursuant to this subsection as of the time of actual payment of such dividends or distributions; and (b) that no such adjustment shall be made if the holders of the applicable series of Preferred Stock simultaneously receive a dividend or other distribution of shares of Common Stock in a number equal to the number of shares of Common Stock as they would have received if all outstanding shares of such series of Preferred Stock had been converted into Common Stock on the date of such event.

4.7 Adjustments for Other Dividends and Distributions. In the event the Corporation at any time or from time to time after the Series A-1 Original Issue Date shall make or issue, or fix a record date for the determination of holders of Common Stock entitled to receive, a dividend or other distribution payable in securities of the Corporation (other than a distribution of shares of Common Stock in respect of outstanding shares of Common Stock) or in other property and the provisions of Section 1 do not apply to such dividend or distribution, then and in each such event the holders of each series of Preferred Stock shall receive, simultaneously with the distribution to the holders of Common Stock, a dividend or other distribution of such securities or other property in an amount equal to the amount of such securities or other property as they would have received if all outstanding shares of such series of Preferred Stock had been converted into Common Stock on the date of such event.

4.8 Adjustment for Merger or Reorganization, etc. Subject to the provisions of Subsection 2.3, if there shall occur any reorganization, recapitalization, reclassification, consolidation or merger involving the Corporation in which the Common Stock (but not all outstanding Preferred Stock) is converted into or exchanged for securities, cash or other property (other than a transaction covered by Subsections 4.4, 4.6 or 4.7), then, following any such reorganization, recapitalization, reclassification, consolidation or merger, each outstanding share of each series of Preferred Stock not so converted shall thereafter be convertible in lieu of the Common Stock into which it was convertible prior to such event into the kind and amount of securities, cash or other property which a holder of the number of shares of Common Stock of the Corporation issuable upon conversion of one share of such series of Preferred Stock immediately prior to such reorganization, recapitalization, reclassification, consolidation or merger would have been entitled to receive pursuant to such transaction; and, in such case, appropriate adjustment (as determined in good faith by the Board) shall be made in the application of the provisions in this Section 4 with respect to the rights and interests thereafter of the holders of such series of Preferred Stock, to the end that the provisions set forth in this Section 4 (including provisions with respect to changes in and other adjustments of the Conversion Price of such series of Preferred Stock) shall thereafter be applicable, as nearly as reasonably may be, in relation to any securities or other property thereafter deliverable upon the conversion of such series of Preferred Stock. For the avoidance of doubt, nothing in this Subsection 4.8 shall be construed as preventing the holders of any series of Preferred Stock from seeking any appraisal rights to which they are otherwise entitled under the General Corporation Law in connection with a merger triggering an adjustment hereunder, nor shall this Subsection 4.8 be deemed conclusive evidence of the fair value of the outstanding shares of any series of Preferred Stock in any such appraisal proceeding.

4.9 Certificate as to Adjustments. Upon the occurrence of each adjustment or readjustment of the Conversion Price of any series of Preferred Stock pursuant to this Section 4, the Corporation at its expense shall, as promptly as reasonably practicable but in any event not later than 10 days thereafter, compute such adjustment or readjustment in accordance with the terms hereof and furnish to each holder of Preferred Stock a certificate setting forth such adjustment or readjustment (including the kind and amount of securities, cash or other property into which the applicable series of Preferred Stock is convertible as a result of such adjustment or readjustment) and showing in detail the facts upon which such adjustment or readjustment is based. The Corporation shall, as promptly as reasonably practicable after the written request at any time of any holder of Preferred Stock (but in any event not later than 10 days thereafter), furnish or cause to be furnished to such holder a certificate setting forth (i) the Conversion Price

of each series of Preferred Stock then in effect, and (ii) the number of shares of Common Stock and the amount, if any, of other securities, cash or property which then would be received upon the conversion of each series of Preferred Stock.

4.10 Notice of Record Date. In the event:

(a) the Corporation shall take a record of the holders of its Common Stock (or other capital stock or securities at the time issuable upon conversion of any series of Preferred Stock) for the purpose of entitling or enabling them to receive any dividend or other distribution, or to receive any right to subscribe for or purchase any shares of capital stock of any class or any other securities, or to receive any other security; or

(b) of any capital reorganization of the Corporation, any reclassification of the Common Stock of the Corporation, or any Deemed Liquidation Event; or

(c) of the voluntary or involuntary dissolution, liquidation or winding-up of the Corporation,

then, and in each such case, the Corporation will send or cause to be sent to the holders of each series of Preferred Stock a notice specifying, as the case may be, (i) the record date for such dividend, distribution or right, and the amount and character of such dividend, distribution or right, or (ii) the effective date on which such reorganization, reclassification, consolidation, merger, transfer, dissolution, liquidation or winding-up is proposed to take place, and the time, if any is to be fixed, as of which the holders of record of Common Stock (or such other capital stock or securities at the time issuable upon the conversion of any series of Preferred Stock) shall be entitled to exchange their shares of Common Stock (or such other capital stock or securities) for securities or other property deliverable upon such reorganization, reclassification, consolidation, merger, transfer, dissolution, liquidation or winding-up, and the amount per share and character of such exchange applicable to each series of Preferred Stock and the Common Stock. Such notice shall be sent at least 10 days prior to the record date or effective date for the event specified in such notice.

5. Mandatory Conversion.

5.1 Trigger Events. Upon either (a) the closing of the sale of shares of Common Stock to the public at a price of at least $1.00 per share (subject to appropriate adjustment in the event of any Recapitalization with respect to the Common Stock that is effected at any time after the Series A-1 Original Issue Date) in a firm-commitment underwritten public offering pursuant to an effective registration statement under the Securities Act of 1933, as amended, resulting in at least $50,000,000 of gross proceeds to the Corporation or (b) the date and time specified by, or upon the occurrence of an event specified by, the Requisite Series A Holders (the time of such closing or the date and time specified or the time of the event specified in such vote or written consent is referred to herein as the "**Mandatory Conversion Time**"), then (i) all outstanding shares of Preferred Stock shall automatically be converted into shares of Common Stock, at the then effective conversion rate applicable to each series of Preferred Stock, as calculated pursuant to Subsection 4.1.1, and (ii) such shares may not be reissued by the Corporation.

5.2 Procedural Requirements. All holders of record of shares of Preferred Stock shall be sent written notice of the Mandatory Conversion Time and the place designated for mandatory conversion of all shares of Preferred Stock pursuant to this Section 5. Such notice need not be sent in advance of the occurrence of the Mandatory Conversion Time. Upon receipt of such notice, each holder of shares of Preferred Stock in certificated form shall surrender his, her or its certificate or certificates for all such shares (or, if such holder alleges that such certificate has been lost, stolen or destroyed, a lost certificate affidavit and agreement reasonably acceptable to the Corporation to indemnify the Corporation against any claim that may be made against the Corporation on account of the alleged loss, theft or destruction of such certificate) to the Corporation at the place designated in such notice. If so required by the Corporation, any certificates surrendered for conversion shall be endorsed or accompanied by written instrument or instruments of transfer, in form satisfactory to the Corporation, duly executed by the registered holder or by his, her or its attorney duly authorized in writing. All rights with respect to any shares of Preferred Stock converted pursuant to Subsection 5.1, including the rights, if any, to receive notices and vote (other than as a holder of Common Stock), will terminate at the Mandatory Conversion Time (notwithstanding the failure of the holder or holders thereof to surrender any certificates at or prior to such time), except only the rights of the holders thereof, upon surrender of any certificate or certificates (or lost certificate affidavit and agreement) therefor, to receive the items provided for in the next sentence of this Subsection 5.2. As soon as practicable after the Mandatory Conversion Time and, if applicable, the surrender of the certificate or certificates (or lost certificate affidavit and agreement) for any shares of Preferred Stock, the Corporation shall (a) issue and deliver to such holder, or to his, her or its nominees, a certificate or certificates for the number of full shares of Common Stock issuable on such mandatory conversion in accordance with the provisions hereof and (b) pay cash as provided in Subsection 4.2 in lieu of any fraction of a share of Common Stock otherwise issuable upon such conversion and the payment of any declared but unpaid dividends on the shares of Preferred Stock converted. Such converted shares of any series of Preferred Stock shall be retired and cancelled and may not be reissued as shares of such series of Preferred Stock, and the Corporation may thereafter take such appropriate action (without the need for stockholder action) as may be necessary to reduce the authorized number of shares of such series of Preferred Stock accordingly.

6. Redeemed or Otherwise Acquired Shares. Any shares of Preferred Stock that are redeemed or otherwise acquired by the Corporation or any of its subsidiaries shall be automatically and immediately cancelled and retired and shall not be reissued, sold or transferred. Neither the Corporation nor any of its subsidiaries may exercise any voting or other rights granted to the holders of Preferred Stock following redemption.

7. Waiver. Except to the extent otherwise expressly provided elsewhere in this Certificate of Incorporation, any of the rights, powers, preferences and other terms of any series of Preferred Stock set forth herein may be waived on behalf of all holders of such series of Preferred Stock by the affirmative written consent or vote of holders of a majority of the outstanding shares of such series of Preferred Stock.

8. Notices. Any notice required or permitted by the provisions of this Article Fifth to be given to a holder of shares of Preferred Stock shall be mailed, postage prepaid, to the post office address last shown on the records of the Corporation, or given by electronic

communication in compliance with the provisions of the General Corporation Law, and shall be deemed sent upon such mailing or electronic transmission.

SIXTH: Subject to any additional vote required by this Certificate of Incorporation or Bylaws, in furtherance and not in limitation of the powers conferred by statute, the Board of Directors is expressly authorized to make, repeal, alter, amend and rescind any or all of the Bylaws of the Corporation.

SEVENTH: Subject to any additional vote required by this Certificate of Incorporation, the number of directors of the Corporation shall be determined in the manner set forth in the Bylaws of the Corporation.

EIGHTH: Elections of directors need not be by written ballot unless the Bylaws of the Corporation shall so provide.

NINTH: Meetings of stockholders may be held within or without the State of Delaware, as the Bylaws of the Corporation may provide. The books of the Corporation may be kept outside the State of Delaware at such place or places as may be designated from time to time by the Board of Directors or in the Bylaws of the Corporation.

TENTH: To the fullest extent permitted by law, a director of the Corporation shall not be personally liable to the Corporation or its stockholders for monetary damages for breach of fiduciary duty as a director. If the General Corporation Law or any other law of the State of Delaware is amended after approval by the stockholders of this Article Tenth to authorize corporate action further eliminating or limiting the personal liability of directors, then the liability of a director of the Corporation shall be eliminated or limited to the fullest extent permitted by the General Corporation Law as so amended.

Any repeal or modification of the foregoing provisions of this Article Tenth by the stockholders of the Corporation shall not adversely affect any right or protection of a director of the Corporation existing at the time of, or increase the liability of any director of the Corporation with respect to any acts or omissions of such director occurring prior to, such repeal or modification.

ELEVENTH: To the fullest extent permitted by applicable law, the Corporation is authorized to provide indemnification of (and advancement of expenses to) directors, officers and agents of the Corporation (and any other persons to which General Corporation Law permits the Corporation to provide indemnification) through Bylaw provisions, agreements with such agents or other persons, vote of stockholders or disinterested directors or otherwise, in excess of the indemnification and advancement otherwise permitted by Section 145 of the General Corporation Law.

Any amendment, repeal or modification of the foregoing provisions of this Article Eleventh shall not adversely affect any right or protection of any director, officer or other agent of the Corporation existing at the time of such amendment, repeal or modification.

TWELFTH: The Corporation renounces, to the fullest extent permitted by law, any interest or expectancy of the Corporation in, or in being offered an opportunity to participate in, any Excluded Opportunity. An "**Excluded Opportunity**" is any matter, transaction or

interest that is presented to, or acquired, created or developed by, or which otherwise comes into the possession of, (i) any director of the Corporation who is not an employee of the Corporation or any of its subsidiaries, or (ii) any holder of Preferred Stock or any partner, member, director, stockholder, employee or agent of any such holder, other than someone who is an employee of the Corporation or any of its subsidiaries (collectively, "**Covered Persons**"), unless such matter, transaction or interest is presented to, or acquired, created or developed by, or otherwise comes into the possession of, a Covered Person expressly and solely in such Covered Person's capacity as a director of the Corporation.

THIRTEENTH: Unless the Corporation consents in writing to the selection of an alternative forum, the Court of Chancery in the State of Delaware shall be the sole and exclusive forum for any stockholder (including a beneficial owner) to bring (i) any derivative action or proceeding brought on behalf of the Corporation, (ii) any action asserting a claim of breach of fiduciary duty owed by any director, officer or other employee of the Corporation to the Corporation or the Corporation's stockholders, (iii) any action asserting a claim against the Corporation, its directors, officers or employees arising pursuant to any provision of the Delaware General Corporation Law or the Corporation's certificate of incorporation or bylaws or (iv) any action asserting a claim against the Corporation, its directors, officers or employees governed by the internal affairs doctrine, except for, as to each of (i) through (iv) above, any claim as to which the Court of Chancery determines that there is an indispensable party not subject to the jurisdiction of the Court of Chancery (and the indispensable party does not consent to the personal jurisdiction of the Court of Chancery within ten days following such determination), which is vested in the exclusive jurisdiction of a court or forum other than the Court of Chancery, or for which the Court of Chancery does not have subject matter jurisdiction. If any provision or provisions of this Article Thirteenth shall be held to be invalid, illegal or unenforceable as applied to any person or entity or circumstance for any reason whatsoever, then, to the fullest extent permitted by law, the validity, legality and enforceability of such provisions in any other circumstance and of the remaining provisions of this Article Thirteenth (including, without limitation, each portion of any sentence of this Article Thirteenth containing any such provision held to be invalid, illegal or unenforceable that is not itself held to be invalid, illegal or unenforceable) and the application of such provision to other persons or entities and circumstances shall not in any way be affected or impaired thereby.

* * *

3. That the foregoing amendment and restatement of the Certificate of Incorporation was approved by the holders of the requisite number of shares of this corporation in accordance with Section 228 of the General Corporation Law.

4. That this Third Amended and Restated Certificate of Incorporation, which restates and integrates and further amends the provisions of this Corporation's Second Amended and Restated Certificate of Incorporation, has been duly adopted in accordance with Sections 242 and 245 of the General Corporation Law.

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IN WITNESS WHEREOF, this Third Amended and Restated Certificate of Incorporation has been executed by a duly authorized officer of this corporation on this 21st day of August, 2017.

By: /s/ Keith Gottesdiener
Keith Gottesdiener, Chief Executive Officer

BYLAWS

OF

RHYTHM METABOLIC, INC.

ARTICLE I

STOCKHOLDERS

SECTION 1. Place of Meetings. All meetings of stockholders shall be held at the principal office of the corporation or at such other place as may be named in the notice. Notwithstanding the foregoing, the Board of Directors may, in its sole discretion, determine that the meeting shall not be held at any place, but shall be held solely by means of remote communication, subject to such guidelines and procedures as the Board of Directors may adopt, as permitted by applicable law.

SECTION 2. Annual Meeting. The annual meeting of stockholders for the election of directors and the transaction of such other business as may properly come before the meeting shall be held on such date and at such hour and place as the Board of Directors or an officer designated by the Board of Directors may determine. If the annual meeting is not held on the date designated therefor, the Board of Directors shall cause the meeting to be held as soon thereafter as convenient.

SECTION 3. Remote Communication. For the purposes of these bylaws, if authorized by the Board of Directors in its sole discretion, and subject to such guidelines and procedures as the Board of Directors may adopt, stockholders and proxyholders not physically present at a meeting of the stockholders may, by means of remote communication, participate in a meeting of stockholders and be deemed present in person and vote at a meeting of stockholders whether such meeting is to be held at a designated place or solely by means of remote communication, provided that (i) the corporation shall implement reasonable measures to verify that each person deemed present and permitted to vote at the meeting by means of remote communication is a stockholder or proxyholder, (ii) the corporation shall implement reasonable measures to provide such stockholders and proxyholders a reasonable opportunity to participate in the meeting and to vote on matters submitted to the stockholders, including an opportunity to read or hear the proceedings of the meeting substantially concurrently with such proceedings, and (iii) if any stockholder or proxyholder votes or takes other action at the meeting by means of remote communication, a record of such vote or other action shall be maintained by the corporation.

SECTION 4. Special Meetings. Special meetings of the stockholders may be called at any time by the President or a majority of the Board of Directors. A special meeting of stockholders shall be called by the Secretary, upon written request of stockholders who together own of record a majority of the outstanding shares of each class of stock entitled to vote at such meeting.

SECTION 5. Notice of Meetings. Except where some other notice is required by law, notices of meetings of the stockholders shall state the place, if any, date and hour of the meeting, the means of remote communications, if any, by which stockholders and proxyholders may be deemed to be present in person and vote at such meetings and the purposes for which the meeting is called, shall be given by the Secretary under the direction of the Board of Directors or the President, not less than ten nor more than sixty days before the date fixed for such meeting, to each stockholder of record entitled to vote at such meeting. If the Board of Directors has chosen to make a list of stockholders available on an electronic network, the notice shall provide the information required to gain access to such list. Notice to stockholders may be given in writing or by electronic transmission as permitted pursuant to this Section 5. If given in writing, notice shall be given personally to each stockholder or left at such stockholder's residence or usual place of business or mailed postage prepaid and addressed to the stockholder at such stockholder's address as it appears upon the records of the corporation. In case of the death, absence, incapacity or refusal of the Secretary, such notice may be given by a person designated either by the President or the Board of Directors. Only such business shall be conducted at a special meeting of stockholders as shall have been brought before the meeting pursuant to the corporation's notice of meeting. Notice of any meeting of stockholders need not be given to any stockholder who has waived such notice in writing or by electronic transmission, whether before or after the time such meeting is held. Attendance of a person at a meeting of stockholders shall constitute a waiver of notice of such meeting, except when the stockholder attends a meeting for the express purpose of objecting, at the beginning of the meeting, to the transaction of any business because the meeting is not lawfully called or convened. Neither the business to be transacted at, nor the purpose of, any regular or special meeting of the stockholders need be specified in any written or electronically transmitted waiver of notice. Except as required by statute, notice of any adjourned meeting of the stockholders shall not be required.

Any notice to stockholders given by the corporation shall be effective if given by a form of electronic transmission consented to by the stockholder to whom the notice is given to the extent permitted by applicable law. Any such consent shall be revocable by the stockholder by written notice to the corporation and shall also be deemed revoked if (1) the corporation is unable to deliver by electronic transmission two consecutive notices given by the corporation in accordance with such consent and (2) such inability becomes known to the Secretary or Assistant Secretary of the corporation or to the transfer agent or other person responsible for the giving of notice; provided, however, the inadvertent failure to treat such inability as a revocation shall not invalidate any meeting or other action. Notice given pursuant to this Section shall be deemed given: (1) if by facsimile telecommunication, when directed to a number at which the stockholder has consented to receive notice; (2) if by electronic mail, when directed to an electronic mail address at which the stockholder has consented to receive notice; (3) if by posting on an electronic network together with separate notice to the stockholder of such specific posting, upon the later of (A) such posting and (B) the giving of such separate notice; and (4) if by any other form of electronic transmission consented to by the stockholder, when directed to the stockholder in accordance with such consent. An affidavit of the secretary or an assistant secretary or of the transfer agent or other agent of the corporation that the notice has been given by a form of electronic transmission shall, in the absence of fraud, be prima facie evidence of the facts stated therein.

For purposes of these bylaws, “electronic transmission” means any form of communication, not directly involving the physical transmission of paper, that creates a record that may be retained, retrieved and reviewed by a recipient thereof, and that may be directly reproduced in paper form by such a recipient through an automated process.

SECTION 6. Record Date. The Board of Directors may fix in advance a record date for the determination of the stockholders entitled to notice of or to vote at any meeting of stockholders, or entitled to consent to corporation action in writing without a meeting, or entitled to receive payment of any dividend or other distribution or allotment of any rights, or entitled to exercise any rights in respect of any change, conversion or exchange of stock, or for the purpose of any other lawful action. Such record date shall not be earlier than the date upon which the resolution fixing the record date is adopted by the Board of Directors and shall not be more than 60 nor less than 10 days before the date of such meeting, nor more than 60 days before any other action to which such record date relates. If no record date is fixed, the record date for determining stockholders entitled to notice of or to vote at a meeting of stockholders shall be at the close of business on the day preceding the day on which notice is given, or, if notice is waived, at the close of business on the day preceding the day on which the meeting is held. The record date for determining stockholders for any purpose other than those set forth in this section shall be at the close of business on the day on which the Board of Directors adopts the resolution relating to such purpose. A determination of stockholders of record entitled to notice of or to vote at a meeting of stockholders shall apply to any adjournment of the meeting; provided, however, that the Board of Directors may fix a new record date for the adjourned meeting.

SECTION 7. Voting List. The officer who has charge of the stock ledger of the corporation shall make or have made, at least 10 days before every meeting of stockholders, a complete list of the stockholders entitled to vote at the meeting, arranged in alphabetical order and showing the address of each stockholder and the number of shares registered in the name of each stockholder. Such list shall be open to the examination of any stockholder for any purpose germane to the meeting, during ordinary business hours, for a period of at least 10 days before the meeting either on a reasonably accessible electronic network or during ordinary business hours at the principal place of business of the corporation. The list shall also be produced and kept at the time and place of the meeting during the whole time thereof, and may be inspected by any stockholder who is present. The stock ledger shall be the only evidence as to who are the stockholders entitled to examine the stock ledger, the list required by this section or the books of the corporation, or to vote at any meeting of stockholders.

SECTION 8. Quorum of Stockholders. Unless otherwise provided in the Certificate of Incorporation, at any meeting of the stockholders, the holders of a majority of the voting power of the outstanding shares of capital stock of the corporation entitled to vote generally in the election of directors present in person or represented by proxy, shall constitute a quorum for the consideration of any question, but in the absence of a quorum a smaller group may adjourn any meeting from time to time. When a quorum is present at any meeting, a majority of the votes properly cast shall, except where a different vote is required by law, by the Certificate of Incorporation or by these bylaws, decide any question brought before such meeting. Any election by stockholders shall be determined by a plurality of the vote cast by the stockholders entitled to vote at the election. The stockholders present at a duly organized meeting may

continue to transact business until adjournment, notwithstanding the withdrawal of enough stockholders to leave less than a quorum.

SECTION 9. Proxies and Voting. Unless otherwise provided in the Certificate of Incorporation, each stockholder entitled to vote at a meeting of stockholders may authorize another person or persons to act for such stockholder by proxy, but no such proxy shall be voted or acted upon after three years from its date, unless the proxy provides for a longer period. Shares of the capital stock of the corporation belonging to the corporation or to another corporation, a majority of whose shares entitled to vote in the election of directors is owned by the corporation, shall neither be entitled to vote nor be counted for quorum purposes.

SECTION 10. Conduct of Meeting. Meetings of the stockholders shall be presided over by the Chairman of the Board, if any, or in the absence of the Chairman of the Board by the Vice Chairman of the Board, if any, or in the absence of the Vice Chairman of the Board by the President, or in the absence of the President by a Vice-President, or in the absence of the foregoing persons by a chairman designated by the Board of Directors, or in the absence of such designation by a chairman chosen at the meeting. The Secretary, or in the absence of the Secretary an Assistant Secretary, shall act as secretary of the meeting, but in the absence of the Secretary and any Assistant Secretary the chairman of the meeting may appoint any person to act as secretary of the meeting.

The Board of Directors may adopt such rules, regulations and procedures for the conduct of the meeting of stockholders as it shall deem appropriate. Except to the extent inconsistent with such rules and regulations as adopted by the Board of Directors, the chairman of the meeting shall have the right and authority to prescribe such rules, regulations and procedures and to do all such acts as, in the judgment of such chairman, are appropriate for the proper conduct of the meeting. Such rules, regulations or procedures, whether adopted by the Board of Directors or prescribed by the chairman of the meeting, may include, without limitation, (i) the establishment of an agenda or order of business for the meeting, (ii) rules and procedures for maintaining order at the meeting and the safety of those present, (iii) limitations on attendance at or participation in the meeting to stockholders of record of the corporation, their duly authorized and constituted proxies or such other persons as the chairman of the meeting shall determine, (iv) restrictions on entry to the meeting after the time fixed for the commencement thereof, and (v) limitations on the time allotted to questions or comments by participants. Unless and to the extent determined by the Board of Directors or the chairman of the meeting, meetings of stockholders shall not be required to be held in accordance with the rules of parliamentary procedure.

SECTION 11. Action Without Meeting. Any action required or permitted to be taken at any annual or special meeting of stockholders of the corporation may be taken without a meeting, without prior notice and without a vote, if a consent in writing, setting forth the action so taken, is signed by the holders or by proxy for the holders of outstanding stock having not less than the minimum number of votes that would be necessary to authorize or take such action at a meeting at which all shares entitled to vote on such action were present and voted. Prompt notice of the taking of corporate action without a meeting by less than unanimous written consent shall be given to those stockholders who have not consented in writing.

ARTICLE II

DIRECTORS

SECTION 1. General Powers. The business and affairs of the corporation shall be managed by or under the direction of a Board of Directors, who may exercise all of the powers of the corporation that are not by law required to be exercised by the stockholders. In the event of a vacancy on the Board of Directors, the remaining directors, except as otherwise provided by law or the Certificate of Incorporation, may exercise the powers of the full Board until the vacancy is filled.

SECTION 2. Election. Subject to the provisions of the Certificate of Incorporation, the holders of record of the capital stock of the corporation, voting as a single class, shall be entitled to elect the directors of the Corporation.

SECTION 3. Vacancies. Any vacancy in the Board of Directors, however occurring, including a vacancy resulting from an enlargement of the Board or from the removal of any director, may be filled by vote of a majority of the directors then in office although less than a quorum, or by the sole remaining director. Each director so chosen to fill a vacancy shall serve for a term determined in the manner provided in the Certificate of Incorporation and the General Corporation Law of the State of Delaware. When one or more directors shall resign from the Board, effective at a future date, a majority of the directors then in office, including those who have so resigned, shall have the power to fill such vacancy or vacancies, the vote thereon to take effect when such resignation or resignations shall become effective. If at any time there are no directors in office, then an election of directors may be held in accordance with the General Corporation Law of the State of Delaware.

SECTION 4. Resignation. Any director may resign at any time by giving notice to the corporation in writing or by electronic transmission. Such resignation shall take effect at the time specified therein, or if no time is specified, at the time of its receipt by the Chairman of the Board, if any, the President or the Secretary.

SECTION 5. Removal. Subject to the provisions of the Certificate of Incorporation, directors may be removed from office only by the holders of record of the capital stock of the corporation, voting as a single class.

SECTION 6. Committees. The Board of Directors may, by resolution or resolutions passed by a majority of the whole Board of Directors, designate one or more committees, each committee to consist of one or more directors of the corporation. The Board of Directors may designate one or more directors as alternate members of any committee to replace any absent or disqualified member at any meeting of the committee. In the absence or disqualification of any member of any such committee, the member or members thereof present at any meeting and not disqualified from voting, whether or not such member or members constitute a quorum, may unanimously appoint another member of the Board of Directors to act at the meeting in the place of such absent or disqualified member. The Board of Directors shall have the power to change the members of any such committee at any time, to fill vacancies therein and to discharge any such committee, either with or without cause, at any time.

Any such committee, to the extent permitted by law and to the extent provided in a resolution of the Board of Directors or in these bylaws, shall have and may exercise all the powers and authority of the Board of Directors in the management of the business and affairs of the corporation, and may authorize the seal of the corporation to be affixed to all papers that may require it.

A majority of all the members of any such committee may fix its rules of procedure, determine its actions and fix the time and place, whether within or without the State of Delaware, of its meetings and specify what notice thereof, if any, shall be given, unless the Board of Directors shall otherwise by resolution provide. Each committee shall keep regular minutes of its meetings and make such reports as the Board of Directors may from time to time request.

SECTION 7. Meetings of the Board of Directors. Regular meetings of the Board of Directors may be held without call or formal notice at such places either within or without the State of Delaware and at such times as the Board may by vote from time to time determine. A regular meeting of the Board of Directors may be held without call or formal notice immediately after and at the same place as the annual meeting of the stockholders, or any special meeting of the stockholders at which a Board of Directors is elected.

Special meetings of the Board of Directors may be held at any place either within or without the State of Delaware at any time when called by the Chairman of the Board, if any, the President, the Secretary or two or more directors. Reasonable notice of the time and place of a special meeting shall be given to each director unless such notice is waived by attendance or by waiver in the manner provided in these bylaws for waiver of notice by stockholders. Notice may be given by, or by a person designated by, the Secretary, the person or persons calling the meeting, or the Board of Directors. No notice of any adjourned meeting of the Board of Directors shall be required. In any case it shall be deemed sufficient notice to a director to send notice by mail at least seventy-two hours, by telegram or fax at least forty-eight hours before the meeting, addressed to such director at his or her usual or last known business or home address, by electronic mail at least twenty-four hours before the meeting, when directed to his or her usual or last known electronic mail address, or by any other form of electronic transmission to which such director has consented, when directed to the director consistent therewith.

Directors or members of any committee may participate in a meeting of the Board of Directors or of such committee by means of conference telephone or similar communications equipment by means of which all persons participating in the meeting can hear each other, and participation by such means shall constitute presence in person at such meeting.

SECTION 8. Quorum and Voting. A majority of the total number of directors shall constitute a quorum, except that when a vacancy or vacancies exist in the Board, a majority of the directors then in office (but not less than one-third of the total number of the directors) shall constitute a quorum. A majority of the directors present, whether or not a quorum is present, may adjourn any meeting from time to time. If, at any meeting, a quorum is not present for any reason, then another Board meeting may be convened within not less than two (2) and not more than ten (10) business days after such meeting and, at such other meeting, a majority of all directors shall constitute a quorum for all purposes. The vote of a majority of the directors present at any meeting at which a quorum is present shall be the act of the Board of Directors,

except where a different vote is required by law, by the Certificate of Incorporation or by these bylaws.

SECTION 9. Compensation. The Board of Directors may fix fees for their services and for their membership on committees, and expenses of attendance may be allowed for attendance at each meeting. Nothing herein contained shall be construed to preclude any director from serving the corporation

in any other capacity, as an officer, agent or otherwise, and receiving compensation therefor.

SECTION 10. Action Without Meeting. Any action required or permitted to be taken at any meeting of the Board of Directors or of any committee thereof may be taken without a meeting and without notice if all members of the Board of Directors or of such committee, as the case may be, consent thereto in writing (which may be in counterparts) or by electronic transmission, and the writing or writings or electronic transmission or electronic transmissions are filed with the minutes of proceedings of the Board of Directors or of such committee. Such filings shall be in paper form if the minutes are maintained in paper form and shall be in electronic form if the minutes are maintained in electronic form.

ARTICLE III

OFFICERS

SECTION 1. Titles. The officers of the corporation shall consist of a President, a Secretary, a Treasurer and such other officers with such other titles as the Board of Directors shall determine, who may include without limitation a Chairman of the Board, a Vice-Chairman of the Board and one or more Vice-Presidents, Assistant Treasurers or Assistant Secretaries.

SECTION 2. Election and Term of Office. The officers of the corporation shall be elected from time to time by the Board of Directors to hold office until his or her successor is elected and qualified, unless a different term is specified in the vote electing such officer, or until his or her earlier death, resignation or removal.

SECTION 3. Qualification. Unless otherwise provided by resolution of the Board of Directors, no officer, other than the Chairman or Vice-Chairman of the Board, need be a director. No officer need be a stockholder. Any number of offices may be held by the same person, as the Board of Directors shall determine.

SECTION 4. Removal. Any officer may be removed, with or without cause, at any time, by resolution adopted by the Board of Directors.

SECTION 5. Resignation. Any officer may resign by delivering a written notice to the corporation at its principal office or to the Chairman of the Board, if any, the President or the Secretary. Such resignation shall take effect at the time specified therein, or if no time is specified, at the time of its receipt by the Chairman of the Board, if any, the President or the Secretary.

SECTION 6. Vacancies. The Board of Directors, the Chairman of the Board, if any, or the President may at any time fill any vacancy occurring in any office for the unexpired portion

of the term or may leave unfilled any office other than those of President, Treasurer and Secretary.

SECTION 7. Powers and Duties. The officers of the corporation shall have such powers and perform such duties as are specified herein and as may be conferred upon or assigned to them by the Board of Directors, or, in the case of any officer other than the President, the President, and shall have such additional powers and duties as are incident to their office except to the extent that resolutions of the Board of Directors are inconsistent therewith.

SECTION 8. President and Vice-Presidents. Except to the extent that such duties are assigned by the Board of Directors to the Chairman of the Board, or in the absence of the Chairman or in the event of his or her inability or refusal to act, the President shall be the chief executive officer of the corporation and shall have general and active management of the business of the corporation and general supervision of its officers, agents and employees, and shall see that all orders and resolutions of the Board of Directors are carried into effect. The President shall preside at each meeting of the stockholders and the Board of Directors unless a Chairman or Vice-Chairman of the Board is elected by the Board and is assigned the duty of presiding at such meetings.

The Board of Directors may assign to any Vice-President the title of Executive Vice-President, Senior Vice-President or any other title selected by the Board of Directors. In the absence of the President or in the event of his or her inability or refusal to act, the duties of the President shall be performed by the Executive Vice President, if any, Senior Vice President, if any, or Vice President, if any, in that order (and, in the event there be more than one person in any such office, in the order of their length of time spent in such office), and when so acting, such officer shall have all the powers of and be subject to all the restrictions upon the President.

SECTION 9. Secretary and Assistant Secretaries. The Secretary shall attend all meetings of the Board of Directors and of the stockholders and record all the proceedings of such meetings in a book to be kept for that purpose, shall give, or cause to be given, notice of all meetings of the stockholders and special meetings of the Board of Directors, shall maintain a stock ledger and prepare lists of stockholders and their addresses as required and shall have custody of the corporate seal, which the Secretary or any Assistant Secretary shall have authority to affix to any instrument requiring it and attest by any of their signatures. The Board of Directors may give general authority to any other officer to affix and attest the seal of the corporation.

Any Assistant Secretary, or any other officer, employee or agent designated by the Board of Directors, the Chairman of the Board or the President, may, in the absence of the Secretary or in the event of the Secretary's inability or refusal to act, perform the duties and exercise the powers of the Secretary.

SECTION 10. Treasurer and Assistant Treasurers. The Treasurer shall have the custody of the corporate funds and securities, shall keep full and accurate accounts of receipts and disbursements in books belonging to the corporation and shall deposit all moneys and other valuable effects in the name and to the credit of the corporation in such depositories as may be designated by or pursuant to resolution of the Board of Directors. The Treasurer shall disburse

the funds of the corporation as may be ordered by the Board of Directors, the Chairman of the Board, if any, or the President, taking proper vouchers for such disbursements, and shall render to the Chairman of the Board, if any, the President and the Board of Directors, at its regular meetings or whenever they may require it, an account of all transactions and of the financial condition of the corporation.

Any Assistant Treasurer, or any other officer, employee or agent designated by the Board of Directors, the Chairman of the Board or the President, may, in the absence of the Treasurer or in the event of his or her inability or refusal to act, perform the duties and exercise the powers of the Treasurer.

SECTION 11. Bonded Officers. The Board of Directors may require any officer to give the corporation a bond in such sum and with such surety or sureties as shall be satisfactory to the Board of Directors upon such terms and conditions as the Board of Directors may specify, including without limitation a bond for the faithful performance of the duties of such officer and for the restoration to the corporation of all property in his or her possession or control belonging to the corporation.

ARTICLE IV

STOCK

SECTION 1. Certificates of Stock. Unless otherwise provided by the Board of Directors, the shares of the corporation shall be represented by certificates. One or more stock certificates, signed by (i) the Chairman or Vice-Chairman of the Board of Directors or the President or a Vice-President and (ii) the Treasurer or an Assistant Treasurer or the Secretary or an Assistant Secretary, shall be issued to each stockholder certifying the number of shares owned by the stockholder in the corporation. Any or all signatures on any such certificate may be facsimiles. In case any officer, transfer agent or registrar who shall have signed or whose facsimile signature shall have been placed upon a certificate shall have ceased to be such officer, transfer agent or registrar before such certificate is issued, it may be issued by the corporation with the same effect as if such person or entity were such officer, transfer agent or registrar at the date of issue.

Each certificate for shares of stock that are subject to any restriction on transfer pursuant to the Certificate of Incorporation, these bylaws, applicable securities laws, or any agreement among any number of stockholders or among such holders and the corporation shall have conspicuously noted on the face or back of the certificate either the full text of the restriction or a statement of the existence of such restriction. If the corporation is authorized to issue more than one class or series of stock, each certificate for shares of stock shall have conspicuously noted on the face or back of the certificate a statement that the corporation will furnish without additional charge to each stockholder who so requests the powers, designations, preferences and relative, participating, optional, or other special rights of each class of stock or series thereof and the qualifications, limitations or restrictions of such preferences and/or rights.

SECTION 2. Transfers of Shares of Stock. Subject to the restrictions, if any, stated or noted on a stock certificate, shares of stock represented by a certificate may be transferred on the

books of the corporation by the surrender to the corporation or its transfer agent of the certificate representing such shares properly endorsed or accompanied by a written assignment or power of attorney properly executed, and with such proof of authority or the authenticity of signature as the corporation or its transfer agent may reasonably require. The corporation shall be entitled to treat the record holder of stock as shown on its books as the owner of such stock for all purposes, including the payment of dividends and the right to vote with respect to that stock, regardless of any transfer, pledge or other disposition of that stock, until the shares have been transferred on the books of the corporation in accordance with the requirements of these bylaws.

SECTION 3. Lost Certificates. A new stock certificate may be issued in the place of any certificate theretofore issued by the corporation and alleged to have been lost, stolen or destroyed, upon such terms in conformity with law as the Board of Directors shall prescribe. The Board of Directors may, in their discretion, require the owner of the lost, stolen or destroyed certificate, or the owner's legal representatives, to give the corporation a bond, in such sum as they may direct, to indemnify the corporation against any claim that may be made against it on account of the alleged loss, theft or destruction of any such certificate, or the issuance of any such new certificate.

SECTION 4. Fractional Share Interests. The corporation may, but shall not be required to, issue fractions of a share. If the corporation does not issue fractions of a share, it shall (i) arrange for the disposition of fractional interests by those entitled thereto, (ii) pay in cash the fair value of fractions of a share as of the time when those entitled to receive such fractions are determined, or (iii) issue scrip or warrants in registered or bearer form, which shall entitle the holder to receive a certificate for a full share upon the surrender of such scrip or warrants aggregating a full share. A certificate for a fractional share shall, but scrip or warrants shall not unless otherwise provided therein, entitle the holder to exercise voting rights, to receive dividends thereon, and to participate in any of the assets of the corporation in the event of liquidation. The Board of Directors may cause scrip or warrants to be issued subject to the conditions that they shall become void if not exchanged for certificates representing full shares before a specified date, or subject to the conditions that the shares for which scrip or warrants are exchangeable may be sold by the corporation and the proceeds thereof distributed to the holders of scrip or warrants, or subject to any other conditions that the Board of Directors may impose.

SECTION 5. Dividends. Subject to the provisions of the Certificate of Incorporation, the Board of Directors may, out of funds legally available therefor declare and pay dividends upon the capital stock of the corporation as and when they deem expedient.

ARTICLE V

INDEMNIFICATION OF DIRECTORS AND OFFICERS

The corporation shall indemnify, to the extent permitted by applicable law, any person made, or threatened to be made, a party to any action, suit or proceeding, whether civil, criminal, administrative or investigative, by reason of the fact that such person is or was a director or officer of the corporation or serves or served at the request of the corporation as a director or officer of any other enterprise or in a comparable role at such enterprise. Expenses (including attorneys' fees), judgments, fines and amounts paid in settlement, actually and reasonably

incurred by any such person in connection with any such action, suit or proceeding shall be paid or reimbursed by the corporation promptly upon receipt by it of an undertaking of such person to repay such amounts if it shall ultimately be determined that such person is not entitled to be indemnified by the corporation. The rights provided to any person by this bylaw shall be enforceable against the corporation by such person, who shall be presumed to have relied upon it in serving or continuing to serve as a director or officer, and by such person's heirs and legal representations. No amendment, termination or

repeal of this bylaw shall impair the rights of any person arising at any time with respect to actions, transactions or events occurring, or circumstances existing, before such amendment, termination or repeal. For purposes of this bylaw, the term “corporation” shall include any predecessor of the corporation and any constituent corporation (including any constituent of a constituent) absorbed by the corporation in a consolidation or merger; the term “other enterprise” shall include employee benefit plans; the term “fines” shall include any excise taxes assessed on a person with respect to any employee benefit plan; service “at the request of the corporation” shall include service as a director or officer of the corporation which imposes duties on, or involves services by, such director or officer with respect to an employee benefit plan, its participants or beneficiaries; and action by a person with respect to an employee benefit plan which such person reasonably believes to be in the interest of the participants and beneficiaries of such plan shall be deemed to be action not opposed to the best interests of the corporation.

ARTICLE VI

GENERAL PROVISIONS

SECTION 1. Fiscal Year. Except as otherwise designated from time to time by the Board of Directors, the fiscal year of the corporation shall begin on the first day of January and end on the last day of December.

SECTION 2. Corporate Seal. The corporate seal shall be in such form as shall be approved by the Board of Directors. The Secretary shall be the custodian of the seal, and a duplicate seal may be kept and used by each Assistant Secretary and by any other officer the Board of Directors may authorize.

SECTION 3. Certificate of Incorporation. All references in these bylaws to the Certificate of Incorporation shall be deemed to refer to the Certificate of Incorporation of the corporation, as in effect from time to time.

SECTION 4. Execution of Instruments. The President, the Treasurer and the Secretary shall have power to execute and deliver on behalf and in the name of the corporation any instrument requiring the signature of an officer of the corporation, including deeds, contracts, mortgages, bonds, notes, debentures, checks, drafts and other orders for the payment of money. In addition, the Board of Directors, the President, the Treasurer and the Secretary may expressly delegate such powers to any other officer or agent of the corporation.

SECTION 5. Voting of Securities. The President, the Treasurer and the Secretary, and each other person authorized by the Board of Directors, each acting singly, may waive notice of, and act as, or appoint any person or persons to act as, proxy or attorney-in-fact for this

corporation (with or without power of substitution) at any meeting of stockholders or owners of other interests of any other corporation or organization the securities of which may be held by this corporation. In addition, the Board of Directors, the President and the Treasurer may expressly delegate such powers to any other officer or agent of the corporation.

SECTION 6. Evidence of Authority. A certificate by the Secretary, an Assistant Secretary or a temporary secretary as to any action taken by the stockholders, directors, a committee or any officer or representative of the corporation shall, as to all persons who rely on the certificate in good faith, be conclusive evidence of that action.

SECTION 7. Books and Records. The books and records of the corporation shall be kept at such places within or without the State of Delaware as the Board of Directors may from time to time determine.

SECTION 8. Amendments. Subject to any vote of the holders of any class or series of capital stock of the corporation required by the Delaware General Corporation Law or by the Certificate of Incorporation, the Board of Directors is expressly empowered to adopt, amend or repeal the bylaws of the corporation.

Adopted by the Incorporator of the Corporation on February 26, 2013.

Exhibit 4.2

RHYTHM PHARMACEUTICALS, INC.

AMENDED AND RESTATED INVESTORS' RIGHTS AGREEMENT

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Schedule A - Schedule of Initial Investors

AMENDED AND RESTATED INVESTORS' RIGHTS AGREEMENT

THIS AMENDED AND RESTATED INVESTORS' RIGHTS AGREEMENT (this "**Agreement**") is made as of the 21st day of August, 2017, by and among (i) Rhythm Pharmaceuticals, Inc. (formerly known as Rhythm Metabolic, Inc.), a Delaware corporation (the "**Company**"), (ii) each of the persons listed on Schedule A hereto (the "**Initial Investors**"), and (iii) each person who hereafter becomes a party to this Agreement in accordance with Subsection 6.1 or Subsection 6.9 hereof.

RECITALS

WHEREAS, the Initial Investors, including, without limitation, Rhythm Holding Company LLC, a Delaware limited liability company and majority stockholder of the Company ("**Parent**"), are parties to that certain Investors' Rights Agreement, dated as of August 3, 2015 (the "**Prior Agreement**"); and

WHEREAS, Parent holds 93,500,000 shares of Common Stock of the Company and all of such 93,500,000 shares of Common Stock are held by Parent subject to the provisions of the Prior Agreement in Parent's capacity as an Investor (as such term is defined in the Prior Agreement) thereunder; and

WHEREAS, simultaneously with the execution of this Agreement, the Company and Parent are entering into an Exchange Agreement, dated of even date herewith (as amended and in effect from time to time, the "**Exchange Agreement**"), whereby Parent will transfer, assign and surrender to the Company 78,666,209 shares of Common Stock owned by Parent in exchange for 78,666,209 shares of Series A-1 Junior Preferred Stock (as defined in Section 1 below) issued by the Company to Parent (the "**Exchange**"); and

WHEREAS, the Initial Investors, including, without limitation, Parent, desire to amend and restate the Prior Agreement for purposes of, among other things, providing that all 78,666,209 shares of Series A-1 Junior Preferred Stock and all 14,833,791 shares of Common Stock (as defined in Section 1 below) owned by Parent immediately after the Exchange shall be held by Parent subject to the provisions of this Agreement in Parent's capacity as an Investor hereunder; and

WHEREAS, concurrently with or as promptly as practicable following the consummation of the Exchange and the execution of this Agreement, Parent intends to effect a distribution (the "**Distribution**") of all of the shares of capital stock of the Company owned by Parent to its Members (as such term is defined in the Rhythm Holding Company, LLC Third Amended and Restated Operating Agreement, dated as of August 21, 2017, as amended and in effect from time to time); and

WHEREAS, the Initial Investors, including, without limitation, Parent, represent at least the required number of holders of capital stock of the Company necessary to amend the Prior Agreement, and desire to amend and restate the Prior Agreement in its entirety and to accept the rights created pursuant to this Agreement in lieu of the rights granted to them under the Prior Agreement; and

WHEREAS, the Initial Investors, including, without limitation, Parent, hereby agree that this Agreement shall govern the rights of the Investors to cause the Company to register shares of Common Stock issuable to, or owned by, the Investors, to receive certain information from the Company, and to participate in future equity offerings by the Company, and shall govern certain other matters as set forth in this Agreement.

NOW, THEREFORE, in consideration of mutual covenants set forth herein and other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, the parties hereby agree as follows:

1. Definitions. For purposes of this Agreement:

1.1 "**Affiliate**" means, with respect to any specified Person, any other Person who, directly or indirectly, controls, is controlled by, or is under common control with such Person, including without limitation any general partner, managing member, officer **or** director of such Person or any venture capital or other investment fund now or hereafter existing that is controlled by one or more general partners or managing members of, or shares the same management company or investment advisor with, such Person, and, if the Person referred to is a natural Person, any Immediate Family Member of such Person or any trust for the benefit of such Person or for the benefit of such one or more of such Peron's Immedate Family Members, and, if the Person is a trust, to its beneficiaries.

1.2 "**Common Stock**" means shares of the Company's common stock, par value $0.001 per share.

1.3 "**Damages**" means any loss, damage, claim or liability (joint or several) to which a party hereto may become subject under the Securities Act, the Exchange Act, or other federal or state law, insofar as such loss, damage, claim or liability (or any action in respect thereof) arises out of or is based upon: (i) any untrue statement or alleged untrue statement of a material fact contained in any registration statement of the Company, including any preliminary prospectus or final prospectus contained therein or any amendments or supplements thereto; (ii) an omission or alleged omission to state therein a

material fact required to be stated therein, or necessary to make the statements therein not misleading; or (iii) any violation or alleged violation by the indemnifying party (or any of its agents or Affiliates) of the Securities Act, the Exchange Act, any state securities law, or any rule or regulation promulgated under the Securities Act, the Exchange Act, or any state securities law.

1.4 "**Derivative Securities**" means any securities or rights convertible into, or exercisable or exchangeable for (in each case, directly or indirectly), Common Stock, including options and warrants.

1.5 "**Exchange Act**" means the Securities Exchange Act of 1934, as amended, and the rules and regulations promulgated thereunder.

1.6 "**Excluded Registration**" means (i) a registration relating to the sale of securities to employees of the Company or a subsidiary pursuant to a stock option, stock purchase, or similar plan; (ii) a registration relating to an SEC Rule 145 transaction; (iii) a registration on any form that does not include substantially the same information as would be

required to be included in a registration statement covering the sale of the Registrable Securities; or (iv) a registration in which the only Common Stock being registered is Common Stock issuable upon conversion of debt securities that are also being registered.

1.7 "**Form S-1**" means such form under the Securities Act as in effect on the date hereof or any successor registration form under the Securities Act subsequently adopted by the SEC.

1.8 "**Form S-3**" means such form under the Securities Act as in effect on the date hereof or any registration form under the Securities Act subsequently adopted by the SEC that permits incorporation of substantial information by reference to other documents filed by the Company with the SEC.

1.9 "**GAAP**" means generally accepted accounting principles in the United States.

1.10 "**Holder**" means any holder of Registrable Securities who is a party to this Agreement.

1.11 "**Immediate Family Member**" means a child, stepchild, grandchild, parent, stepparent, grandparent, spouse, sibling, mother-in-law, father-in-law, son-in-law, daughter-in-law, brother-in-law, or sister-in-law, including, adoptive relationships, of a natural person referred to herein.

1.12 "**Initiating Holders**" means, collectively, Holders who properly initiate a registration request under this Agreement.

1.13 "**Investment Securities**" means (1) shares of Preferred Stock, (2) shares of Common Stock issued or issuable upon conversion of any shares of Preferred Stock and (3) shares of Common Stock acquired by any Investor at any time and from time to time after the date of this Agreement upon the exercise by such Investor of its rights of first refusal under the Rights of First Refusal and Co-Sale Agreement.

1.14 "**Investor Directors**" shall have the meaning ascribed to such term in the Restated Certificate.

1.15 "**Investors**" shall mean, collectively, (i) the Initial Investors, (ii) each person who hereafter becomes a party to this Agreement pursuant to Subsection 6.1 hereof and (iii) each person who hereafter becomes a party to this Agreement pursuant to Subsection 6.9 hereof. Notwithstanding the foregoing, a person shall cease being an Investor for all purposes of this Agreement if and when such person no longer owns or holds any Registrable Securities.

1.16 "**IPO**" means the Company's first underwritten public offering of its Common Stock under the Securities Act.

1.17 "**New Securities**" means, collectively, equity securities of the Company, whether or not currently authorized, as well as rights, options, or warrants to purchase such

equity securities, or securities of any type whatsoever that are, or may become, convertible or exchangeable into or exercisable for such equity securities.

1.18 "**Person**" means any individual, corporation, association, general partnership, limited partnership, joint venture, trust, estate, limited liability company, limited liability partnership, unincorporated organization, government (or any agency or political subdivision thereof) or other legal entity or organization.

1.19 "**Pfizer**" means Pfizer Inc.

1.20 "**Preferred Stock**" means, as the context may require or permit, any or all of (i) the Series A Preferred Stock and (ii) the Series A-1 Junior Preferred Stock**.**

1.21 "**Registrable Securities**" means (i) the Common Stock issuable or issued upon conversion of any series of Preferred Stock; (ii) any Common Stock held by the Investors as of the date of this Agreement or acquired by the Investors at any time and from time to time after the date of this Agreement; (iii) any Common Stock issued or issuable (directly or indirectly) upon conversion and/or exercise of any other securities of the Company held by the Investors as of the date of this Agreement or acquired by the Investors at any time and from time to time after the date of this Agreement; and (iv) any Common Stock issued as (or issuable upon the conversion or exercise of any warrant, right, or other security that is issued as) a dividend or other distribution with respect to, or in exchange for or in replacement of, the securities referenced in clauses (i), (ii) and (iii) above; excluding in all cases, however, (x) any Registrable Securities sold by a Person in a transaction in which the applicable rights under this Agreement are not assigned pursuant to Subsection 6.1, and (y) in the case of any Service Provider Investor, any and all shares of Common Stock held or that may be acquired by any such Service Provider Investor at any time and from time to time after the date of this Agreement, except if and to the extent that such shares of Common Stock are

Investment Securities (which Investment Securities shall be Registrable Securities); and excluding for purposes of Section 2 any shares for which registration rights have terminated pursuant to Subsection 2.13 of this Agreement.

1.22 "**Registrable Securities then outstanding**" means the number of shares determined by adding the number of shares of outstanding Common Stock that are Registrable Securities and the number of shares of Common Stock issuable (directly or indirectly) pursuant to then exercisable and/or convertible securities that are Registrable Securities.

1.23 "**Restated Certificate**" means the Company's Third Amended and Restated Certificate of Incorporation, as may be further amended, restated and in effect from time to time.

1.24 "**Restricted Securities**" means the securities of the Company required to be notated with the legend set forth in Subsection 2.12(b) hereof.

1.25 "**Right of First Refusal and Co-Sale Agreement**" means that certain Amended and Restated Right of First Refusal and Co-Sale Agreement, dated of even date herewith, by and among the Company, the Initial Investors and any other stockholders of the Company that are parties thereto, as amended and in effect from time to time.

1.26 "**SEC**" means the Securities and Exchange Commission.

1.27 "**SEC Rule 144**" means Rule 144 promulgated by the SEC under the Securities Act.

1.28 "**SEC Rule 145**" means Rule 145 promulgated by the SEC under the Securities Act.

1.29 "**Securities Act**" means the Securities Act of 1933, as amended, and the rules and regulations promulgated thereunder.

1.30 "**Selling Expenses**" means all underwriting discounts, selling commissions, and stock transfer taxes applicable to the sale of Registrable Securities, and fees and disbursements of counsel for any Holder, except for the fees and disbursements of the Selling Holder Counsel borne and paid by the Company as provided in Subsection 2.6.

1.31 "**Series A Preferred Stock**" means the Company's Series A Preferred Stock, par value $0.001 per share.

1.32 "**Series A-1 Junior Preferred Stock**" means the Company's Series A-1 Junior Preferred Stock, par value $0.001 per share.

1.33 "**Service Provider Investor**" means any Investor that is a current or former officer, director, employee or consultant of the Company or that is a permitted transferee under clause (ii) of Subsection 6.1 hereof or an Affiliate of any current or former officer, director, employee or consultant of the Company.

2. Registration Rights. The Company covenants and agrees as follows:

2.1 Demand Registration.

(a) Form S-1 Demand.If, at any time after one hundred eighty (180) days after the effective date of the registration statement for the IPO, the Company receives a written request from Holders holding at least a majority of the Registrable Securities then outstanding and held by the Holders that the Company file a Form S-1 registration statement with respect to Registrable Securities owned by such Holder or Holders having an anticipated aggregate offering price, net of Selling Expenses, of at least Fifteen Million Dollars ($15,000,000), then the Company shall (i) within ten (10) days after the date such request is given, give notice thereof (the "**Demand Notice**") to all Holders other than the Initiating Holders and (ii) as soon as practicable, and in any event within sixty (60) days after the date such request is given by the Initiating Holders, file a Form S-1 registration statement under the Securities Act covering all Registrable Securities that the Initiating Holders request to be registered and any additional Registrable Securities requested to be included in such registration by any other Holders, as specified by notice given by each such Holder to the Company within twenty (20) days of the date the Demand Notice is given, and in each case, subject to the limitations of Subsections 2.1(c), 2.1(d) and 2.3.

(b) Form S-3 Demand. If at any time when it is eligible to use a Form S-3 registration statement, the Company receives a request from Holders of at least ten percent (10%) of the Registrable Securities then outstanding that the Company file a Form S-3 registration statement with respect to outstanding Registrable Securities of such Holders (x) that cannot be sold by such Holders pursuant to Rule 144 during the three month period immediately following such request and (y) that have an anticipated aggregate offering price, net of Selling Expenses, of at least Ten Million Dollars ($10,000,000), then the Company shall (i) within ten (10) days after the date such request is given, give a Demand Notice to all Holders other than the Initiating Holders; and (ii) as soon as practicable, and in any event within forty-five (45) days after the date such request is given by the Initiating Holders, file a Form S-3 registration statement under the Securities Act covering all Registrable Securities that the Initiating Holders request to be registered and any additional Registrable Securities requested to be included in such registration by any other Holders, as specified by notice given by each such Holder to the Company within twenty (20) days of the date the Demand Notice is given, and in each case, subject to the limitations of Subsections 2.1(c), 2.1(d) and 2.3.

(c) Notwithstanding the foregoing obligations, if the Company furnishes to Holders requesting a registration pursuant to this Subsection 2.1 a certificate signed by the Company's chief executive officer stating that in the good faith judgment of the Company's Board of Directors it would be materially detrimental to the Company and its stockholders for such registration statement to either become effective or remain effective for as long as such registration statement otherwise would be required to remain effective, because such action would (i) materially interfere with a significant acquisition, corporate reorganization, or other similar transaction involving the Company; (ii) require premature disclosure of material information that the Company has a bona fide business purpose for preserving as confidential; or (iii) render the Company unable to comply with requirements under the Securities Act or Exchange Act, then the Company shall have the right to defer taking action with respect to such filing, and any time periods with respect to filing or effectiveness thereof shall be tolled correspondingly, for a period of not more than one hundred twenty (120) days after the request of the Initiating

Holders is given; provided, however, that the Company may not invoke this right more than once in any twelve (12) month period; and provided further that the Company shall not register any securities for its own account or that of any other stockholder during such one hundred twenty (120) day period other than an Excluded Registration.

(d) The Company shall not be obligated to effect, or to take any action to effect, any registration pursuant to Subsection 2.1(a) (i) during the period that is sixty (60) days before the Company's good faith estimate of the date of filing of, and ending on a date that is one hundred eighty (180) days after the effective date of, a Company-initiated registration, provided that the Company is actively employing in good faith commercially reasonable efforts to cause such registration statement to become effective; (ii) after the Company has effected two registrations pursuant to Subsection 2.1(a); or (iii) if the Initiating Holders propose to dispose of shares of Registrable Securities that may be immediately registered on Form S-3 pursuant to a request made pursuant to Subsection 2.1(b). The Company shall not be obligated to effect, or to take any action to effect, any registration pursuant to Subsection 2.1(b) (i) during the period that is thirty (30) days before the Company's good faith estimate of the date of filing of, and ending on a date that is ninety (90) days after the effective date of, a Company-initiated registration, provided that the Company is actively employing in good faith commercially reasonable efforts

to cause such registration statement to become effective; or (ii) if the Company has effected two registrations pursuant to Subsection 2.1(b) within the twelve (12) month period immediately preceding the date of such request. A registration shall not be counted as "effected" for purposes of this Subsection 2.1(d) until such time as the applicable registration statement has been declared effective by the SEC, unless the Initiating Holders withdraw their request for such registration, elect not to pay the registration expenses therefor, and forfeit their right to one demand registration statement pursuant to Subsection 2.6, in which case such withdrawn registration statement shall be counted as "effected" for purposes of this Subsection 2.1(d).

2.2 Company Registration. If the Company proposes to register (including, for this purpose, a registration effected by the Company for stockholders other than the Holders) any of its Common Stock under the Securities Act in connection with the public offering of such securities solely for cash (other than in an Excluded Registration or in a registration effected by the Company for its own account that is not underwritten), the Company shall, at such time, promptly give each Holder notice of such registration. Upon the request of each Holder given within twenty (20) days after such notice is given by the Company, the Company shall, subject to the provisions of Subsection 2.3, cause to be registered all of the Registrable Securities that each such Holder has requested to be included in such registration. If the Company proposes to sell shares of Common Stock that have already been registered "off the shelf" by means of a prospectus supplement in connection with a public offering of shares of Common Stock solely for cash by the Company for the account of the Company or any stockholders of the Company other than the Holders, the Company shall, at such time, promptly give the Holders notice of such contemplated offering. Upon the request of a Holder given within (10) days after such notice is given by the Company, the Company shall, subject to the provisions of Section 2.3, include in such offering all of the Registrable Securities that each such Holder has requested to be included in such offering. The Company shall have the right to terminate or withdraw any registration initiated by it under this Subsection 2.2 before the effective date of such registration, whether or not any Holder has elected to include Registrable Securities in such registration. The expenses (other than Selling Expenses) of such withdrawn registration shall be borne by the Company in accordance with Subsection 2.6.

2.3 Underwriting Requirements.

(a) If, pursuant to Subsection 2.1**,** the Initiating Holders intend to distribute the Registrable Securities covered by their request by means of an underwriting, they shall so advise the Company as a part of their request made pursuant to Subsection 2.1, and the Company shall include such information in the Demand Notice. The underwriter(s) will be selected by the Company and shall be reasonably acceptable to a majority in interest of the Initiating Holders. In such event, the right of any Holder to include such Holder's Registrable Securities in such registration shall be conditioned upon such Holder's participation in such underwriting and the inclusion of such Holder's Registrable Securities in the underwriting to the extent provided herein. All Holders proposing to distribute their securities through such underwriting shall (together with the Company as provided in Subsection 2.4(e)) enter into an underwriting agreement in customary form with the underwriter(s) selected for such underwriting. Notwithstanding any other provision of this Subsection 2.3, if the managing underwriter(s) advise(s) the Initiating Holders in writing that marketing factors require a limitation on the number of shares to be underwritten, then the Initiating Holders shall so advise

all Holders of Registrable Securities that otherwise would be underwritten pursuant hereto, and the number of Registrable Securities that may be included in the underwriting shall be allocated among such Holders of Registrable Securities, including the Initiating Holders, in proportion (as nearly as practicable) to the number of Registrable Securities owned by each Holder or in such other proportion as shall mutually be agreed to by all such selling Holders; provided, however, that the number of Registrable Securities held by the Holders to be included in such underwriting shall not be reduced unless all other securities are first entirely excluded from the underwriting. To facilitate the allocation of shares in accordance with the above provisions, the Company or the underwriters may round the number of shares allocated to any Holder to the nearest one hundred (100) shares.

(b) In connection with any offering involving an underwriting of shares of the Company's capital stock pursuant to Subsection 2.2, the Company shall not be required to include any of the Holders' Registrable Securities in such underwriting unless the Holders accept the terms of the underwriting as agreed upon between the Company and its underwriters, and then only in such quantity as the underwriters in their sole discretion determine will not jeopardize the success of the offering by the Company. If the total number of securities, including Registrable Securities, requested by stockholders to be included in such offering exceeds the number of securities to be sold (other than by the Company) that the underwriters in their reasonable discretion determine is compatible with the success of the offering, then the Company shall be required to include in the offering only that number of such securities, including Registrable Securities, which the underwriters and the Company in their sole discretion determine will not jeopardize the success of the offering. In no event shall any Registrable Securities be excluded from such offering unless all other stockholders' securities have been first excluded. If the underwriters determine that less than all of the Registrable Securities requested to be registered can be included in such offering, then the Registrable Securities that are included in such offering shall be allocated among the selling Holders in proportion (as nearly as practicable to) the number of Registrable Securities owned by each selling Holder or in such other proportions as shall mutually be agreed to by all such selling Holders. To facilitate the allocation of shares in accordance with the above provisions, the Company or the underwriters may round the number of shares allocated to any Holder to the nearest one hundred (100) shares. Notwithstanding the foregoing, in no event shall (i) the number of Registrable Securities included in the offering be reduced unless all other securities (other than securities to be sold by the Company) are first entirely excluded from the offering or (ii) the number of Registrable Securities included in the offering be reduced below thirty percent (30%) of the total number of securities included in such offering, unless such

offering is the IPO, in which case the selling Holders may be excluded further if the underwriters make the determination described above and no other stockholder's securities are included in such offering. For purposes of the provision in this Subsection 2.3(b) concerning apportionment, for any selling Holder that is a partnership, limited liability company, or corporation, the partners, members, retired partners, retired members, stockholders, and Affiliates of such Holder, or the estates and Immediate Family Members of any such partners, retired partners, members, and retired members and any trusts for the benefit of any of the foregoing Persons, shall be deemed to be a single "selling Holder," and any pro rata reduction with respect to such "selling Holder" shall be based upon the aggregate number of Registrable Securities owned by all Persons included in such "selling Holder," as defined in this sentence.

(c) For purposes of Section 2.1, a registration shall not be counted as "effected" if, as a result of an exercise of an underwriter's cutback provisions in Section 2.3(a), fewer than seventy percent (70%) of the total number of Registrable Securities that Holders have requested to be included in such registration statement are actually included.

2.4 Obligations of the Company. Whenever required under this Section to effect the registration of any Registrable Securities, the Company shall, as expeditiously as reasonably possible:

(a) prepare and file with the SEC a registration statement with respect to such Registrable Securities and use its commercially reasonable efforts to cause such registration statement to become effective and, upon the request of the Holders of a majority of the Registrable Securities registered thereunder, keep such registration statement effective for a period of up to one hundred twenty (120) days or, if earlier, until the distribution contemplated in the registration statement has been completed; provided, however, that (i) such one hundred twenty (120) day period shall be extended for a period of time equal to the period the Holder refrains, at the request of an underwriter of Common Stock (or other securities) of the Company, from selling any securities included in such registration, and (ii) in the case of any registration of Registrable Securities on Form S-3 that are intended to be offered on a continuous or delayed basis, subject to compliance with applicable SEC rules, such one hundred twenty (120) day period shall be extended for up to one hundred eighty (180) days, if necessary, to keep the registration statement effective until all such Registrable Securities are sold;

(b) prepare and file with the SEC such amendments and supplements to such registration statement, and the prospectus used in connection with such registration statement, as may be necessary to comply with the Securities Act in order to enable the disposition of all securities covered by such registration statement;

(c) furnish to the selling Holders such numbers of copies of a prospectus, including a preliminary prospectus, as required by the Securities Act, and such other documents as the Holders may reasonably request in order to facilitate their disposition of their Registrable Securities;

(d) use its commercially reasonable efforts to register and qualify the securities covered by such registration statement under such other securities or blue-sky laws of such jurisdictions as shall be reasonably requested by the selling Holders; provided that the Company shall not be required to qualify to do business or to file a general consent to service of process in any such states or jurisdictions, unless the Company is already subject to service in such jurisdiction and except as may be required by the Securities Act;

(e) in the event of any underwritten public offering, enter into and perform its obligations under an underwriting agreement, in usual and customary form, with the underwriter**(s)** of such offering;

(f) use its commercially reasonable efforts to cause all such Registrable Securities covered by such registration statement to be listed on a national securities

exchange or trading system and each securities exchange and trading system (if any) on which similar securities issued by the Company are then listed;

(g) provide a transfer agent and registrar for all Registrable Securities registered pursuant to this Agreement and provide a CUSIP number for all such Registrable Securities, in each case not later than the effective date of such registration;

(h) promptly make available for inspection by the selling Holders, any managing underwriter(s) participating in any disposition pursuant to such registration statement, and any attorney or accountant or other agent retained by any such underwriter or selected by the selling Holders, all financial and other records, pertinent corporate documents, and properties of the Company, and cause the Company's officers, directors, employees, and independent accountants to supply all information reasonably requested by any such seller, underwriter, attorney, accountant, or agent, in each case, as necessary or advisable to verify the accuracy of the information in such registration statement and to conduct appropriate due diligence in connection therewith;

(i) notify each selling Holder, promptly after the Company receives notice thereof, of the time when such registration statement has been declared effective or a supplement to any prospectus forming a part of such registration statement has been filed;

(j) after such registration statement becomes effective, notify each selling Holder of any request by the SEC that the Company amend or supplement such registration statement or prospectus;

(k) as promptly as possible notify each seller of Registrable Securities and each underwriter under such registration statement, at any time when a prospectus relating thereto is required to be delivered under the Securities Act, of the happening of any event of which the Company has knowledge as a result of which the prospectus contained in such registration statement, as then in effect, includes an untrue statement of a material fact or omits to state a material fact required to be stated therein or necessary to make the statements therein not misleading in light of the circumstances then existing; and

(l) in the case of an underwritten offering, use its best efforts to furnish, at the request of any Holder requesting registration of Registrable Securities pursuant to this Section 2 on the date on which such Registrable Securities are sold to the underwriter, (1) an opinion, dated such date, of the counsel representing the Company for the purposes of such registration, in form and substance as is customarily given to underwriters in an

underwritten public offering, addressed to the underwriters, and (ii) a "comfort" letter dated such date, from the independent certified public accountants of the Company, in form and substance as is customarily given by independent certified public accountants to underwriters in an underwritten public offering, addressed to the underwriters, if any.

In addition, the Company shall ensure that, at all times after any registration statement covering a public offering of securities of the Company under the Securities Act shall have become effective, its insider trading policy shall provide that the Company's directors may implement a trading program under Rule 10b5-1 of the Exchange Act.

2.5 Furnish Information. It shall be a condition precedent to the obligations of the Company to take any action pursuant to this Section 2 with respect to the Registrable Securities of any selling Holder that such Holder shall furnish to the Company such information regarding itself, the Registrable Securities held by it, and the intended method of disposition of such securities as is reasonably required to effect the registration of such Holder's Registrable Securities.

2.6 Expenses of Registration. All expenses (other than Selling Expenses) incurred in connection with registrations, filings, or qualifications pursuant to Section 2, including all registration, filing, and qualification fees; printers' and accounting fees; fees and disbursements of counsel for the Company; and the reasonable fees and disbursements, not to exceed $50,000, of one counsel for the selling Holders ("**Selling Holder Counsel**"), shall be borne and paid by the Company; provided, however, that the Company shall not be required to pay for any expenses of any registration proceeding begun pursuant to Subsection 2.1 if the registration request is subsequently withdrawn at the request of the Holders of a majority of the Registrable Securities to be registered (in which case all selling Holders shall bear such expenses pro rata based upon the number of Registrable Securities that were to be included in the withdrawn registration), unless the Holders of a majority of the Registrable Securities then outstanding and held by the Holders agree to forfeit their right to one registration pursuant to Subsections 2.1(a) or 2.1(b), as the case may be; and provided further that if, at the time of such withdrawal, the Holders shall have learned of a material adverse change in the condition, business, or prospects of the Company from that known to the Holders at the time of their request and have withdrawn the request with reasonable promptness after learning of such information then the Holders shall not be required to pay any of such expenses and shall not forfeit their right to one registration pursuant to Subsections 2.1(a) or 2.1(b), as the case may be. All Selling Expenses relating to Registrable Securities registered pursuant to this Section shall be borne and paid by the Holders pro rata on the basis of the number of Registrable Securities registered on their behalf.

2.7 Delay of Registration. No Holder shall have any right to obtain or seek an injunction restraining or otherwise delaying any registration pursuant to this Agreement as the result of any controversy that might arise with respect to the interpretation or implementation of this Section 2.

2.8 Indemnification. If any Registrable Securities are included in a registration statement under this Section:

(a) To the extent permitted by law, the Company will indemnify and hold harmless each selling Holder, and the partners, members, officers, directors, and stockholders of each such Holder; legal counsel, accountants and investment advisors for each such Holder; any underwriter (as defined in the Securities Act) for each such Holder; and each Person, if any, who controls such Holder or underwriter within the meaning of the Securities Act or the Exchange Act, against any Damages, and the Company will pay to each such Holder, underwriter, controlling Person, or other aforementioned Person any legal or other expenses reasonably incurred thereby in connection with investigating or defending any claim or proceeding from which Damages may result, as such expenses are incurred; provided, however, that the indemnity agreement contained in this Subsection 2.8(a) shall not apply to amounts paid

in settlement of any such claim or proceeding if such settlement is effected without the consent of the Company, which consent shall not be unreasonably withheld, nor shall the Company be liable for any Damages to the extent that they arise out of or are based upon actions or omissions made in reliance upon and in conformity with written information furnished by or on behalf of any such Holder, underwriter, controlling Person, or other aforementioned Person expressly for use in connection with such registration.

(b) To the extent permitted by law, each selling Holder, severally and not jointly, will indemnify and hold harmless the Company, and each of its directors, each of its officers who has signed the registration statement, each Person (if any), who controls the Company within the meaning of the Securities Act, legal counsel and accountants for the Company, any underwriter (as defined in the Securities Act), any other Holder selling securities in such registration statement, and any controlling Person of any such underwriter or other Holder, against any Damages, in each case only to the extent that such Damages arise out of or are based upon actions or omissions made in reliance upon and in conformity with written information furnished by or on behalf of such selling Holder expressly for use in connection with such registration; and each such selling Holder will pay to the Company and each other aforementioned Person any legal or other expenses reasonably incurred thereby in connection with investigating or defending any claim or proceeding from which Damages may result, as such expenses are incurred; provided, however, that the indemnity agreement contained in this Subsection 2.8(b) shall not apply to amounts paid in settlement of any such claim or proceeding if such settlement is effected without the consent of the Holder, which consent shall not be unreasonably withheld; and provided further that in no event shall the aggregate amounts payable by any Holder by way of indemnity or contribution under Subsections 2.8(b) and 2.8(d) exceed the proceeds from the offering received by such Holder (net of any Selling Expenses paid by such Holder), except in the case of fraud or willful misconduct by such Holder.

(c) Promptly after receipt by an indemnified party under this Subsection 2.8 of notice of the commencement of any action (including any governmental action) for which a party may be entitled to indemnification hereunder, such indemnified party will, if a claim in respect thereof is to be made against any indemnifying party under this Subsection 2.8, give the indemnifying party notice of the commencement thereof. The indemnifying party shall have the right to participate in such action and, to the extent the indemnifying party so desires, participate jointly with any other indemnifying party to which notice has been given, and to assume the defense thereof with counsel mutually satisfactory to the parties; provided, however, that an indemnified party (together with all other indemnified parties that may be represented without conflict by one counsel) shall have the right to retain one separate counsel, with the fees and expenses to be paid by the indemnifying party, if representation of such indemnified party by the counsel retained by the indemnifying party would be inappropriate due to actual or potential differing interests between such indemnified party and any other party represented by such counsel in such action. The failure to give notice to the indemnifying party within a reasonable time of the commencement of any such action shall relieve such indemnifying party of any liability to the indemnified party under this Subsection 2.8, to the extent that such failure materially prejudices the

indemnifying party's ability to defend such action. The failure to give notice to the indemnifying party will not relieve it of any liability that it may have to any indemnified party otherwise than under this Subsection 2.8.

(d) To provide for just and equitable contribution to joint liability under the Securities Act in any case in which either: (i) any party otherwise entitled to indemnification hereunder makes a claim for indemnification pursuant to this Subsection 2.8 but it is judicially determined (by the entry of a final judgment or decree by a court of competent jurisdiction and the expiration of time to appeal or the denial of the last right of appeal) that such indemnification may not be enforced in such case, notwithstanding the fact that this Subsection 2.8 provides for indemnification in such case, or (ii) contribution under the Securities Act may be required on the part of any party hereto for which indemnification is provided under this Subsection 2.8, then, and in each such case, such parties will contribute to the aggregate losses, claims, damages, liabilities, or expenses to which they may be subject (after contribution from others) in such proportion as is appropriate to reflect the relative fault of each of the indemnifying party and the indemnified party in connection with the statements, omissions, or other actions that resulted in such loss, claim, damage, liability, or expense, as well as to reflect any other relevant equitable considerations. The relative fault of the indemnifying party and of the indemnified party shall be determined by reference to, among other things, whether the untrue or allegedly untrue statement of a material fact, or the omission or alleged omission of a material fact, relates to information supplied by the indemnifying party or by the indemnified party and the parties' relative intent, knowledge, access to information, and opportunity to correct or prevent such statement or omission; provided, however, that, in any such case (x) no Holder will be required to contribute any amount in excess of the public offering price of all such Registrable Securities offered and sold by such Holder pursuant to such registration statement, and (y) no Person guilty of fraudulent misrepresentation (within the meaning of Section 11(f) of the Securities Act) will be entitled to contribution from any Person who was not guilty of such fraudulent misrepresentation; and provided further that in no event shall a Holder's liability pursuant to this Subsection 2.8(d), when combined with the amounts paid or payable by such Holder pursuant to Subsection 2.8(b), exceed the proceeds from the offering received by such Holder (net of any Selling Expenses paid by such Holder), except in the case of willful misconduct or fraud by such Holder.

(e) Notwithstanding the foregoing, to the extent that the provisions on indemnification and contribution contained in the underwriting agreement entered into in connection with the underwritten public offering are in conflict with the foregoing provisions, the provisions in the underwriting agreement shall control.

(f) Unless otherwise superseded by an underwriting agreement entered into in connection with the underwritten public offering, the obligations of the Company and Holders under this Subsection 2.8 shall survive the completion of any offering of Registrable Securities in a registration under this Section 2, and otherwise shall survive the termination of this Agreement.

2.9 Reports Under Exchange Act. With a view to making available to the Holders the benefits of SEC Rule 144 and any other rule or regulation of the SEC that may at any time permit a Holder to sell securities of the Company to the public without registration or pursuant to a registration on Form S-3, the Company shall:

(a) make and keep available adequate current public information, as those terms are understood and defined in SEC Rule 144, at all times after the effective date of the registration statement filed by the Company for the IPO;

(b) use commercially reasonable efforts to file with the SEC in a timely manner all reports and other documents required of the Company under the Securities Act and the Exchange Act (at any time after the Company has become subject to such reporting requirements); and

(c) furnish to any Holder, so long as the Holder owns any Registrable Securities, forthwith upon request (i) to the extent accurate, a written statement by the Company that it has complied with the reporting requirements of SEC Rule 144 (at any time after ninety (90) days after the effective date of the registration statement filed by the Company for the IPO), the Securities Act, and the Exchange Act (at any time after the Company has become subject to such reporting requirements), or that it qualifies as a registrant whose securities may be resold pursuant to Form S-3 (at any time after the Company so qualifies); and (ii) such other information as may be reasonably requested in availing any Holder of any rule or regulation of the SEC that permits the selling of any such securities without registration (at any time after the Company has become subject to the reporting requirements under the Exchange Act) or pursuant to Form S-3 (at any time after the Company so qualifies to use such form).

2.10 Limitations on Subsequent Registration Rights. From and after the date of this Agreement, the Company shall not, without the prior written consent of the Holders of a majority of the Registrable Securities then outstanding and held by the Holders, enter into any agreement with any holder or prospective holder of any securities of the Company that would (i) provide to such holder the right to include securities in any registration on other than either a pro rata basis with respect to the Registrable Securities or on a subordinate basis after all Holders have had the opportunity to include in the registration and offering all shares of Registrable Securities that they wish to so include or (ii) allow such holder or prospective holder to initiate a demand for registration of any securities held by such holder or prospective holder; provided that this limitation shall not apply to any additional Investor who becomes a party to this Agreement in accordance with Subsection 6.9.

2.11 "Market Stand-off" Agreement. Each Holder hereby agrees that it will not, without the prior written consent of the managing underwriter, during the period commencing on the date of the final prospectus relating to the IPO, and ending on the date specified by the Company and the managing underwriter (such period not to exceed one hundred eighty (180) days, or such other period as may be requested by the Company or an underwriter to accommodate regulatory restrictions on (1) the publication or other distribution of research reports, and (2) analyst recommendations and opinions, including, but not limited to, the restrictions contained in FINRA Rule 2711(f)(4) or NYSE Rule 472(f)(4), or any successor provisions or amendments thereto), (i) lend; offer; pledge; sell; contract to sell; sell any option or contract to purchase; purchase any option or contract to sell; grant any option, right, or warrant to purchase; or otherwise transfer or dispose of, directly or indirectly, any shares of Common Stock (or any securities convertible into or exercisable or exchangeable (directly or indirectly) for Common Stock) held immediately before the effective date of the registration statement for the IPO or any shares of Common Stock acquired at any time after such effective date upon exercise

or conversion of any exercisable or convertible securities of the Company held immediately before such effective date or (ii) enter into any swap or other arrangement that transfers to another, in whole or in part, any of the economic consequences of ownership of such securities, whether any such transaction described in clause (i) or (ii) above is to be settled by delivery of Common Stock or other securities, in cash, or otherwise. The foregoing provisions of this Subsection 2.11 shall not apply with respect to any offering of securities of the Company other than the IPO, shall not apply to the purchase of any shares in the IPO itself or in the open market following the IPO, shall not apply to the sale of any shares to an underwriter pursuant to an underwriting agreement or to the transfer of any shares to any trust for the direct or indirect benefit of the Holder or the immediate family of the Holder, provided that the trustee of the trust agrees to be bound in writing by the restrictions set forth herein, and provided further that any such transfer shall not involve a disposition for value, and the foregoing provisions of this Subsection 2.11 shall be applicable to the Holders only if all officers, directors, Holders and other stockholders individually owning more than one percent (1%) of the Company's outstanding Common Stock (after giving effect to conversion into Common Stock of all outstanding Preferred Stock) are subject to the same restrictions. The underwriters in connection with such registration are intended third-party beneficiaries of this Subsection 2.11 and shall have the right, power and authority to enforce the provisions hereof as though they were a party hereto. Each Holder further agrees to execute such agreements as may be reasonably requested by the underwriters in connection with such registration that are consistent with this Subsection 2.11 or that are necessary to give further effect thereto. If any of the obligations described in this Subsection 2.11 are waived or terminated with respect to any of the securities of any officer, director, Holder or greater than one-percent (1%) stockholder (in any such case, the "**Released Securities**"), the foregoing provisions shall be waived or terminated, as applicable, to the same extent and with respect to the same percentage of securities of each Holder as the percentage of Released Securities represent with respect to the securities held by the applicable officer, director, Holder or greater than one-percent stockholder.

2.12 Restrictions on Transfer.

(a) The Preferred Stock and the Registrable Securities shall not be sold, pledged, or otherwise transferred, and the Company shall not recognize and shall issue stop-transfer instructions to its transfer agent with respect to any such sale, pledge, or transfer, except upon the conditions specified in this Agreement, which conditions are intended to ensure compliance with the provisions of the Securities Act. A transferring Holder will cause any proposed purchaser, pledgee or other transferee of shares of Preferred Stock or other Registrable Securities held by such Holder to agree in writing to take and hold such securities subject to the provisions and upon the conditions specified in Subsection 2.11 and this Subsection 2.12. Notwithstanding the foregoing, the Company shall not require any transferee of shares pursuant to an effective registration statement or, following the IPO, SEC Rule 144, to be bound by such subsections with respect to such transferred shares.

(b) Each certificate, instrument, or book entry representing (i) the Preferred Stock, (ii) the Registrable Securities, and (iii) any other securities issued in respect of the securities referenced in clauses (i) and (ii), upon any stock split, stock dividend, recapitalization, merger, consolidation, or similar event, shall (unless otherwise permitted by the provisions of Subsection 2.12(c)) be notated with a legend substantially in the following form:

THE SECURITIES REPRESENTED HEREBY HAVE BEEN ACQUIRED FOR INVESTMENT AND HAVE NOT BEEN REGISTERED UNDER THE SECURITIES ACT OF 1933. SUCH SHARES MAY NOT BE SOLD, PLEDGED, OR TRANSFERRED IN THE ABSENCE OF SUCH REGISTRATION OR A VALID EXEMPTION FROM THE REGISTRATION AND PROSPECTUS DELIVERY REQUIREMENTS OF SAID ACT.

THE SECURITIES REPRESENTED HEREBY MAY BE TRANSFERRED ONLY IN ACCORDANCE WITH THE TERMS OF AN AMENDED AND RESTATED INVESTORS' RIGHTS AGREEMENT, DATED AS OF AUGUST 21, 2017, AMONG THE COMPANY, AND CERTAIN STOCKHOLDERS OF THE COMPANY, AS AMENDED AND IN EFFECT FROM TIME TO TIME. A COPY OF SUCH AMENDED AND RESTATED INVESTORS' RIGHTS AGREEMENT IS ON FILE WITH THE SECRETARY OF THE COMPANY.

The Holders consent to the Company making a notation in its records and giving instructions to any transfer agent of the Restricted Securities in order to implement the restrictions on transfer set forth in this Subsection 2.12.

(c) The holder of any Restricted Securities, by acceptance of ownership thereof, agrees to comply in all respects with the provisions of this Section 2. Before any proposed sale, pledge, or transfer of any Restricted Securities, unless there is in effect a registration statement under the Securities Act covering the proposed transaction or, following the IPO, the transfer is made pursuant to SEC Rule 144, the Holder thereof shall give notice to the Company of such Holder's intention to effect such sale, pledge, or transfer. Each such notice shall describe the manner and circumstances of the proposed sale, pledge, or transfer in sufficient detail and, if reasonably requested by the Company, shall be accompanied at such Holder's expense by either (i) a written opinion of legal counsel who shall, and whose legal opinion shall, be reasonably satisfactory to the Company, addressed to the Company, to the effect that the proposed transaction may be effected without registration under the Securities Act; (ii) a "no action" letter from the SEC to the effect that the proposed sale, pledge, or transfer of such Restricted Securities without registration will not result in a recommendation by the staff of the SEC that action be taken with respect thereto; or (iii) any other evidence reasonably satisfactory to counsel to the Company to the effect that the proposed sale, pledge, or transfer of the Restricted Securities may be effected without registration under the Securities Act, whereupon the Holder of such Restricted Securities shall be entitled to sell, pledge, or transfer such Restricted Securities in accordance with the terms of the notice given by the Holder to the Company. The Company will not require such a legal opinion or "no action" letter (x) in any transaction in compliance with SEC Rule 144; or (y) in any transaction in which such Holder distributes Restricted Securities to an Affiliate of such Holder for no consideration; provided that, with respect to transfers under the foregoing clause (x) at any time prior to the IPO and with respect to transfers under the foregoing clause (y) at any time, each transferee agrees in writing to be subject to the terms of Subsection 2.11 and this Subsection 2.12. Each certificate, instrument, or book entry representing the Restricted Securities transferred as above provided shall be notated with, except if such transfer is made pursuant to SEC Rule 144 at any time after the IPO or pursuant to an effective registration statement, the appropriate restrictive legend set forth in Subsection 2.12(b), except that such certificate, instrument or book entry shall not be

notated with the first of such restrictive legends if, in the opinion of counsel for such Holder and the Company, such legend is not required in order to establish compliance with any provisions of the Securities Act.

2.13 Termination of Registration Rights. The right of any Holder to request registration or inclusion of Registrable Securities in any registration pursuant to Subsections 2.1 or 2.2 shall terminate upon the earliest to occur of:

(a) the closing of a Deemed Liquidation Event, as such term is defined in the Restated Certificate, as amended and in effect from time to time;

(b) following the IPO, such time as Rule 144 or another similar exemption under the Securities Act is available for the sale of all of such Holder's shares without limitation during a three-month period without registration and without the requirement for the Company to be in compliance with the current public information required under Rule 144(c)(1); and

(c) the fifth (5th) anniversary of the date of the IPO.

3. Information Rights.

3.1 Delivery of Financial Statements. The Company shall deliver to each Investor, provided that the Board of Directors has not reasonably determined that such Investor is a competitor of the Company:

(a) as soon as practicable, but in any event within one hundred eighty (180) days after the end of each fiscal year of the Company (i) a balance sheet as of the end of such year, (ii) statements of income and of cash flows for such year, and a comparison between (x) the actual amounts as of and for such fiscal year and (y) the comparable amounts for the prior year and as included in the Budget (as defined in Subsection 3.1(c)) for such year, with an explanation of any material differences between such amounts and a schedule as to the sources and applications of funds for such year, and (iii) a statement of stockholders' equity as of the end of such year, all such financial statements audited and certified by independent public accountants of regional or national reputation and recognized standing selected by the Company;

(b) as soon as practicable, but in any event within forty-five (45) days after the end of each of the first three (3) quarters of each fiscal year of the Company, an unaudited statement of income and cash flow for such fiscal quarter, and an unaudited balance sheet as of the end of such fiscal quarter, all prepared in accordance with GAAP (except that such financial statements may (i) be subject to normal year-end audit adjustments, and (ii) not contain all notes thereto that may be required in accordance with GAAP);

(c) as soon as practicable, but in any event no later than thirty (30) days before the end of each fiscal year, a budget for the next fiscal year (the "**Budget**"), approved by the Board of Directors;

(d) with respect to the financial statements called for in Subsection 3.1(a) and Subsection 3.1(b) an instrument executed by the chief financial officer,

treasurer or chief executive officer of the Company certifying that such financial statements were prepared in accordance with GAAP consistently applied with prior practice for earlier periods (except as otherwise set forth in Subsection 3.1(b)) and fairly present the financial condition of the Company and its results of operation for the periods specified therein; and

(e) such other information relating to the financial condition, business, prospects, or corporate affairs of the Company as any Investor may from time to time reasonably request; provided, however, that the Company shall not be obligated under this Section 3.1 to provide information to any Investor if it determines in good faith that disclosure of such information would (i) be disadvantageous to the Company from a competitive standpoint, (ii) breach any confidentiality obligation of the Company, (iii) provide access to, or otherwise result in the disclosure of, any trade secret of the Company, (iv) otherwise pertain to an actual or potential conflict of interest or (v) adversely affect the attorney-client privilege between the Company and its counsel. Notwithstanding anything to the contrary contained in this Agreement, the foregoing clauses (i) and (iv) shall not be deemed to prevent the investment, legal, finance, tax, accounting and audit personnel of Pfizer and its Affiliates from obtaining access to information under this Section 3.1 relating to the financial condition of the Company solely for the purpose of managing, evaluating and reporting on Pfizer's investment in the Company.

If, for any period, the Company has any subsidiary whose accounts are consolidated with those of the Company, then in respect of such period the financial statements delivered pursuant to the foregoing sections shall be the consolidated and consolidating financial statements of the Company and all such consolidated subsidiaries.

Notwithstanding anything else in this Subsection 3.1 to the contrary, the Company may cease providing the information set forth in this Subsection 3.1 during the period starting with the date sixty (60) days before the Company's good-faith estimate of the date of filing of a registration statement if it reasonably concludes it must do so to comply with the SEC rules applicable to such registration statement and related offering; provided that the Company's covenants under this Subsection 3.1 shall be reinstated at such time as the Company is no longer actively employing its commercially reasonable efforts to cause such registration statement to become effective.

3.2 Inspection. The Company shall permit each Investor (provided that the Board of Directors has not reasonably determined that such Investor is a competitor of the Company), at such Investor's expense, to visit and inspect the Company's and each of its subsidiaries' properties, examine its books of account and records, and discuss the Company's affairs, finances, and accounts with its officers, during normal business hours of the Company as may be reasonably requested by the Investor and upon reasonable notice to the Company; provided, however, that the Company shall not be obligated under this Section 3.2 to provide any Investor with access to any such information if it determines in good faith that such access would (i) be disadvantageous to the Company from a competitive standpoint, (ii) breach any confidentiality obligation of the Company, (iii) provide access to, or otherwise result in the disclosure of, any trade secret of the Company, (iv) otherwise pertain to an actual or potential conflict of interest or (v) adversely affect the attorney-client privilege between the Company and its counsel. Notwithstanding anything to the contrary contained in this Agreement, the foregoing

clauses (i) and (iv) shall not be deemed to prevent the investment, legal, finance, tax, accounting and audit personnel of Pfizer and its Affiliates from obtaining access to information under this Section 3.2 relating to the financial condition of the Company solely for the purpose of managing, evaluating and reporting on Pfizer's investment in the Company.

3.3 Observer Rights. As long as OrbiMed Private Investments V, LP ("**OrbiMed**"), Baker Brothers Life Sciences, L.P. ("**Baker**"), Deerfield Private Design Fund III, L.P. ("**Deerfield**"), any Investor advised by Wellington Management Company LLP ("**Wellington**"), New Enterprise Associates 13, L.P. ("**NEA**") or Pfizer Inc. ("**Pfizer**") owns any shares of Preferred Stock, the Company shall invite a representative of OrbiMed, Baker, Deerfield, Wellington, NEA and Pfizer, as the case may be, to attend all meetings of its Board of Directors in a nonvoting observer capacity (an "**Observer**") and, in this respect, shall give such Observer copies of all notices, minutes, consents, and other materials that it provides to its directors contemporaneously with the delivery of such notices, minutes, consents, or other materials to the directors; provided, however, that such Observer shall agree to hold in confidence and trust and to act in a fiduciary manner with respect to all information so provided; and provided further, that the Company reserves the right to withhold any information and to exclude such Observer from any meeting or portion thereof if access to such information or attendance at such meeting could adversely affect the attorney-client privilege between the Company and its counsel or result in disclosure of trade secrets or a conflict of interest, or if such Investor or its Observer is a competitor of the Company.

3.4 Termination of Information Rights and Observer Rights. The covenants set forth in Subsections 3.1, 3.2 and 3.3 shall terminate and be of no further force or effect (i) immediately before the consummation of the IPO, (ii) when the Company first becomes subject to the periodic reporting requirements of Section 12(g) or 15(d) of the Exchange Act, or (iii) upon a Deemed Liquidation Event, as such term is defined in the Restated Certificate, in which the consideration received by the Investors is in the form of cash and/or marketable securities, whichever event occurs first.

3.5 Confidentiality. Each Investor agrees that such Investor will keep confidential and will not disclose, divulge, or use for any purpose (other than to monitor its investment in the Company) any confidential information obtained from the Company pursuant to the terms of this Agreement (including notice of the Company's intention to file a registration statement), unless such confidential information (a) is known or becomes known to the public in general (other than as a result of a breach of this Subsection 3.5 by such Investor), (b) is or has been independently developed or conceived by the Investor without use of the Company's confidential information, or (c) is or has been made known or disclosed to the Investor by a third party without a breach of any obligation of confidentiality such third party may have to the Company; provided, however, that an Investor may disclose confidential information (i) to its attorneys, accountants, consultants, and other professionals to the extent necessary to obtain their services in connection with monitoring its investment in the Company; (ii) to any prospective purchaser of any Registrable Securities from such Investor, if such prospective purchaser agrees to be bound by the provisions of this Subsection 3.5; (iii) to any existing or prospective Affiliate, partner (and partners of such partner), equityholder, member, stockholder, or wholly owned subsidiary of such Investor in the ordinary course of business, provided that such Investor informs such Person that such information is confidential and directs such Person to maintain the

confidentiality of such information and provided, however, that, notwithstanding anything express or implied to the contrary in the foregoing provisions of this clause (iii) or in any of the other provisions of this Subsection 3.5, the rights of Pfizer to disclose or use confidential information (including, without limitation, the right to disclose confidential information to Affiliates or officers, directors, employees, agents of Pfizer or any Affiliate of Pfizer) shall be subject to the restrictions and limitations set forth in that certain letter agreement regarding confidentiality, dated of even date herewith, by and between the Company and Pfizer, as amended and in effect from time to time,; or; or (iv) as may otherwise be required by law, or requested by any governmental, regulatory or other legal authority, provided that the Investor promptly notifies the Company of such disclosure and takes reasonable steps to minimize the extent of any such required disclosure and seek confidential treatment for the information so disclosed to the extent practicable. The Company acknowledges that at least some of the Investors are in the business of venture capital and other investing and therefore review the business plans and related proprietary information of many enterprises, including enterprises which may have products or services which compete directly or indirectly with those of the Company or its subsidiaries. Nothing in this Agreement shall preclude or in any way restrict the Investors from investing or participating in any particular enterprise whether or not such enterprise has products or services which compete with those of the Company or its subsidiaries. The Company and each Investor acknowledges and agrees that Pfizer or its Affiliates may presently have, or may engage in the future, in internal development programs, or may receive information from third parties that relates to, and may develop and commercialize products independently or in cooperation with such third parties, that are similar to or that are directly or indirectly competitive with, the Company's or its subsidiaries' development programs, products or services. Nothing in this Agreement or any other agreement related to the transactions contemplated by this Agreement shall in any way preclude or restrict Pfizer or its Affiliates from conducting any development program, commercializing any product or service or otherwise engaging in any enterprise, whether or not such development program, product, service or enterprise competes with those of the Company or its subsidiaries, so long as such activities do not result in a violation of the confidentiality provisions of this Agreement. Notwithstanding the foregoing, in the case of any Investor that is advised by a registered investment adviser or Affiliates thereof, such Investor may identify the Company and the value of such Investor's security holdings in the Company in accordance with applicable investment reporting and disclosure regulations or internal policies and respond to routine examinations, demands, requests or reporting requirements of a regulator without prior notice to or consent from the Company.

4. Rights to Future Stock Issuances.

4.1 Right of First Offer. Subject to the terms and conditions of this Subsection 4.1 and applicable securities laws, if the Company proposes to offer or sell any New Securities, the Company shall first offer such New Securities to each Investor. Each Investor shall be entitled to purchase a sufficient participation in the New Securities to retain such Investor's *pro rata* percentage of ownership in the Company in accordance with the provisions of this Subsection 4.1 (including, without limitation, Subsection 4.1(b) below).

(a) The Company shall give notice (the "**Offer Notice**") to each Investor, stating (i) its bona fide intention to offer such New Securities, (ii) the number of such

New Securities to be offered, and (iii) the price and terms, if any, upon which it proposes to offer such New Securities.

(b) By notification to the Company within twenty (20) days after the Offer Notice is given, each Investor may elect to purchase or otherwise acquire, at the price and on the terms specified in the Offer Notice, up to that portion of such New Securities which equals the

proportion that the Common Stock then held by such Investor, including, without limitation, all shares of Common Stock then issuable (directly or indirectly) upon conversion and/or exercise, as applicable, of the Preferred Stock and any other Derivative Securities then held by such Investor (except that, in the case of any Service Provider Investor, it will be the proportion that the Investment Securities then held by such Service Provider Investor) bears to the total Common Stock of the Company then outstanding (assuming full conversion and/or exercise, as applicable, of all Preferred Stock and other Derivative Securities). At the expiration of such twenty (20) day period, the Company shall promptly notify each Investor that elects to purchase or acquire all the shares available to it (each, a "**Fully Exercising Investor**") of any other Investor's failure to do likewise. During the ten (10) day period commencing after the Company has given such notice, each Fully Exercising Investor may, by giving notice to the Company, elect to purchase or acquire, in addition to the number of shares specified above, up to that portion of the New Securities for which Investors were entitled to subscribe but that were not subscribed for by the Investors which is equal to the proportion that the Common Stock issued and held, or issuable (directly or indirectly) upon conversion and/or exercise, as applicable, of Preferred Stock and any other Derivative Securities then held, by such Fully Exercising Investor (except that, in the case of any such Fully Exercising Investor that is a Service Provider Investor, it will be the proportion that the Investment Securities then held by such Service Provider Investor) bears to the Common Stock issued and held, or issuable (directly or indirectly) upon conversion and/or exercise, as applicable, of the Preferred Stock and any other Derivative Securities then held, by all Fully Exercising Investors who wish to purchase such unsubscribed shares (except that, in the case that any of the Fully Exercising Investors is a Service Provider Investor, only the Investment Securities then held by such Service Provider Investor shall be taken into account for purposes of any allocation of New Securities among the Fully Exercising Investors pursuant to this Subsection 4.1(b)). The closing of any sale pursuant to this Subsection 4.1(b) shall occur within the later of ninety (90) days of the date that the Offer Notice is given and the date of initial sale of New Securities pursuant to Subsection 4.1(c).

(c) If all New Securities referred to in the Offer Notice are not elected to be purchased or acquired as provided in Subsection 4.1(b), the Company may, during the ninety (90) day period following the expiration of the periods provided in Subsection 4.1(b), offer and sell the remaining unsubscribed portion of such New Securities to any Person or Persons at a price not less than, and upon terms no more favorable to the offeree than, those specified in the Offer Notice. If the Company does not enter into an agreement for the sale of the New Securities within such period, or if such agreement is not consummated within thirty (30) days of the execution thereof, the right provided hereunder shall be deemed to be revived and such New Securities shall not be offered unless first reoffered to the Investors in accordance with this Subsection 4.1.

(d) The right of first offer in this Subsection 4.1 shall not be applicable to (i) Exempted Securities (as defined in the Restated Certificate) and (ii) shares of Common Stock issued in the IPO.

(e) Notwithstanding any provision hereof to the contrary, in lieu of complying with the provisions of this Subsection 4.1, the Company may elect to give notice to the Investors within thirty (30) days after the issuance of New Securities. Such notice shall describe the type, price, and terms of the New Securities. Each Investor shall have twenty (20) days from the date notice is given to elect to purchase up to the number of New Securities that would, if purchased by such Investor, maintain such Investor's percentage-ownership position, calculated as set forth in Subsection 4.1(b) before giving effect to the issuance of such New Securities. The closing of such sale shall occur within sixty (60) days of the date notice is given to the Investors.

(f) Each Investor shall have a right of first offer to purchase any equity securities offered by any majority-owned subsidiary of the Company. Such right of first offer shall be on the same terms and conditions as the right of first offer set forth in this Subsection 4.1 with respect to any New Securities offered by the Company, and for purposes of implementing the foregoing provisions of this Subsection 4.1(f) any reference in this Section 4.1 or in the definition of the term "New Securities" to the Company shall be deemed and treated as a reference to the applicable majority-owned subsidiary of the Company that is offering any of its equity securities. The Company hereby covenants and agrees that it will cause each of its majority-owned subsidiaries that is offering any of such majority-owned subsidiary's equity securities to comply with the provisions of this Subsection 4.1 with respect to any such offering to the same extent as the Company is required to comply with the provisions of this Subsection 4.1 with respect to any offering of New Securities by the Company.

(g) The rights of first offer of each Investor pursuant to this Subsection 4.1 shall be applicable only if and for so long as such Investor qualifies as an "accredited investor" pursuant to Regulation D promulgated under the Securities Act.

(h) In the event that the rights of an Investor to purchase New Securities under this Subsection 4.1 are waived with respect to a particular offering of New Securities without such Investor's prior written consent (a "**Waived Investor**") and any Investor that participated in waiving such rights actually purchases New Securities in such offering, then the Company shall grant, and hereby grants, each Waived Investor the right to purchase, twenty (20) days following written notice of the sale of such New Securities, in a subsequent closing of such issuance on substantially the same terms and conditions, the same percentage of its full pro rata share of such New Securities as the highest percentage of any such purchasing Investor.

4.2 Termination. The covenants set forth in Subsection 4.1 shall terminate and be of no further force or effect (i) immediately before the consummation of the IPO**,** (ii) when the Company first becomes subject to the periodic reporting requirements of Section 12(g) or 15(d) of the Exchange Act, or (iii) upon a Deemed Liquidation Event, as such term is defined in the Restated Certificate, whichever event occurs first.

5. Additional Covenants.

5.1 Insurance. The Company shall use its commercially reasonable efforts to obtain, within ninety (90) days of the date hereof, from financially sound and reputable insurers Directors and Officers liability insurance, in an amount and on terms and conditions satisfactory to the Board of Directors, and will use commercially reasonable efforts to cause such insurance policy to be maintained until such time as the Board of Directors determines that such insurance should be discontinued. Such policy shall not be cancelable by the Company without prior approval by the Board of Directors.

5.2 Employee Agreements. The Company will cause each person now or hereafter employed by it or by any subsidiary (or engaged by the Company or any subsidiary as a consultant/independent contractor) with access to confidential information and/or trade secrets to enter into a nondisclosure and proprietary rights assignment agreement. In addition, the Company shall not amend, modify, terminate, waive, or otherwise alter, in whole or in part, any of the above-referenced agreements or any restricted stock agreement between the Company and any employee, without the consent of the Board of Directors.

5.3 Employee Stock. Unless otherwise approved by the Board of Directors (which approval shall include the approval of the Investor Directors so long as there are any Investor Directors), all future employees and consultants of the Company who purchase, receive options to purchase, or receive awards of shares of the Company's capital stock (an "**Award**") after the date hereof shall be required to execute restricted stock or option agreements, as applicable, providing for (i) vesting of shares over a four (4) year period, with the first twenty-five percent (25%) of such shares vesting following twelve (12) months of continued employment or service, and the remaining shares vesting in equal monthly installments over the following thirty-six (36) months, and (ii) a market stand-off provision substantially similar to that in Subsection 2.11. In addition, unless otherwise approved by the Board of Directors, the Company shall retain a "right of first refusal" on employee transfers until the Company's IPO and shall have the right to repurchase unvested shares at cost upon termination of employment of a holder of restricted stock. The Company shall not issue any Common Stock pursuant to an Award, unless and until such time, if ever, as the applicable recipient of such Award shall have become a party to and bound by the Right of First Refusal and Co-Sale Agreement and any other agreement that the Board of Directors of the Company, in its sole discretion, requires that such individual enter into prior to, and as a condition to, the issuance of such Common Stock by the Company to such individual.

5.4 Qualified Small Business Stock. The Company shall use commercially reasonable efforts to cause those shares of Series A Preferred Stock that are Registrable Securities, as well as any shares of Common Stock into which such shares of Series A Preferred Stock are converted, within the meaning of Section 1202(f) of the Internal Revenue Code (the "**Code**"), to constitute "qualified small business stock" as defined in Section 1202(c) of the Code; provided, however, that such requirement shall not be applicable if the Board of Directors of the Company determines, in its good-faith business judgment, that such qualification is inconsistent with the best interests of the Company. The Company shall submit to its stockholders (including the Investors) and to the Internal Revenue Service any reports that may be required under Section 1202(d)(1)(C) of the Code and the regulations promulgated thereunder. In addition, within twenty (20) business days after any Investor's written request therefor, the Company shall, at its option, either (i) deliver to such Investor a written statement

indicating whether (and what portion of) such Investor's interest in the Company constitutes "qualified small business stock" as defined in Section 1202(c) of the Code or (ii) deliver to such Investor such factual information in the Company's possession as is reasonably necessary to enable such Investor to determine whether (and what portion of) such Investor's interest in the Company constitutes "qualified small business stock" as defined in Section 1202(c) of the Code.

5.5 Matters Requiring Investor Director Approval. The Company hereby covenants and agrees with each of the Investors that it shall not, without approval of the Board of Directors, which approval must include the affirmative vote of a majority of the Investor Directors so long as there are any Investor Directors:

(a) make, or permit any subsidiary to make, any loan or advance to, or own any stock or other securities of, any subsidiary or other corporation, partnership or other entity, unless it is wholly owned by the Company;

(b) make, or permit any subsidiary to make, any loan or advance to any Person, including, without limitation, any employee or director of the Company or any subsidiary, except loans, advances and similar expenditures in the ordinary course of business or under the terms of an employee stock or option plan approved by the Board of Directors or that are permitted under Subsection 5.5(a) above;

(c) guarantee, directly or indirectly, or permit any subsidiary to guarantee, directly or indirectly, any indebtedness except for trade accounts of the Company or any subsidiary arising in the ordinary course of business;

(d) make any investment, other than investments in (1) prime commercial paper, (2) money market funds, (3) certificates of deposit in any United States bank having a net worth in excess of $100,000,000 or (4) obligations issued or guaranteed by the Unted States of America, in each case having a maturity not in excess of one year;

(e) incur any aggregate indebtedness in excess of $100,000 that is not already included in a budget approved by the Board of Directors, other than trade credit incurred in the ordinary course of business;

(f) otherwise enter into or be a party to any transaction with any director, officer, or employee of the Company or any "associate" (as defined in Rule 12b-2 promulgated under the Exchange Act) of any such Person, including without limitation any "management bonus" or similar plan providing payments to employees in connection with a Deemed Liquidation Event, as such term is defined in the Restated Certificate, except for the following: (1) transactions contemplated by this Agreement; (2) any grant or issuance of stock options or other equity incentives under any stock option plan or equity incentive plan approved by a majority of the Board of Directors; (3) any payments or benefits provided under any employee benefit plan approved by a majority of the Board of Directors; (4) payment of salary or other cash compensation to officers, directors or employees in amounts that have been approved by a majority of the Board of Directors, that are reflected in a budget approved by a majority of the Board of Directors or that are required or permitted to be paid pursuant to a written agreement to which the Company is a party; (4) transactions resulting in payments to or by the

Company in an aggregate amount less than $60,000 per year; or (5) transactions made in the ordinary course of business and pursuant to reasonable requirements of the Company's business and upon fair and reasonable terms that are approved by a majority of the Board of Directors;

(g) hire or terminate any of the executive officers of the Company, or change any of the compensation of (including approving the payment of bonues to) any of the executive officers unless contemplated in the Company's budget or any agreement between the Company and such executive officer;

(h) enter new lines of business that are not primarily related to the business of the Company as conducted as of the date of this Agreement, or exit the current line of business of the Company as conducted as of the date of this Agreement, or change the principal business of the Company;

(i) sell, assign, license, pledge, or encumber material technology or intellectual property, other than licenses granted in the ordinary course of business;

(j) the acquisition of all or substantially all of the properties, assets or stock of another company or entity; or

(k) increase the size of the Board of Directors of the Company above nine (9) members.

5.6 Board Matters. Unless otherwise determined by the vote of a majority of the directors then in office, the Board of Directors shall meet in person at least four (4) times per year in accordance with an agreed-upon schedule. The Company shall reimburse the directors for all reasonable out-of-pocket travel expenses incurred (consistent with the Company's travel policy) in connection with attending meetings of the Board of Directors, including committees thereof. The Company shall maintain an audit and compensation committee of the Board of Directors.

5.7 Successor Indemnification. If the Company or any of its successors or assignees consolidates with or merges into any other Person and is not the continuing or surviving corporation or entity of such consolidation or merger, then to the extent necessary, proper provision shall be made so that the successors and assignees of the Company assume the obligations of the Company with respect to indemnification of members of the Board of Directors as in effect immediately before such transaction, whether such obligations are contained in the Company's Bylaws, its Certificate of Incorporation, or elsewhere, as the case may be.

5.8 Indemnification Matters. The Company hereby acknowledges that one (1) or more of the directors nominated to serve on the Board of Directors by the Investors (each a "**Fund Director**") may have certain rights to indemnification, advancement of expenses and/or insurance provided by one or more of the Investors and certain of their affiliates (collectively, the "**Fund Indemnitors**"). The Company hereby agrees (a) that it is the indemnitor of first resort (*i.e.*, its obligations to any such Fund Director are primary and any obligation of the Fund Indemnitors to advance expenses or to provide indemnification for the same expenses or liabilities incurred by such Fund Director are secondary), (b) that it shall be required to advance

the full amount of expenses incurred by such Fund Director and shall be liable for the full amount of all expenses, judgments, penalties, fines and amounts paid in settlement by or on behalf of any such Fund Director to the extent legally permitted and as required by the Restated Certificate or By-laws of the Company (or any agreement between the Company and such Fund Director, each as may be amended an in effect from time to time), without regard to any rights such Fund Director may have against the Fund Indemnitors, and, (c) that it irrevocably waives, relinquishes and releases the Fund Indemnitors from any and all claims against the Fund Indemnitors for contribution, subrogation or any other recovery of any kind in respect thereof. The Company further agrees that no advancement or payment by the Fund Indemnitors on behalf of any such Fund Director with respect to any claim for which such Fund Director has sought indemnification from the Company shall affect the foregoing and the Fund Indemnitors shall have a right of contribution and/or be subrogated to the extent of such advancement or payment to all of the rights of recovery of such Fund Director against the Company.

5.9 FCPA. The Company represents that it shall not (and shall not permit any of its subsidiaries or affiliates or any of its or their respective directors, officers, managers, employees, independent contractors, representatives or agents to) promise, authorize or make any payment to, or otherwise contribute any item of value to, directly or indirectly, to any third party, including any Non-U.S. Official (as such term is defined in the U.S. Foreign Corrupt Practices Act of 1977, as amended (the "**FCPA**")), in each case, in violation of the FCPA, the U.K. Bribery Act, or any other applicable anti-bribery or anti-corruption law. The Company further represents that it shall (and shall cause each of its subsidiaries and affiliates to) cease all of its or their respective activities, as well as remediate any actions taken by the Company, its subsidiaries or affiliates, or any of their respective directors, officers, managers, employees, independent contractors, representatives or agents in violation of the FCPA, the U.K. Bribery Act, or any other applicable anti-bribery or anti-corruption law. The Company further represents that it shall (and shall cause each of its subsidiaries and affiliates to) maintain systems of internal controls (including, but not limited to, accounting systems, purchasing systems and billing systems) to ensure compliance with the FCPA, the U.K. Bribery Act, or any other applicable anti-bribery or anti-corruption law. Upon request, the Company agrees to provide responsive information and/or certifications concerning its compliance with applicable anti-corruption laws. The Company shall promptly notify each Investor if the Company becomes aware of any enforcement action. The Company shall, and shall cause any direct or indirect subsidiary or entity controlled by it, whether now in existence or formed in the future, to comply with the FCPA. The Company shall use its best efforts to cause any direct or indirect subsidiary, whether now in existence or formed in the future, to comply in all material respects with all applicable laws.

5.10 Termination of Covenants. The covenants set forth in this Section 5, except for Subsection 5.7 and Subsection 5.8, shall terminate and be of no further force or effect (i) immediately before the consummation of the IPO, (ii) when the Company first becomes subject to the periodic reporting requirements of Section 12(g) or 15(d) of the Exchange Act, or (iii) upon a Deemed Liquidation Event, as such term is defined in the Restated Certificate, whichever event occurs first.

6. Miscellaneous.

6.1 Successors and Assigns. The rights under this Agreement may be assigned (but only with all related obligations) by a Holder to a transferee of Registrable Securities that (i) is an Affiliate, partner, member, limited partner, retired or former partner or former or retired member or shareholder of such Holder, (ii) is such Holder's Immediate Family Member or is a trust for the benefit of such Holder or one or more of such Holder's Immediate Family Members, in either case if such Holder is an individual or (iii) after such transfer either holds at least 200,000 shares of Registrable Securities (subject to appropriate adjustment for stock splits, stock dividends, combinations, and other recapitalizations) or all of the Registrable Securities held by such Holder prior to such transfer; provided, however, that (x) the Company is, within a reasonable time after such transfer, furnished with written notice of the name and address of such transferee and the Registrable Securities with respect to which such rights are being transferred; and (y) such transferee becomes a party to this Agreement by executing and delivering an Adoption Agreement, substantially in the form attached hereto as Exhibit A, whereupon such transferee shall be deemed an "Investor" for all purposes of this Agreement and shall be bound by and subject to the terms and conditions of this Agreement that are applicable to Investors, including the provisions of Subsection 2.11. For the purposes of determining the number of shares of Registrable Securities held by a transferee, the holdings of shares of Registrable Securities of a transferee (1) that is an Affiliate or stockholder of a Holder; (2) who is a Holder's Immediate Family Member; or (3) that is a trust for the benefit of an individual Holder or such Holder's Immediate Family Member shall be aggregated together and with those shares of Registrable Securities of the transferring Holder; provided further that all transferees who would not qualify individually for assignment of rights shall have a single attorney-in-fact for the purpose of exercising any rights, receiving notices, or taking any action under this Agreement. The terms and conditions of this Agreement inure to the benefit of and are binding upon the respective successors and permitted

assignees of the parties. Nothing in this Agreement, express or implied, is intended to confer upon any person other than the parties hereto or their respective successors and permitted assignees any rights, remedies, obligations or liabilities under or by reason of this Agreement, except as expressly provided herein.

6.2 Governing Law. This Agreement and any controversy arising out of or relating to this Agreement shall be governed by and construed in accordance with the internal laws of the State of Delaware, without regard to conflict of law principles that would result in the application of any law other than the law of the State of Delaware.

6.3 Counterparts. This Agreement may be executed in two (2) or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument. Counterparts may be delivered via facsimile, electronic mail (including pdf or any electronic signature complying with the federal ESIGN Act of 2000, e.g., www.docusign.com) or other transmission method and any counterpart so delivered shall be deemed to have been duly and validly delivered and be valid and effective for all purposes.

6.4 Titles and Subtitles. The titles and subtitles used in this Agreement are for convenience only and are not to be considered in construing or interpreting this Agreement.

6.5 Notices. All notices and other communications given or made pursuant to this Agreement shall be in writing and shall be deemed effectively given upon the earlier of actual receipt or (i) personal delivery to the party to be notified; (ii) when sent, if sent by

electronic mail or facsimile during the recipient's normal business hours, and if not sent during normal business hours, then on the recipient's next business day; (iii) five (5) days after having been sent by registered or certified mail, return receipt requested, postage prepaid; or (iv) one (1) business day after the business day of deposit with a nationally recognized overnight courier, freight prepaid, specifying next-day delivery, with written verification of receipt. All communications shall be sent to the respective parties only at their addresses as set forth on Schedule A hereto, or to the principal office of the Company and to the attention of the Chief Executive Officer, in the case of the Company, or to such email address, facsimile number, or address as subsequently modified by written notice given in accordance with this Subsection 6.5. If notice is given to the Company, it shall be sent to

Rhythm Pharmaceuticals, Inc.
500 Boylston Street
11th Floor
Boston, MA 02116
Attention: Keith Gottesdiener, Chief Executive Officer

and a copy (which shall not constitute notice) to:

Morgan, Lewis & Bockius LLP
One Federal Street
Boston, MA 02110
Attention: Julio E. Vega, Esq.
Fax No.: (617) 951-8736

If notice is given to any of the Investors, a copy (which shall not constitute notice) also shall be sent to the party designated as the notice party by such Investor on Schedule A.

6.6 Amendments and Waivers. Any term of this Agreement may be amended and the observance of any term of this Agreement may be waived (either generally or in a particular instance, and either retroactively or prospectively) only with the written consent of the Company and the holders of a majority of the Registrable Securities then outstanding and held by the Holders; provided that (i) the Company may in its sole discretion waive compliance with Subsection 2.12; (ii) any provision hereof may be waived by any waiving party on such party's own behalf, without the consent of any other party; and (iii) Subsection 3.3 shall not be amended or waived with respect to the observer rights of OrbiMed, Baker, Deerfield, Wellington, NEA or Pfizer without the written consent of such Holder for so long as such Holder is entitled to exercise such rights set forth in Subsection 3.3. Notwithstanding the foregoing, (x) this Agreement may not be amended or terminated and the observance of any term hereof may not be waived with respect to any Investor without the written consent of such Investor, unless such amendment, termination, or waiver applies to all Investors in the same fashion (it being agreed that a waiver of the provisions of Section 4 with respect to a particular transaction shall be deemed to apply to all Investors in the same fashion if such waiver does so by its terms, notwithstanding the fact that certain Investors may nonetheless, by agreement with the Company, purchase securities in such transaction), and (y) Schedule A attached hereto may be amended by written instrument executed by the Company without the consent, approval or agreement of any Investor if any such amendment is solely for purposes of reflecting any permitted assignment or

transfer in accordance with Subsection 6.1 hereof or any person that hereafter becomes a party to this Agreement pursuant to any of Subsections 6.1 and 6.9 hereof. The Company shall give prompt notice of any amendment or termination hereof or waiver hereunder to any party hereto that did not consent in writing to such amendment, termination, or waiver. Any amendment, termination, or waiver effected in accordance with this Subsection 6.6 shall be binding on all parties hereto, regardless of whether any such party has consented thereto. No waivers of or exceptions to any term, condition, or provision of this Agreement, in any one or more instances, shall be deemed to be or construed as a further or continuing waiver of any such term, condition, or provision.

6.7 Severability. In case any one or more of the provisions contained in this Agreement is for any reason held to be invalid, illegal or unenforceable in any respect, such invalidity, illegality, or unenforceability shall not affect any other provision of this Agreement, and such invalid, illegal, or unenforceable provision shall be reformed and construed so that it will be valid, legal, and enforceable to the maximum extent permitted by law.

6.8 Aggregation of Stock. All shares of Registrable Securities held or acquired by Affiliates shall be aggregated together for the purpose of determining the availability of any rights under this Agreement and such Affiliated persons may apportion such rights as among themselves in any manner they deem appropriate.

6.9 Additional Investors. Notwithstanding anything to the contrary contained herein, if the Company issues additional shares of Preferred Stock after the date hereof, any purchaser or acquiror of such shares of Preferred Stock may become a party to this Agreement by executing and delivering an Adoption Agreement, substantially in the form attached hereto as Exhibit A, and thereafter shall be deemed an "Investor" for all purposes hereunder. No action or consent by the Investors shall be required for such joinder to this Agreement by such additional Investor, so long as such additional Investor has agreed in writing to be bound by all of the obligations as an "Investor" hereunder.

6.10 Entire Agreement. This Agreement (including any Schedules and Exhibits hereto) constitutes the full and entire understanding and agreement among the parties with respect to the subject matter hereof, and any other written or oral agreement relating to the subject matter hereof existing between the parties is expressly canceled, including, without limitation, the Prior Agreement.

6.11 Dispute Resolution. The parties (a) hereby irrevocably and unconditionally submit to the jurisdiction of the state courts of the State of Delaware and to the jurisdiction of the United States District Court for the District of Delaware for the purpose of any suit, action or other proceeding arising out of or based upon this Agreement, (b) agree not to commence any suit, action or other proceeding arising out of or based upon this Agreement except in the state courts of the State of Delaware or the United States District Court for the District of Delaware, and (c) hereby waive, and agree not to assert, by way of motion, as a defense, or otherwise, in any such suit, action or proceeding, any claim that it is not subject personally to the jurisdiction of the above-named courts, that its property is exempt or immune from attachment or execution, that the suit, action or proceeding is brought in an inconvenient

forum, that the venue of the suit, action or proceeding is improper or that this Agreement or the subject matter hereof may not be enforced in or by such court.

6.12 Waiver of Jury Trial. EACH PARTY HEREBY WAIVES ITS RIGHTS TO A JURY TRIAL OF ANY CLAIM OR CAUSE OF ACTION BASED UPON OR ARISING OUT OF THIS AGREEMENT, THE OTHER TRANSACTION DOCUMENTS, THE SECURITIES OR THE SUBJECT MATTER HEREOF OR THEREOF. THE SCOPE OF THIS WAIVER IS INTENDED TO BE ALL-ENCOMPASSING OF ANY AND ALL DISPUTES THAT MAY BE FILED IN ANY COURT AND THAT RELATE TO THE SUBJECT MATTER OF THIS TRANSACTION, INCLUDING, WITHOUT LIMITATION, CONTRACT CLAIMS, TORT CLAIMS (INCLUDING NEGLIGENCE), BREACH OF DUTY CLAIMS, AND ALL OTHER COMMON LAW AND STATUTORY CLAIMS. THIS SECTION HAS BEEN FULLY DISCUSSED BY EACH OF THE PARTIES HERETO AND THESE PROVISIONS WILL NOT BE SUBJECT TO ANY EXCEPTIONS. EACH PARTY HERETO HEREBY FURTHER WARRANTS AND REPRESENTS THAT SUCH PARTY HAS REVIEWED THIS WAIVER WITH ITS LEGAL COUNSEL, AND THAT SUCH PARTY KNOWINGLY AND VOLUNTARILY WAIVES ITS JURY TRIAL RIGHTS FOLLOWING CONSULTATION WITH LEGAL COUNSEL.

6.13 Delays or Omissions. No delay or omission to exercise any right, power, or remedy accruing to any party under this Agreement, upon any breach or default of any other party under this Agreement, shall impair any such right, power, or remedy of such nonbreaching or nondefaulting party, nor shall it be construed to be a waiver of or acquiescence to any such breach or default, or to any similar breach or default thereafter occurring, nor shall any waiver of any single breach or default be deemed a waiver of any other breach or default theretofore or thereafter occurring. All remedies, whether under this Agreement or by law or otherwise afforded to any party, shall be cumulative and not alternative.

6.14 Acknowledgment. The Company acknowledges that the Investors are in the business of venture capital investing and therefore review the business plans and related proprietary information of many enterprises, including enterprises which may have products or services which compete directly or indirectly with those of the Company. Nothing in this Agreement shall preclude or in any way restrict the Investors from investing or participating in any particular enterprise whether or not such enterprise has products or services which compete with those of the Company.

[Remainder of Page Intentionally Left Blank]

IN WITNESS WHEREOF, the parties have executed this Agreement as of the date first above written.

COMPANY:

RHYTHM PHARMACEUTICALS, INC.

By: /s/ Keith M. Gottesdiener
Name: Keith M. Gottesdiener
Title: Chief Executive Officer

SIGNATURE PAGE TO AMENDED AND RESTATED INVESTORS' RIGHTS AGREEMENT

INITIAL INVESTORS:

ORBIMED PRIVATE INVESTMENTS V, LP

By: OrbiMed Capital GP V LLC,
Its General Partner

By: OrbiMed Advisors LLC,

Its Managing Member

By: /s/ Jonathan Silverstein
Name: Jonathan Silverstein
Title: Member

INITIAL INVESTORS:

667, L.P.

By: Baker Bros. Advisors LP, management company and investment adviser to 667, L.P., pursuant to authority granted to it by Baker Biotech Capital, L.P., general partner to 667, L.P., and not as the general partner.

By: /s/ Scott Lessing
Name: Scott Lessing
Title: President

BAKER BROTHERS LIFE SCIENCES, L.P.

By: Baker Bros. Advisors LP, management company and investment adviser to Baker Brothers Life Sciences, L.P., pursuant to authority granted to it by Baker Brothers Life Sciences Capital, L.P., general partner to Baker Brothers Life Sciences, L.P., and not as the general partner.

By: /s/ Scott Lessing
Name: Scott Lessing
Title: President

INITIAL INVESTORS:

Hadley Harbor Master Investors (Cayman) L.P.

By: Wellington Management Company LLP, as investment adviser

By: /s/ Emily D. Babalas
Name: Emily D. Babalas
Title: Managing Director and Counsel

INITIAL INVESTORS:

DEERFIELD SPECIAL SITUATIONS FUND, L.P.

By: Deerfield Mgmt, L.P.
General Partner

By: J.E. Flynn Capital, LLC
General Partner

By: /s/ David J. Clark
Name: David J. Clark
Title: Authorized Signatory

DEERFIELD PRIVATE DESIGN FUND III, L.P.

By: Deerfield Mgmt III, L.P.
General Partner

By: J.E. Flynn Capital III, LLC
General Partner

By: /s/ David J. Clark
Name: David J. Clark
Title: Authorized Signatory

SIGNATURE PAGE TO AMENDED AND RESTATED INVESTORS' RIGHTS AGREEMENT

INITIAL INVESTORS:

NEW ENTERPRISE ASSOCIATES 13, L.P.

By: NEA Partners 13, L.P., its general partner
By: NEA 13 GP, LTD, its general partner

By: /s/ Louis S. Citron
Name: Louis S. Citron
Title: Chief Legal Officer

NEA VENTURES 2009, LIMITED PARTNERSHIP

By: /s/ Louis S. Citron
Name: Louis S. Citron
Title: Vice-President

SIGNATURE PAGE TO AMENDED AND RESTATED INVESTORS' RIGHTS AGREEMENT

INITIAL INVESTORS:

MPM BIOVENTURES V, L.P.

By: MPM BIOVENTURES V GP LLC, its General Partner

By: MPM BIOVENTURES V LLC, its Managing Member

By: /s/ Todd Foley
Name: Todd Foley
Title: Member

MPM ASSET MANAGEMENT INVESTORS BV5 LLC

By: MPM BIOVENTURES V LLC, its Manager

By: /s/ Todd Foley
Name: Todd Foley
Title: Member

SIGNATURE PAGE TO AMENDED AND RESTATED INVESTORS' RIGHTS AGREEMENT

INITIAL INVESTORS:

PFIZER INC.

By: /s/ Barbara Dalton
Name: Barbara Dalton
Title: Vice President, Venture Capital
Worldwide Business Development

INITIAL INVESTORS:

THIRD ROCK VENTURES, LP

By: Third Rock Ventures GP, L.P., its general partner

By: TRV GP, LLC, its general partner

By: /s/ Kevin Gillis
Name: Kevin Gillis
Title: CFO

SIGNATURE PAGE TO AMENDED AND RESTATED INVESTORS' RIGHTS AGREEMENT

INITIAL INVESTORS:

SUTREPA SAS

By: /s/ Olivier Jochem
Name: Olivier Jochem
Title: President

SIGNATURE PAGE TO AMENDED AND RESTATED INVESTORS' RIGHTS AGREEMENT

INITIAL INVESTORS:

RHYTHM HOLDING COMPANY, LLC

By: /s/ Keith Gottesdiener
Name Keith Gottesdiener
Title: Chief Executive Officer

SIGNATURE PAGE TO AMENDED AND RESTATED INVESTORS' RIGHTS AGREEMENT

INITIAL INVESTORS:

/s/ David Meeker
David Meeker

SIGNATURE PAGE TO AMENDED AND RESTATED INVESTORS' RIGHTS AGREEMENT

INITIAL INVESTORS:

/s/ Keith Gottesdiener
Keith Gottesdiener

SIGNATURE PAGE TO AMENDED AND RESTATED INVESTORS' RIGHTS AGREEMENT

INITIAL INVESTORS:

/s/ Bart Henderson
Bart Henderson

SIGNATURE PAGE TO AMENDED AND RESTATED INVESTORS' RIGHTS AGREEMENT

SCHEDULE A

INITIAL INVESTORS

Name and Address	Number of Shares of Series A Preferred Stock
OrbiMed Private Investments V, LP 601 Lexington Avenue, 54th Floor New York, NY 10022 Attention: Jonathan Silverstein Email:SilversteinJ@OrbiMed.com With a copy (which shall not constitute notice) to: Sidley Austin LLP 787 Seventh Avenue New York, New York 10019 Attention: Geoffrey W. Levin, Esq. Email:glevin@sidley.com	23,349,531
667, L.P. 667 Madison Avenue, 21st Floor New York, NY 10065 Attention: Scott L. Lessing Email: slessing@bbinvestments.com	760,829
Baker Brothers Life Sciences, L.P. 667 Madison Avenue, 21st Floor New York, NY 10065 Attention: Scott L. Lessing Email: slessing@bbinvestments.com	9,913,242
ItalianFlare & Co. c/o Wellington Management Company LLP 280 Congress Street Boston, MA 02210 Attention: Steven M. Hoffman Email: seclaw@wellington.com	5,000,000
Deerfield Private Design Fund III, L.P. c/o Deerfield Management Company, L.P. Attn: Lawrence Atinsky 780 Third Ave., 37th Fl. New York, NY 10017 latinsky@deerfield.com	2,668,518
Deerfield Special Situations Fund, L.P. c/o Deerfield Management Company, L.P. Attn: Lawrence Atinsky 780 Third Ave., 37th Fl. New York, NY 10017 latinsky@deerfield.com	2,668,518
New Enterprise Associates 13, L.P. c/o New Enterprise Associates 1954 Greenspring Drive, Suite 600 Timonium, MD 21093	12,864,324
MPM Bioventures V, L.P. c/o MPM Capital LLC 450 Kendall Street Cambridge, MA 02142	7,365,688

MPM Asset Management Investors BV5 LLC c/o MPM Capital LLC 450 Kendall Street Cambridge, MA 02142	286,143
Pfizer Inc. 235 East 42nd Street New York, NY 10017 Attn: Barbara Dalton	4,103,704
Third Rock Ventures, L.P. 29 Newbury Street Boston, MA 02116	9,479,502
Sutrepa SAS 65 quai Georges Gorse 92100 Boulogne- Billancourt, France Attn: Olivier Jochem	1,540,000
David Meeker 20 Garland Road Lincoln, MA 01773	500,000
Keith Gottesdiener c/o Rhythm Pharmaceuticals, Inc. 500 Boylston Street	250,000

11th Floor Boston, MA 02116	
Bart Henderson 48 Prentiss Lane Belmont, MA 02478	200,000

Name and Address	**Number of Shares of Series A-1 Junior Preferred Stock**
Rhythm Holding Company LLC 500 Boylston Street 11th Floor Boston, MA 02116	78,666,209

Name and Address	**Number of Shares of Common Stock**
Rhythm Holding Company LLC 500 Boylston Street 11th Floor Boston, MA 02116	14,833,791
David Meeker 20 Garland Road Lincoln, MA 01773	200,000

EXHIBIT A

ADOPTION AGREEMENT

This Adoption Agreement ("**Adoption Agreement**") is executed on [ ], by the undersigned (the "**Holder**") pursuant to the terms of that certain Amended and Restated Investors' Rights Agreement dated as of August 21, 2017 (the "**Agreement**"), by and among the Company and certain holders of securities of the Company, as such Agreement may be amended or amended and restated hereafter. Capitalized terms used but not defined in this Adoption Agreement shall have the respective meanings ascribed to such terms in the Agreement. By the execution of this Adoption Agreement, the Holder agrees as follows.

1.1 Acknowledgement. Holder acknowledges that Holder is acquiring certain Registrable Securities of the Company, and desires to become an Investor party to the Agreement with respect to such Registrable Securities.

1.2 Agreement. Holder hereby (a) agrees that the Registrable Securities and any other securities of the Company required by the Agreement to be bound thereby, shall be bound by and subject to the terms of the Agreement and (b) adopts the Agreement with the same force and effect as if Holder were originally an Investor party thereto.

1.3 Notice. Any notice required or permitted by the Agreement shall be given to Holder at the address or facsimile number listed below Holder's signature hereto.

[Signature Page to Follow]

IN WITNESS WHEREOF, the parties have executed this Adoption Agreement as of the date first above written.

HOLDER: _____

By: _____
Name:
Title:

Address:

Facsimile Number:

ACCEPTED AND AGREED:

RHYTHM PHARMACEUTICALS, INC.

By: _____
Name:
Title:

Exhibit 10.3

6Rhythm Pharmaceuticals, Inc.
500 Boylston Street — 11th Floor
Boston, MA 02116
Main Telephone: 617-585-2090
www.rhythmtx.com

November 16, 2016

Bart Henderson
c/o Rhythm Pharmaceuticals
500 Boylston Street, 11th Floor
Boston, MA 02116

Dear Bart:

On behalf of Rhythm Pharmaceuticals, Inc., formerly known as Rhythm Metabolic, Inc. (the "Company" or "Rhythm"), I am pleased to set forth below the terms of your employment with the Company.

Employment. You are currently the President of the Company but are an employee of Motus Therapeutics, Inc., an affiliate of the Company ("Motus"). Your employment with Motus will terminate, and your employment with the Company will begin, on November 16, 2016 (the "Start Date"). During the term of your employment with the Company, you will continue to hold the position and title of President, reporting to the Chief Executive Officer. While your employment is with the Company, you will also hold the title of President of Rhythm Holding Company, LLC (the "Parent") and Motus. During the term of your employment with the Company, you will be responsible for performing the duties associated with the position above or as the Company may otherwise assign to you. Your primary place of employment will initially be in the Company's offices located in Boston, Massachusetts; however, you will be expected to travel as may be necessary to fulfill your responsibilities. In the course of your employment with Company, you will be subject to, and required to comply with, all company policies and all applicable laws and regulations.

Base Salary. During your employment, your salary will be $335,000 annualized, subject to all required and elected taxes and other withholdings. Your salary may be adjusted from time to time in accordance with normal business practice and in the sole discretion of the Company.

Annual Target Cash Incentive. Following the end of each fiscal year and subject to the approval by the Company's Board of Directors, you will be eligible to earn a performance and retention bonus, based on your performance and the Company's performance, each during the applicable fiscal year, and your continued employment in good standing on the date of incentive distribution. Your target annual incentive opportunity is 50% of your annualized base salary.

Equity Grant. Any existing grants of equity you have in the Parent or the Company will be treated consistent with the terms of the applicable agreements under which such awards have been granted. You may be awarded additional equity grants from time to time in accordance with normal business practice and in the sole discretion of the Company's Board of Directors or the Parent's Board of Managers, as the case may be. The terms of any future equity grant will be consistent with any plan under which they are granted and the terms of the applicable agreement under which the award(s) are granted.

Benefits. You may participate in any and all benefit programs that the Company establishes and makes available to its employees from time to time, subject to the terms and conditions of those programs. The Company's benefits programs are subject to change at any time in the Company's sole discretion. You currently are eligible to receive reimbursement from the Company for the actual amounts of your medical insurance premiums for yourself and your eligible dependents, until such time as the Company establishes a medical insurance plan.

Vacation. You will be entitled to such annual paid vacation as may be offered or made available by the Company from time to time to its employees. Your accrual and use of vacation time will be pursuant to any vacation or time off policy the Company may establish or modify from time to time. The Company's vacation policy is subject to change at any time in the Company's sole discretion.

Severance. If the Company terminates your employment without Cause (as defined below) or you resign your employment with the Company for Good Reason (as defined below) (in either event, a "Qualifying Termination"), subject to your execution of a release acceptable to the Company (the "Release"), the expiration of any revocation period provided in the Release and your continued compliance with the terms of the NDA (as defined below), the Company will pay you an amount equal to your then-current base salary rate for a period of six (6) months (the "Regular Severance Amount").

If there is a Qualifying Termination within the three (3) months immediately preceding or the twelve (12) months immediately following a "Sale of the Company" (as such term is defined in the Operating Agreement of the Parent, as amended and in effect from time to time), subject to your execution of a Release following your Separation from Service (as defined below), the expiration of any revocation period provided in the Release and your continued compliance with the terms of the NDA, in lieu of any Regular Severance Amount, the Company will pay you an amount equal to your then-current base salary rate for a period of twelve (12) months (the "Sale of the Company Severance Amount") plus an amount equal to 100% of your annual target cash incentive.

Notwithstanding anything express or implied in this letter to the contrary, if your employment with the Company is terminated by the Company or you at any time prior to or after a Sale of the Company and at the time of such termination you are offered employment on the same terms with either Parent or any

subsidiary of Parent and neither Parent nor such subsidiary is at that time itself subject to a Sale of the Company, then the termination of your employment with the Company shall not be deemed or treated as a Qualifying Termination for any purposes of this letter.

Any severance amount to which you may be entitled under this letter will be paid in substantially equal installments in accordance with the Company's ordinary payroll practices, beginning on the first payroll date following the date that is either (i) 60 days after the date of your Separation from Service, or (ii) in the case of a Separation from Service that is a Qualifying Termination that occurs within the three (3)

months immediately preceding a Sale of the Company, 60 days after the date of such Sale of the Company. To be eligible for either the Regular Severance Amount or the Sale of the Company Severance Amount, as applicable, you must execute and deliver the Release to the Company and allow it to become effective within 30 days of your Separation from Service or, if later, a Sale of the Company giving rise to a Sale of the Company Severance Amount entitlement.

In addition, if following your Separation from Service, you are eligible for and timely elect continued medical insurance coverage pursuant to COBRA, the Company will reimburse you for the applicable premiums for you and your eligible dependents during the period commencing on the date of your Separation from Service and ending on the earlier to occur of (a) the final day of the Severance Period and (b) the date you otherwise become ineligible for continued coverage under COBRA. Notwithstanding the foregoing, if the Company determines that it cannot provide such reimbursement of premiums to you without potentially violating applicable law, the Company shall not be obligated to make any such payments or reimbursements to you.

If the Qualifying Termination occurs within the three (3) months immediately preceding or the twelve (12) months immediately following a Sale of the Company, then each outstanding equity award in the Parent or the Company held by you shall immediately vest and, if applicable, become exercisable with respect to one hundred percent (100%) of the shares of equity of the Parent or the Company subject thereto. The foregoing provisions of this paragraph shall apply notwithstanding anything express or implied to the contrary in any agreement or award between you and the Company or the Parent, or in any plan of the Company or the Parent, that is applicable to such outstanding equity award.

Notwithstanding anything herein to the contrary, in the event that any compensation or benefit that constitutes "nonqualified deferred compensation" within the meaning of Section 409A of the Internal Revenue Code of 1986, as amended (the "Code"), becomes payable upon the occurrence of a Sale of the Company, such compensation or benefit shall not be paid unless such Sale of the Company constitutes a "change in control event" within the meaning of Section 409A of the Code.

If any payment or benefit you would receive under this letter, when combined with any other payment or benefit you receive pursuant to the termination of your employment with the Company ("Payment") would (i) constitute a "parachute payment" within the meaning of Section 280G of the Code, and (ii) but for this sentence, be subject to the excise tax imposed by Section 4999 of the Code (the "Excise Tax"), then such Payment shall be either (x) the full amount of such Payment or (y) such lesser amount (with your choice of whether to reduce cash payments or stock option compensation or both) as would result in no portion of the Payment being subject to the Excise Tax, whichever of the foregoing amounts, taking into account the applicable federal, state and local employment taxes, income taxes and the Excise Taxes results in your receipt, on an after-tax basis, of the greater amount of the Payment notwithstanding that all or some portion of the Payment may be subject to the Excise Tax.

Definitions

Separation from Service. For purposes of this letter, "Separation from Service" means a "separation from service" within the meaning of Section 409A of the Code. Each installment payment provided under this letter shall at all times be considered a separate and distinct payment for purposes of Section 409A of the Code. Notwithstanding anything in this letter to the contrary, to the extent required to avoid a

prohibited distribution under Section 409A of the Code, the benefits provided under this letter will not be provided to you until the earlier of (a) the expiration of the six-month period measured from the date of your Separation from Service with the Company or (b) the date of your death. Upon the first business day after expiration of the relevant period, all payments delayed pursuant to the preceding sentence will be paid in a lump sum and any remaining payments due will be paid as otherwise provided herein.

Cause. "Cause" shall mean the occurrence of any of the following events by the individual: (i) commission of any crime involving the Company, or any crime involving fraud, breach of trust, or physical or emotional harm to any person, moral turpitude or dishonesty; (ii) any unauthorized use or disclosure of the Company's proprietary information (other than any such use or disclosure that is not intentional and is not material); (iii) any intentional misconduct or gross negligence that has a material adverse effect on the Company's business or reputation; (iv) any material breach by you of any agreement between you and the Company that is not cured within thirty (30) days after receipt of written notice from the Company describing any such breach; or (v) repeated and willful failure to perform the duties, functions and responsibilities of the individual's position after a written warning from the Company.

Good Reason. "Good Reason" shall mean your resignation from all positions you then hold with the Company if: (A) without your written consent (i) there is a material diminution in the nature or scope of your authorities, duties, or authority; (ii) there is a material reduction of your base salary; provided, however, that a material reduction in your base salary pursuant to a salary reduction program affecting all or substantially all of the employees of the Company and that does not adversely affect you to a greater extent than other similarly situated employees shall not constitute Good Reason; or (iii) you are required to relocate your primary work location to a facility or location that would increase your one way commute distance by more than thirty-five (35) miles from your primary work location as of immediately prior to such change, (B) you provide written notice outlining such conditions, acts or omissions to the Company's Chief Executive Officer, Chief Financial Officer or General Counsel within thirty (30) days immediately following such material change or reduction, (C) such material change or reduction is not remedied by the Company within thirty (30) days following the Company's receipt of such written notice and (D) your resignation is effective not later than thirty (30) days after the expiration of such thirty (30) day cure period. "Good Reason" shall also mean your resignation on the one year anniversary of a Sale of the Company from all positions you then hold with the Company or its successor if by that date you have not entered into a written letter or agreement with the Company or such successor that provides for your continued employment with the Company or such successor. For purposes of clarification, any Qualifying Termination that occurs on the first anniversary of a Sale of the Company shall be deemed and treated as occurring within the twelve (12) months immediately following a Sale of the Company for all purposes of this letter.

Invention, Non-Disclosure, Non-Competition and Non-Solicitation Obligations. At or prior to the Start Date, you will be required to execute and deliver the Company's standard form of Employee Confidentiality, Assignment of Inventions, Non-Competition and Non-Solicitation Agreement (the "NDA"), a copy of which has been or will be provided to you separately.

At-Will Employment. This letter shall not be construed as an agreement, either express or implied, to employ you for any stated term, and shall in no way alter the Company's policy of employment at-will. Similarly, nothing in this letter shall be construed as an agreement, either express or implied, to pay you

any compensation or grant you any benefit beyond the end of your employment with the Company, except as otherwise explicitly set forth in this letter. This letter supersedes all prior understandings, whether written or oral, including, without limitation, your current employment agreement, with respect to the subject matter of this letter.

Please indicate your acceptance of this letter agreement by signing below in the space provided for your signature.

Sincerely,

/s/ Keith Gottesdiener
Keith Gottesdiener
Chief Executive Officer

The foregoing correctly sets forth the terms of my at-will employment with the Company. I am not relying on any representations other than those set forth above.

/s/ Bart Henderson	11/16/16
Bart Henderson	Date

Rhythm Pharmaceuticals, Inc.
500 Boylston Street — 11th Floor
Boston, MA 02116
Main Telephone: 617-585-2090
www.rhythmtx.com

November 16, 2016

Keith M. Gottesdiener, M.D.
c/o Rhythm Pharmaceuticals
500 Boylston Street, 11th Floor
Boston, MA 02116

Dear Keith:

On behalf of Rhythm Pharmaceuticals, Inc., formerly known as Rhythm Metabolic, Inc. (the "Company" or "Rhythm"), I am pleased to set forth below the terms of your employment with the Company.

Employment. You are currently the Chief Executive Officer of the Company but are an employee of Motus Therapeutics, Inc., an affiliate of the Company ("Motus"). Your employment with Motus will terminate, and your employment with the Company will begin, on November 16, 2016 (the "Start Date"). During the term of your employment with the Company, you will continue to hold the position and title of Chief Executive Officer. While your employment is with the Company, you will also hold the title of Chief Executive Officer of each of Rhythm Holding Company, LLC (the "Parent") and Motus. During the term of your employment with the Company, you will be responsible for performing the duties associated with the position above or as the Company may otherwise assign to you. Your primary place of employment will initially be in the Company's offices located in Boston, Massachusetts; however, you will be expected to travel as may be necessary to fulfill your responsibilities. In the course of your employment with Company, you will be subject to, and required to comply with, all company policies and all applicable laws and regulations.

Base Salary. During your employment, your salary will be $476,500 annualized, subject to all required and elected taxes and other withholdings. Your salary may be adjusted from time to time in accordance with normal business practice and in the sole discretion of the Company.

Annual Target Cash Incentive. Following the end of each fiscal year and subject to the approval by the Company's Board of Directors, you will be eligible to earn a performance and retention bonus, based on your performance and the Company's performance, each during the applicable fiscal year, and your continued employment in good standing on the date of incentive distribution. Your target annual incentive opportunity is 50% of your annualized base salary.

Equity Grant. Any existing grants of equity you have in the Parent or the Company will be treated consistent with the terms of the applicable agreements under which such awards have been granted. You may be awarded additional equity grants from time to time in accordance with normal business practice and in the sole discretion of the Company's Board of Directors or the Parent's Board of Managers, as the case may be. The terms of any future equity grant will be consistent with any plan under which they are granted and the terms of the applicable agreement under which the award(s) are granted.

Benefits. You may participate in any and all benefit programs that the Company establishes and makes available to its employees from time to time, subject to the terms and conditions of those programs. The Company's benefits programs are subject to change at any time in the Company's sole discretion. You currently are eligible to receive reimbursement from the Company for the actual amounts of your medical insurance premiums for yourself and your eligible dependents, until such time as the Company establishes a medical insurance plan.

Vacation. You will be entitled to such annual paid vacation as may be offered or made available by the Company from time to time to its employees. Your accrual and use of vacation time will be pursuant to any vacation or time off policy the Company may establish or modify from time to time. The Company's vacation policy is subject to change at any time in the Company's sole discretion.

Severance. If the Company terminates your employment without Cause (as defined below) or you resign your employment with the Company for Good Reason (as defined below) (in either event, a "Qualifying Termination"), subject to your execution of a release acceptable to the Company (the "Release"), the expiration of any revocation period provided in the Release and your continued compliance with the terms of the NDA (as defined below), the Company will pay you an amount equal to your then-current base salary rate for a period of twelve (12) months (the "Regular Severance Amount").

If there is a Qualifying Termination within the three (3) months immediately preceding or the twelve (12) months immediately following a "Sale of the Company" (as such term is defined in the Operating Agreement of the Parent, as amended and in effect from time to time), subject to your execution of a Release following your Separation from Service (as defined below), the expiration of any revocation period provided in the Release and your continued compliance with the terms of the NDA, in lieu of any Regular Severance Amount, the Company will pay you an amount equal to your then-current base salary rate for a period of twelve (12) months (the "Sale of the Company Severance Amount") plus an amount equal to 100% of your annual target cash incentive.

Notwithstanding anything express or implied in this letter to the contrary, if your employment with the Company is terminated by the Company or you at any time prior to or after a Sale of the Company and at the time of such termination you are offered employment on the same terms with either Parent or any

subsidiary of Parent and neither Parent nor such subsidiary is at that time itself subject to a Sale of the Company, then the termination of your employment with the Company shall not be deemed or treated as a Qualifying Termination for any purposes of this letter.

Any severance amount to which you may be entitled under this letter will be paid in substantially equal installments in accordance with the Company's ordinary payroll practices, beginning on the first payroll date following the date that is either (i) 60 days after the date of your Separation from Service, or (ii) in the case of a Separation from Service that is a Qualifying Termination that occurs within the three (3)

months immediately preceding a Sale of the Company, 60 days after the date of such Sale of the Company. To be eligible for either the Regular Severance Amount or the Sale of the Company Severance Amount, as applicable, you must execute and deliver the Release to the Company and allow it to become effective within 30 days of your Separation from Service or, if later, a Sale of the Company giving rise to a Sale of the Company Severance Amount entitlement.

In addition, if following your Separation from Service, you are eligible for and timely elect continued medical insurance coverage pursuant to COBRA, the Company will reimburse you for the applicable premiums for you and your eligible dependents during the period commencing on the date of your Separation from Service and ending on the earlier to occur of (a) the final day of the Severance Period and (b) the date you otherwise become ineligible for continued coverage under COBRA. Notwithstanding the foregoing, if the Company determines that it cannot provide such reimbursement of premiums to you without potentially violating applicable law, the Company shall not be obligated to make any such payments or reimbursements to you.

If the Qualifying Termination occurs within the three (3) months immediately preceding or the twelve (12) months immediately following a Sale of the Company, then each outstanding equity award in the Parent or the Company held by you shall immediately vest and, if applicable, become exercisable with respect to one hundred percent (100%) of the shares of equity of the Parent or the Company subject thereto. The foregoing provisions of this paragraph shall apply notwithstanding anything express or implied to the contrary in any agreement or award between you and the Company or the Parent, or in any plan of the Company or the Parent, that is applicable to such outstanding equity award.

Notwithstanding anything herein to the contrary, in the event that any compensation or benefit that constitutes "nonqualified deferred compensation" within the meaning of Section 409A of the Internal Revenue Code of 1986, as amended (the "Code"), becomes payable upon the occurrence of a Sale of the Company, such compensation or benefit shall not be paid unless such Sale of the Company constitutes a "change in control event" within the meaning of Section 409A of the Code.

If any payment or benefit you would receive under this letter, when combined with any other payment or benefit you receive pursuant to the termination of your employment with the Company ("Payment") would (i) constitute a "parachute payment" within the meaning of Section 280G of the Code, and (ii) but for this sentence, be subject to the excise tax imposed by Section 4999 of the Code (the "Excise Tax"), then such Payment shall be either (x) the full amount of such Payment or (y) such lesser amount (with your choice of whether to reduce cash payments or stock option compensation or both) as would result in no portion of the Payment being subject to the Excise Tax, whichever of the foregoing amounts, taking into account the applicable federal, state and local employment taxes, income taxes and the Excise Taxes results in your receipt, on an after-tax basis, of the greater amount of the Payment notwithstanding that all or some portion of the Payment may be subject to the Excise Tax.

Definitions

Separation from Service. For purposes of this letter, "Separation from Service" means a "separation from service" within the meaning of Section 409A of the Code. Each installment payment provided under this letter shall at all times be considered a separate and distinct payment for purposes of Section 409A of the Code. Notwithstanding anything in this letter to the contrary, to the extent required to avoid a

prohibited distribution under Section 409A of the Code, the benefits provided under this letter will not be provided to you until the earlier of (a) the expiration of the six-month period measured from the date of your Separation from Service with the Company or (b) the date of your death. Upon the first business day after expiration of the relevant period, all payments delayed pursuant to the preceding sentence will be paid in a lump sum and any remaining payments due will be paid as otherwise provided herein.

Cause. "Cause" shall mean the occurrence of any of the following events by the individual: (i) commission of any crime involving the Company, or any crime involving fraud, breach of trust, or physical or emotional harm to any person, moral turpitude or dishonesty; (ii) any unauthorized use or disclosure of the Company's proprietary information (other than any such use or disclosure that is not intentional and is not material); (iii) any intentional misconduct or gross negligence that has a material adverse effect on the Company's business or reputation; (iv) any material breach by you of any agreement between you and the Company that is not cured within thirty (30) days after receipt of written notice from the Company describing any such breach; or (v) repeated and willful failure to perform the duties, functions and responsibilities of the individual's position after a written warning from the Company.

Good Reason. "Good Reason" shall mean your resignation from all positions you then hold with the Company if: (A) without your written consent (i) there is a material diminution in the nature or scope of your authorities, duties, or authority; (ii) there is a material reduction of your base salary; provided, however, that a material reduction in your base salary pursuant to a salary reduction program affecting all or substantially all of the employees of the Company and that does not adversely affect you to a greater extent than other similarly situated employees shall not constitute Good Reason; or (iii) you are required to relocate your primary work location to a facility or location that would increase your one way commute distance by more than thirty-five (35) miles from your primary work location as of immediately prior to such change, (B) you provide written notice outlining such conditions, acts or omissions to the Company's President, Chief Financial Officer or General Counsel within thirty (30) days immediately following such material change or reduction, (C) such material change or reduction is not remedied by the Company within thirty (30) days following the Company's receipt of such written notice and (D) your resignation is effective not later than thirty (30) days after the expiration of such thirty (30) day cure period. "Good Reason" shall also mean your resignation on the one year anniversary of a Sale of the Company from all positions you then hold with the Company or its successor if by that date you have not entered into a written letter or agreement with the Company or such successor that provides for your continued employment with the Company or such successor. For purposes of clarification, any Qualifying Termination that occurs on the first anniversary of a Sale of the Company shall be deemed and treated as occurring within the twelve (12) months immediately following a Sale of the Company for all purposes of this letter.

Invention, Non-Disclosure, Non-Competition and Non-Solicitation Obligations. At or prior to the Start Date, you will be required to execute and deliver the Company's standard form of Employee Confidentiality, Assignment of Inventions, Non-Competition and Non-Solicitation Agreement (the "NDA"), a copy of which has been or will be provided to you separately.

At-Will Employment. This letter shall not be construed as an agreement, either express or implied, to employ you for any stated term, and shall in no way alter the Company's policy of employment at-will. Similarly, nothing in this letter shall be construed as an agreement, either express or implied, to pay you

any compensation or grant you any benefit beyond the end of your employment with the Company, except as otherwise explicitly set forth in this letter. This letter supersedes all prior understandings, whether written or oral, including, without limitation, your current employment agreement, with respect to the subject matter of this letter.

Please indicate your acceptance of this letter agreement by signing below in the space provided for your signature.

Sincerely,

/s/ Bart Henderson
Bart Henderson
President

The foregoing correctly sets forth the terms of my at-will employment with the Company. I am not relying on any representations other than those set forth above.

/s/ Keith Gottesdiener 11/16/16

Keith M. Gottesdiener, M.D. Date

Exhibit 10.5

Rhythm Pharmaceuticals, Inc.
500 Boylston Street — 11th Floor
Boston, MA 02116
Main Telephone: 617-585-2090
www.rhythmtx.com

November 16, 2016

Dr. Fred Fiedorek
c/o Rhythm Pharmaceuticals
500 Boylston Street, 11th Floor
Boston, MA 02116

Dear Fred:

On behalf of Rhythm Pharmaceuticals, Inc., formerly known as Rhythm Metabolic, Inc. (the "Company" or "Rhythm"), I am pleased to set forth below the terms of your employment with the Company.

Employment. You are currently the Chief Medical Officer of the Company but are an employee of Motus Therapeutics, Inc., an affiliate of the Company ("Motus"). Your employment with Motus will terminate, and your employment with the Company will begin, on November 16, 2016 (the "Start Date"). During the term of your employment with the Company, you will continue to hold the position and title of Chief Medical Officer, reporting to the Chief Executive Officer. While your employment is with the Company, you will also hold the title of Chief Medical Officer of Rhythm Holding Company, LLC (the "Parent") and Motus. During the term of your employment with the Company, you will be responsible for performing the duties associated with the position above or as the Company may otherwise assign to you. Your primary place of employment will initially be in the Company's offices located in Boston, Massachusetts; however, you will be expected to travel as may be necessary to fulfill your responsibilities. In the course of your employment with Company, you will be subject to, and required to comply with, all Company policies and all applicable laws and regulations.

Base Salary. During your employment, your salary will be $344,400 annualized, subject to all required and elected taxes and other withholdings. Your salary may be adjusted from time to time in accordance with normal business practice and in the sole discretion of the Company.

Annual Target Cash Incentive. Following the end of each fiscal year and subject to the approval by the Company's Board of Directors, you will be eligible to earn a performance and retention bonus, based on your performance and the Company's performance, each during the applicable fiscal year, and your continued employment in good standing on the date of incentive distribution. Your target annual incentive opportunity is 35% of your annualized base salary.

Equity Grant. Any existing grants of equity you have in the Parent or the Company will be treated consistent with the terms of the applicable agreements under which such awards have been granted. You may be awarded additional equity grants from time to time in accordance with normal business practice and in the sole discretion of the Company's Board of Directors or the Parent's Board of Managers, as the case may be. The terms of any future equity grant will be consistent with any plan under which they are granted and the terms of the applicable agreement under which the award(s) are granted.

Benefits. You may participate in any and all benefit programs that the Company establishes and makes available to its employees from time to time, subject to the terms and conditions of those programs. The Company's benefits programs are subject to change at any time in the Company's sole discretion. You currently are eligible to receive reimbursement from the Company for 80% of the actual amounts of your medical insurance premiums for yourself and your eligible dependents, until such time as the Company establishes a medical insurance plan.

Vacation. You are eligible for a maximum of 20 paid vacation days per calendar year. Your accrual and use of vacation time will be pursuant to any vacation or time off policy the Company may establish or modify from time to time. The Company's vacation policy is subject to change at any time in the Company's sole discretion.

Severance. If the Company terminates your employment without Cause (as defined below) or you resign your employment with the Company for Good Reason (as defined below) (in either event, a "Qualifying Termination"), subject to your execution of a release acceptable to the Company (the "Release"), the expiration of any revocation period provided in the Release and your continued compliance with the terms of the NDA (as defined below), the Company will pay you an amount equal to your then-current base salary rate (or, if greater, your base salary rate prior to any reduction) for a period of six (6) months (the "Regular Severance Amount").

If there is a Qualifying Termination within the three (3) months immediately preceding or the twelve (12) months immediately following a "Sale of the Company" (as such term is defined in the Operating Agreement of the Parent, as amended and in effect from time to time), subject to your execution of a Release following your Separation from Service (as defined below), the expiration of any revocation period provided in the Release and your continued compliance with the terms of the NDA, in lieu of any Regular Severance Amount, the Company will pay you an amount equal to your then-current base salary rate for a period of twelve (12) months (the "Sale of the Company Severance Amount") plus an amount equal to 100% of your annual target cash incentive.

Notwithstanding anything express or implied in this letter to the contrary, if your employment with the Company is terminated by the Company or you at any time prior to or after a Sale of the Company and at the time of such termination you are offered employment on the same terms with either Parent or any

subsidiary of Parent and neither Parent nor such subsidiary is at that time itself subject to a Sale of the Company, then the termination of your employment with the Company shall not be deemed or treated as a Qualifying Termination for any purposes of this letter.

Any severance amount to which you may be entitled under this letter will be paid in substantially equal installments in accordance with the Company's ordinary payroll practices, beginning on the first payroll date following the date that is either (i) 60 days after the date of your Separation from Service, or (ii) in

the case of a Separation from Service that is a Qualifying Termination that occurs within the three (3) months immediately preceding a Sale of the Company, 60 days after the date of such Sale of the Company. To be eligible for either the Regular Severance Amount or the Sale of the Company Severance Amount, as applicable, you must execute and deliver the Release to the Company and allow it to become effective within 30 days of your Separation from Service or, if later, a Sale of the Company giving rise to a Sale of the Company Severance Amount entitlement.

In addition, if following your Separation from Service, you are eligible for and timely elect continued medical insurance coverage pursuant to COBRA, the Company will reimburse you for the applicable premiums for you and your eligible dependents during the period commencing on the date of your Separation from Service and ending on the earlier to occur of (a) the final day of the Severance Period and (b) the date you otherwise become ineligible for continued coverage under COBRA. Notwithstanding the foregoing, if the Company determines that it cannot provide such reimbursement of premiums to you without potentially violating applicable law, the Company shall not be obligated to make any such payments or reimbursements to you.

If the Qualifying Termination occurs within the three (3) months immediately preceding or the twelve (12) months immediately following a Sale of the Company, then each outstanding equity award in the Parent or the Company held by you shall immediately vest and, if applicable, become exercisable with respect to one hundred percent (100%) of the shares of equity of the Parent or the Company subject thereto. For purposes of clarity, if at the time of any such Qualifying Termination at least one half of all equity awards granted to you by the Parent or the Company and then held by you are then vested, there will be no further acceleration of vesting as a result of the provisions of this paragraph upon any such Qualifying Termination. The foregoing provisions of this paragraph shall apply notwithstanding anything express or implied to the contrary in any agreement or award between you and the Company or the Parent, or in any plan of the Company or the Parent, that is applicable to such outstanding equity award.

Notwithstanding anything herein to the contrary, in the event that any compensation or benefit that constitutes "nonqualified deferred compensation" within the meaning of Section 409A of the Internal Revenue Code of 1986, as amended (the "Code"), becomes payable upon the occurrence of a Sale of the Company, such compensation or benefit shall not be paid unless such Sale of the Company constitutes a "change in control event" within the meaning of Section 409A of the Code.

If any payment or benefit you would receive under this letter, when combined with any other payment or benefit you receive pursuant to the termination of your employment with the Company ("Payment") would (i) constitute a "parachute payment" within the meaning of Section 280G of the Code, and (ii) but for this sentence, be subject to the excise tax imposed by Section 4999 of the Code (the "Excise Tax"), then such Payment shall be either (x) the full amount of such Payment or (y) such lesser amount (with your choice of whether to reduce cash payments or stock option compensation or both) as would result in no portion of the Payment being subject to the Excise Tax, whichever of the foregoing amounts, taking into account the applicable federal, state and local employment taxes, income taxes and the Excise Taxes results in your receipt, on an after-tax basis, of the greater amount of the Payment notwithstanding that all or some portion of the Payment may be subject to the Excise Tax.

Definitions

Separation from Service. For purposes of this letter, "Separation from Service" means a "separation from service" within the meaning of Section 409A of the Code. Each installment payment provided under this letter shall at all times be considered a separate and distinct payment for purposes of Section 409A of the Code. Notwithstanding anything in this letter to the contrary, to the extent required to avoid a prohibited distribution under Section 409A of the Code, the benefits provided under this letter will not be provided to you until the earlier of (a) the expiration of the six-month period measured from the date of your Separation from Service with the Company or (b) the date of your death. Upon the first business day after expiration of the relevant period, all payments delayed pursuant to the preceding sentence will be paid in a lump sum and any remaining payments due will be paid as otherwise provided herein.

Cause. "Cause" shall mean the occurrence of any of the following events by the individual: (i) commission of any crime involving the Company, or any crime involving fraud, breach of trust, or physical or emotional harm to any person, moral turpitude or dishonesty; (ii) any unauthorized use or disclosure of the Company's proprietary information (other than any such use or disclosure that is not intentional and is not material); (iii) any intentional misconduct or gross negligence that has a material adverse effect on the Company's business or reputation; (iv) any material breach by you of any agreement between you and the Company that is not cured within thirty (30) days after receipt of written notice from the Company describing any such breach; or (v) repeated and willful failure to perform the duties, functions and responsibilities of the individual's position after a written warning from the Company.

Good Reason. "Good Reason" shall mean your resignation from all positions you then hold with the Company if: (A) without your written consent (i) there is a material diminution in the nature or scope of your authorities, duties, or authority; (ii) there is a material reduction of your base salary; provided, however, that a material reduction in your base salary pursuant to a salary reduction program affecting all or substantially all of the employees of the Company and that does not adversely affect you to a greater extent than other similarly situated employees shall not constitute Good Reason; or (iii) you are required to relocate your primary work location to a facility or location that would increase your one way commute distance by more than thirty-five (35) miles from your primary work location as of immediately prior to such change, (B) you provide written notice outlining such conditions, acts or omissions to the Company's Chief Executive Officer, Chief Financial Officer or General Counsel within thirty (30) days immediately following such material change or reduction, (C) such material change or reduction is not remedied by the Company within thirty (30) days following the Company's receipt of such written notice and (D) your resignation is effective not later than thirty (30) days after the expiration of such thirty (30) day cure period. "Good Reason" shall also mean your resignation on the one year anniversary of a Sale of the Company from all positions you then hold with the Company or its successor if by that date you have not entered into a written letter or agreement with the Company or such successor that provides for your continued employment with the Company or such successor. For purposes of clarification, any Qualifying Termination that occurs on the first anniversary of a Sale of the Company shall be deemed and treated as occurring within the twelve (12) months immediately following a Sale of the Company for all purposes of this letter.

Invention, Non-Disclosure, Non-Competition and Non-Solicitation Obligations. At or prior to the Start Date, you will be required to execute and deliver the Company's standard form of Employee Confidentiality, Assignment of Inventions, Non-Competition and Non-Solicitation Agreement (the "NDA"), a copy of which has been or will be provided to you separately.

At-Will Employment. This letter shall not be construed as an agreement, either express or implied, to employ you for any stated term, and shall in no way alter the Company's policy of employment at-will. Similarly, nothing in this letter shall be construed as an agreement, either express or implied, to pay you any compensation or grant you any benefit beyond the end of your employment with the Company, except as otherwise explicitly set forth in this letter. This letter supersedes all prior understandings, whether written or oral, including, without limitation, your current employment agreement, with respect to the subject matter of this letter.

Please indicate your acceptance of this letter agreement by signing a copy of this offer letter below in the space provided for your signature.

Sincerely,

/s/ Keith Gottesdiener
Keith Gottesdiener
Chief Executive Officer

The foregoing correctly sets forth the terms of my at-will employment with the Company. I am not relying on any representations other than those set forth above.

/s/ Fred Fiedorek	11/16/16
Fred Fiedorek, MD	Date

LICENSE AGREEMENT

BETWEEN

IPSEN PHARMA SAS

AND

RHYTHM METABOLIC, INC.

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* CONFIDENTIAL TREATMENT REQUESTED. OMITTED PORTIONS FILED WITH THE SECURITIES AND EXCHANGE COMMISSION PURSUANT TO RULE 406 PROMULGATED UNDER THE SECURITIES ACT OF 1933, AS AMENDED.

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LICENSE AGREEMENT

This License Agreement (this "**Agreement**") is entered into on March 21, 2013 by and between, on the one hand, IPSEN PHARMA S.A.S., a French corporation, with its principal office at 65 Quai Georges Gorse, 92100 Boulogne-Billancourt, France, on behalf of itself and its Affiliates (collectively, "**Ipsen**"), and, on the other hand, RHYTHM METABOLIC, INC., a corporation organized under the laws of the State of Delaware, U.S.A., with its principal office at 855 Boylston Street, 11th Floor, Boston MA 02116, on behalf of itself and its Affiliates (collectively, "**Licensee**"), and is effective as of the Effective Date (as defined below).

Recitals

1. The rights granted herein were originally granted to Rhythm Pharmaceuticals, Inc. pursuant to that certain License Agreement by and among Ipsen and Rhythm Pharmaceuticals, Inc., dated as of February 26, 2010 (the "**Original Agreement**")

2. Rhythm Pharmaceuticals, Inc. is undergoing a reorganization as a result of which Rhythm Pharmaceuticals Inc. and Rhythm Metabolic, Inc. will become wholly-owned subsidiaries of, a new parent company, Rhythm Holding Company, LLC.

3. As a result of the reorganization described above, the Original Agreement is being amended and restated simultaneously with the execution and delivery of this Agreement to narrow the rights granted thereunder to only those rights related to the Ghrelin Program, allowing the rights related to the MC4 Program originally granted thereunder to be licensed to Rhythm Metabolic, Inc. pursuant to this Agreement. All rights related to the MC4 Program licensed to Licensee hereunder shall be considered granted as of the Effective Date.

4. As a further result of the reorganization, Ipsen and Rhythm Holding Company, LLC will enter into an agreement whereby Ipsen will grant to Rhythm Holding Company, LLC the right to cause Ipsen to license to any wholly-owned subsidiaries of Rhythm Holding Company, LLC all rights related to the GIP Program and any Ipsen Metabolic Compounds.

5. Rhythm Pharmaceuticals, Inc. and Ipsen have entered into the MC4 [ ]* Agreement (as described in Section 2.11 of the Original Agreement), and such Agreement, including all title and rights granted therein, shall be assigned to Licensee in connection with the reorganization described above.

6. Ipsen has discovered and developed certain proprietary compounds that have shown activity against the MC4 protein target and may be drug candidates for use in the treatment of metabolic diseases. Ipsen also has developed and owns certain intellectual property rights useful or necessary for the development, manufacture, use and commercialization of such proprietary compounds.

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* CONFIDENTIAL TREATMENT REQUESTED. OMITTED PORTIONS FILED WITH THE SECURITIES AND EXCHANGE COMMISSION PURSUANT TO RULE 406 PROMULGATED UNDER THE SECURITIES ACT OF 1933, AS AMENDED.

7. Licensee has interest in exclusively licensing the Ipsen Patent Rights (as defined below) and having access to [ ]* thereunder, to pursue a worldwide development program, and thereafter, to commercialize the resulting products.

8. The Parties have prepared this Agreement to govern the development and commercialization of products resulting from this Agreement.

Now, Therefore, in consideration of the premises and the mutual covenants and agreements contained in this Agreement, the Parties, intending to be legally bound, do hereby agree as follows:

ARTICLE 1 INTERPRETATION — DEFINITIONS

1.1 In this Agreement, unless the context otherwise requires, all references to a particular Article, Section, or Appendix, shall be a reference to that Article, Section or Appendix, in or to this Agreement, as it may be amended from time to time pursuant to this Agreement.

1.1.1 Headings are inserted for convenience only and shall not affect the meaning or interpretation of any provision of this Agreement.

1.1.2 This Agreement incorporates all Appendices as a part of this Agreement by reference.

1.1.3 The term "including" (or any variation thereof such as "include") shall be without limitation to the generality of the preceding words.

1.1.4 Unless the contrary intention appears, words in the singular shall include the plural and vice versa.

1.1.5 Unless the contrary intention appears, words denoting persons shall include any individual, partnership, company, corporation, joint venture, trust, association, organization or other entity.

1.1.6 Reference to any statute or regulation includes any modification or re-enactment of that statute or regulation.

The following capitalized terms, whether used in the singular or the plural, shall have the following meanings as used in this Agreement unless otherwise specifically indicated:

1.2 Accounting Period shall mean each [ ]* commencing respectively on [ ]*, each being the first day of an Accounting Period, and finishing respectively on [ ]*, each being the last day of an Accounting Period.

1.3 **Affiliate** shall mean (a) an entity which owns, directly or indirectly, a controlling interest in a Party, by stock ownership or otherwise, (b) any entity in which a

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* CONFIDENTIAL TREATMENT REQUESTED. OMITTED PORTIONS FILED WITH THE SECURITIES AND EXCHANGE COMMISSION PURSUANT TO RULE 406 PROMULGATED UNDER THE SECURITIES ACT OF 1933, AS AMENDED.

Party owns a controlling interest, by stock ownership or otherwise; or (c) any entity, under direct or indirect common control with a Party. For purposes of this paragraph, "controlling interest" and "control" mean ownership of fifty percent (50%) or more of the voting stock permitted to vote for the election of the board of directors or any other arrangement resulting in control or the right to control the management and the affairs of the Party. Notwithstanding anything express or implied in the foregoing provisions of this definition, none of (x) the stockholders of Licensee or any entities affiliated with any of such stockholders, including, without limitation, other portfolio companies of any of such stockholders or (y) Ipsen or any Affiliate of Ipsen shall be deemed or treated as an Affiliate of Licensee for any purposes of this Agreement.

1.4 **Agreement** shall have the meaning set forth in preamble to this Agreement.

1.5 **Arbitration Request** shall have the meaning set forth in Section 16.3.

1.6 **Breaching Party** shall have the meaning set forth in Section 14.2.

1.7 **Bundled Product** shall mean Licensed Product(s) sold to a third party with one or more other products or services in circumstances where either (i) the price of the Licensed Product(s) is not shown separately on the invoice or (ii) the Licensed Product(s) (or a portion of the units of Licensed Product(s)) are detailed on a separate invoice where the price is shown as nil (free of charge) for the Licensed Product(s) (or for those units of the Licensed Product(s)). Licensed Product supplied with a delivery device (and not otherwise supplied together with, or bundled or combined with, any other product or service) shall not be considered a Bundled Product.

1.8 **Change-of-Control** shall have the meaning ascribed to it in Section 2.10.2.

1.9 **Clinical Supply Agreements** shall have the meaning set forth in Section 8.1.

1.10 **Competing Product** shall mean any [ ]*; provided, however, that a Licensed Product shall not be deemed or treated as a Competing Product for purposes of this Agreement.

1.11 **Confidential Information** shall have the meaning set forth in Section 11.1.

1.12 **Contractor** shall mean any third party with whom Licensee enters into an agreement pursuant to which Licensee grants to such third party the right to perform any services for, and on behalf of, Licensee with respect to any Licensed Product in any country of the Territory, including, without limitation, contract research, contract manufacturing or contract sales or commercialization activities. Notwithstanding the foregoing, the term "**Contractor**" shall in no event include (i) any Affiliate of Licensee, (ii) any Sublicensee and (iii) any such third party with whom Licensee enters into an

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agreement if the relationship established between Licensee and such third party pursuant to such agreement is for such third party to be a wholesale distributor of Licensed Product in any country of the Territory.

1.13 **Control** or **Controlled** shall mean, with respect to any intellectual property right or other intangible property, the possession (whether by license from a third party or ownership, or by control over an Affiliate having possession by license from a third party or ownership) by a Party of the ability to grant to the other Party access, ownership and/or a license or sublicense to such intellectual property right or other intangible property without violating the terms of any agreement with any third party.

1.14 **Cover** (as an adjective or as a verb including conjugations and variations such as "**Covered**," "**Coverage**" or "**Covering**") shall mean that the developing, making, using, offering for sale, promoting, selling or importing of a given compound, formulation or product would infringe a Valid Claim of an issued patent in the absence of a license under such Valid Claim. The determination of whether a compound, formulation or product is Covered by a particular Valid Claim shall be made on a country-by-country basis.

1.15 **Delay** shall have the meaning set forth in Section 17.5.

1.16 **Development** shall mean the pre-clinical studies, Phase I, II & III Clinical Trials, filing of NDAs, and other activities, including pharmaceutical and manufacturing development as well as regulatory work, necessary to obtain Regulatory Approval of a Licensed Product.

1.17 **Development Plan** shall mean any version and variations of a document prepared for the Development of each Licensed Product in the Territory, that outlines the Development activities including regulatory strategies, to be performed by Licensee under this Agreement. Such a document shall contain targeted timelines of the Development phases and clinical endpoints.

1.18 **Discloser** shall have the meaning set forth in Section 11.1.

1.19 **Effective Date** shall mean February 26, 2010.

1.20 **EMEA** shall mean the European Medicines Agency or any successor agency.

1.21 **FDA** shall mean the United States of America Food and Drug Administration or any successor agency.

1.22 **First Commercial Sale** shall mean, in each country of the Territory, each first invoiced sale by Licensee, Affiliate or Sub-Licensee to a third party of Licensed Product in the country after obtaining Regulatory Approval in such country.

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1.23 **FTE** shall mean a period equivalent to the number of hours that an employee in the full time employment of either Party would be obliged to spend at work in any twelve (12) month period of continuous employment.

1.24 **Gross Sales** shall mean the gross amount invoiced by Licensee, its Affiliates or Sublicensees for sales of a Licensed Product to third parties in the Territory. For purposes of clarification, [ ]*. Notwithstanding the foregoing provisions of this definition, sales of Licensed Product [ ]* shall not give rise to any Gross Sales for purposes of this Agreement.

1.25 **Health Agency** shall mean a governmental or official body in a given country of the Territory, including FDA and EMEA, as well as any national or international or local regulatory agency, department, bureau or other governmental entity, which reviews, validates and/or delivers Regulatory Approvals.

1.26 **Indemnified Party** shall have the meaning set forth in Section 15.3.

1.27 **Indemnified Person** shall have the meaning set forth in Section 15.3.

1.28 **Infringe** (as a noun, adjective or verb including conjugations and variations such as "**Infringed**," "**Infringes**", "**Infringing**" and "**Infringement**") shall mean infringement, misappropriation, unauthorized use, misuse or other violation of the Patent Rights, know-how, inventions, trade secrets or other intellectual property (except trademarks) of any person or entity, whether such person or entity owns such Patent Rights, Know-How, inventions, trade secrets or other intellectual property (except trademarks) or otherwise has the valid right of use thereof, including, without limitation, pursuant to a license.

1.29 **Initial Development Plan** shall mean the Development Plan attached to this Agreement as Appendix C.

1.30 **Invention** shall mean any invention, whether or not patentable, made as a result of the research or Development activities of a Party or the Parties pursuant to this Agreement. An **"Invention"** may be made by employees of Ipsen solely or jointly with a third party (an **"Ipsen Invention"**), by employees of Licensee solely or jointly with a third party (a **"Licensee Invention"**), or jointly by employees of Ipsen and Licensee with or without a third party (a **"Joint Invention"**), in each instance as determined by U.S. laws of inventorship.

1.31 **Ipsen** shall have the meaning set forth in the preamble to this Agreement.

1.32 **Ipsen Future Know-How** shall mean all Know-How that (A) Ipsen or any of its Affiliates owns or Controls at any time after the Effective Date (and not on or prior to the Effective Date) and during the Term and (B) either (i) is reasonably necessary to research, develop, manufacture, market, promote, use, sell, import or export any

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Licensed Product or any Unlicensed Product or (ii) is used or practiced by Ipsen, its Affiliates, sublicensees or contractors in connection with the research, Development, manufacture, marketing, promotion, use, sale, import or export of any Competing Product. Notwithstanding the foregoing provisions of this definition, the term **"Ipsen Future Know-How"** shall not include Joint Know-How, Ipsen Know-How, Ipsen New Formulation Know-How or Ipsen MC4 [ ]* Know-How.

1.33 Ipsen Future Patent Rights shall mean all Patent Rights that (A) Ipsen or any of its Affiliates owns or Controls at any time after the Effective Date (and not on or prior to the Effective Date) and during the Term and (B) claim any invention included within Ipsen Future Know-How. Notwithstanding the foregoing provisions of this definition, the term **"Ipsen Future Patent Rights"** shall not include Joint Patent Rights, Ipsen Patent Rights, Ipsen New Formulation Patent Rights or Ipsen MC4 [ ]* Patent Rights.

1.34 Ipsen Future Technology shall mean all Ipsen Future Know-How and Ipsen Future Patent Rights.

1.35 Ipsen Indemnitees shall have the meaning set forth in Section 15.2.

1.36 Ipsen Joint Technology Rights shall mean all of Ipsen's right, title and interest in the Joint Patent Rights and the Joint Know-How.

1.37 Ipsen Know-How shall mean, collectively, (A) all Know-How that Ipsen or any of its Affiliates owns or Controls as of the Effective Date and is necessary or useful to the research, Development, manufacture, marketing, promotion, use, sale, import or export of any Licensed Product, including, without limitation, all data and information regarding the safety and efficacy of any Licensed Product, (B) all Know-How, whether or not patentable, conceived, made, generated or developed by Ipsen or any of its Affiliates as a result of the research or Development activities of Ipsen or any of its Affiliates pursuant to this Agreement, including, without limitation, all Ipsen Inventions. The term **"Ipsen Know-How"** shall not include Joint Know-How or Ipsen New Formulation Know-How, but shall include Ipsen MC4 [ ]* Know-How, if any, that is not Joint Know-How.

1.38 Ipsen Licensed Know-How shall mean, collectively, (i) the Ipsen Know-How, (ii) the Ipsen Future Know-How and (iii) Ipsen's right, title and interest in Joint Know-How (including, without limitation, any Joint Know-How that is included in Ipsen MC4 [ ]* Know-How).

1.39 Ipsen Licensed Patent Rights shall mean, collectively, (i) the Ipsen Patent Rights, (ii) the Ipsen [ ]* Patent Rights (if and to the extent not included within the Ipsen Patent Rights), (iii) the Ipsen Future Patent Rights and (iv) Ipsen's right, title and interest in the Joint Patent Rights (including, without limitation, Joint Patent Rights that are included in Ipsen MC4 [ ]* Patent Rights).

1.40 Ipsen Licensed Technology shall mean all Ipsen Licensed Know-How and Ipsen Licensed Patent Rights.

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1.41 Ipsen MC4 Patent Rights shall mean (i) all Patent Rights that are listed in Appendix B of this Agreement and (ii) any and all substitutions, extensions or supplementary protection certificates, reissues, re-examinations, renewals, divisions, continuations, continuations-in-part and foreign counterparts with respect to such Patent Rights.

1.42 Ipsen MC4 Compound shall mean a [ ]*.

1.43 Ipsen MC4 [ ]* shall have the meaning set forth in Section 2.11.1.

1.44 Ipsen MC4 [ ]* Know-How shall mean all Know-How that is included within Ipsen MC4 [ ]* Technology.

1.45 Ipsen MC4 [ ]* Patent Rights shall mean all Patent Rights that are included within Ipsen MC4 [ ]* Technology.

1.46 Ipsen MC4 [ ]* Technology shall have the meaning set forth in Section 2.11.3.

1.47 Ipsen MC4 Product shall mean any [ ]*.

1.48 Ipsen MC4 Program shall mean the [ ]* program conducted by or on behalf of Ipsen or any of its Affiliates (alone or together with one or more Affiliates, partners, contractors or sublicensees) at any time on or prior to the Effective Date for purposes of [ ]*.

1.49 Ipsen MC4 Program Invention shall mean any invention or Know-How that (A) has been conceived, created, used or practiced in the course of carrying out the Ipsen MC4 Program or has been conceived, created or reduced to practice for the purpose of being used in the conduct of the Ipsen MC4 Program or (B) consists of the composition of matter, formulation, any method of use or any method of manufacture of any Ipsen MC4 Compound.

1.50 Ipsen Metabolic Compounds shall mean, collectively, [ ]*.

1.51 Ipsen New Formulation Know-How shall mean all Know-How that is included within Ipsen New Formulation Technology.

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1.52 Ipsen New Formulation Patent Rights shall mean all Patent Rights that are included within Ipsen New Formulation Technology.

1.53 Ipsen New Formulation Technology shall mean all Patent Rights and Know-How that (i) Ipsen or any of its Affiliates owns or Controls at any time after the Effective Date and during the Term and (ii) have been determined pursuant to, and in accordance with, the provisions of Section 2.7 hereof to be necessary or useful to the development of a new formulation for any Licensed Product that is the subject of any evaluation pursuant to Section 2.7. Notwithstanding the foregoing provisions of this definition, the term **"Ipsen New Formulation Technology"** shall not include any Ipsen Licensed Patent Rights or any Ipsen Licensed Know-How.

1.54 Ipsen Ongoing Pre-Clinical Studies shall have the meaning set forth in Section 6.2.

1.55 Ipsen Patent Rights shall mean, collectively, (i) the Ipsen MC4 Patent Rights and (ii) those Ipsen MC4 [ ]* Patent Rights, if any, that are not Joint Patent Rights. In addition, the term "**Ipsen Patent Rights**" shall be deemed automatically modified to include the Ipsen [ ]* Patent Rights if and to the extent that Ipsen obtains an exclusive license to the Ipsen [ ]* Patent Rights from [ ]*.

1.56 Ipsen [ ]* Patent Rights shall mean all Patent Rights in connection with the [ ]* Patent Application that Ipsen or any of its Affiliates owns or Controls at any time during the Term.

1.57 Ipsen Technology shall mean all Ipsen Know-How and Ipsen Patent Rights.

1.58 Joint Know-How shall mean Know-How, whether or not patentable, conceived, created, made, generated or developed jointly by employees of Licensee and Ipsen or any of its Affiliates (with or without a third party) as a result of the research or Development activities of the Parties pursuant to, or contemplated under, this Agreement (including, without limitation, Section 2.11 hereof). The term "**Joint Know-How**" shall include all Joint Inventions.

1.59 Joint Patent Rights shall mean Patent Rights that claim (i) any Joint Invention or (ii) any Joint Know-How.

1.60 Know-How shall mean technical and other information, including information comprising or relating to concepts, discoveries, data, designs, formulae, ideas, inventions, methods, models, assays, research plans, procedures, designs for experiments and tests and results of experimentation and testing (including results of research or Development or other developments), formulations, processes (including manufacturing processes, specifications and techniques), laboratory records, chemical, pharmacological, toxicological, clinical, analytical and quality control data, trial data, case report forms, data analyses, reports, manufacturing data, pre-clinical data and

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summaries and information contained in submissions to, and information from, ethical committees and Health Agencies, including documents containing any of the above.

1.61 Licensed Product Claim shall mean, for a given Licensed Product in a given country of the Territory, a Valid Claim of Ipsen Patent Rights, Ipsen [ ]* Patent Rights (to the extent not included within Ipsen Patent Rights), Ipsen Future Patent Rights or Joint Patent Rights that Covers such Licensed Product in such country.

1.62 Licensed Product shall mean (i) any Ipsen MC4 Product or (ii) any [ ]* that is covered by a Valid Claim of any issued patent or patent application included within Ipsen Patent Rights or Joint Patent Rights.

1.63 Licensed Rights shall have the meaning set forth in Section 2.1.

1.64 Licensee shall have the meaning set forth in the preamble to this Agreement.

1.65 Licensee Indemnitees shall have the meaning set forth in Section 15.1.

1.66 Licensee Joint Technology Rights shall mean all of Licensee's right, title and interest in and to the Joint Patent Rights and the Joint Know-How.

1.67 Licensee Know-How shall mean all Know-How that Licensee or any of its Affiliates owns, Controls or otherwise has in-licensed at any time during the Term. Notwithstanding the foregoing provisions of this definition, the term **"Licensee Know-How"** shall not include Ipsen Licensed Know-How, Ipsen New Formulation Know-How and Joint Know-How.

1.68 Licensee Patent Rights shall mean all Patent Rights that Licensee or any of its Affiliates owns, controls or otherwise has in-licensed at any time during the Term. Notwithstanding the foregoing provisions of this definition, the term **"Licensee Patent Rights"** shall not include Ipsen Licensed Patent Rights, Ipsen New Formulation Patent Rights and Joint Patent Rights.

1.69 Licensee Technology shall mean all Licensee Know-How and Licensee Patent Rights.

1.70 Licensee Trademark shall have the meaning attributed to it under Section 10.1.

1.71 Losses shall have the meaning set forth in Section 15.1.

1.72 Manufacturing Cost shall have the meaning set forth in the Clinical Supply Agreements.

1.73 MC4 Product shall mean any Licensed Product that [ ]*.

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1.74 **NDA Filing** shall mean a New Drug Application filed as a result of activities under this Agreement with the FDA, or the equivalent application to the equivalent agency in any other country of the Territory, the filing of which is necessary to market and sell a Licensed Product, including all amendments and supplements to any of the foregoing.

1.75 **Necessary Third Party IP Rights** shall mean (i) any Valid Claim of Patent Rights owned or controlled by a third party which would be Infringed by the use or practice of the Ipsen Licensed Technology, Ipsen Future Technology, the Ipsen New Formulation Technology (if and to the extent licensed to Licensee) or the Ipsen MC4 [ ]* Technology to research, develop, manufacture, market, promote, use, sell, import or export any Licensed Product in any country of the Territory or (ii) any Patent Rights or Know How owned or controlled by a third party (other than Patent Rights already within the scope of the foregoing clause (i) of this definition) that (1) are reasonably necessary to enable the research, development, manufacture, use or commercialization of a License Product in any country of the Territory, (2) are reasonably likely to materially reduce the risks or the timetable for the development of a License Product in any country of the Territory or (3) are reasonably likely to materially reduce the commercialization risk, or materially increase the anticipated Net Sales, of a Licensed Product in any country of the Territory.

1.76 **Net Sales** shall mean Gross Sales less deductions (not otherwise taken into account) for the [ ]*.

In the event that a Licensed Product is sold as a component of a Bundled Product, then Net Sales shall be determined by multiplying the Net Sales of the Bundled Product by the fraction [ ]* where [ ]* equals the average selling price of such Licensed Product sold separately in finished form and [ ]* equals the aggregate average selling price of the relevant other product(s) included in such Bundled Product sold separately in finished form, in each case in the relevant country in which sales of such Bundled Product were made, during the same Accounting Period and in similar volumes. In the event that no separate sale of such Licensed Product is made during the applicable Accounting Period in similar volumes and in the relevant country in which the sale of such Bundled Product was made and that there are separate sales of the relevant other product(s) included in such Bundled Product in similar volumes and in the relevant country in which the sale of such Bundled Product was made, then Net Sales shall be determined by multiplying the Net Sales of the Bundled Product by the fraction [ ]*

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[ ]*, where [ ]* equals the average selling price of the Bundled Product for the country in which sales were made. In the event that no separate sale of either such Licensed Product or the relevant other product(s) is made during the applicable Accounting Period in similar volumes and in the relevant country in which the sale of such Bundled Product was made, then Net Sales shall be determined by multiplying the Net Sales of the Bundled Product by the fraction [ ]*, where [ ]* equals the fully absorbed cost of manufacturing such Licensed Product and [ ]* equals the full absorbed cost of manufacturing the relevant other product(s).

1.77 **Non-Breaching Party** shall have the meaning set forth in Section 14.2.

1.78 **Party** shall mean, individually, IPSEN PHARMA S.A.S. or RHYTHM METABOLIC, INC., and "**Parties**" shall mean collectively, IPSEN PHARMA S.A.S. and, RHYTHM METABOLIC, INC.

1.79 **Patent Rights** shall mean all rights under any patent or patent application in any country of the world, including any substitution, extension or supplementary protection certificate, reissue, re-examination, renewal, division, continuation or continuation-in-part thereof.

1.80 **[ ]*** shall mean [ ]*.

1.81 **[ ]* Patent Application** shall mean [ ]*.

1.82 **Phase I Clinical Trial** shall mean a human clinical trial normally conducted in healthy volunteers with the aim of establishing the pharmacokinetic, pharmacodynamic and early safety profile.

1.83 **Phase II Clinical Trial** shall mean a human clinical trial that is required for Regulatory Approval where a product is tested in a limited number of patients for the purpose of establishing dose ranging and/or first indication of efficacy of product for a therapeutic or prophylactic use.

1.84 **Phase III Clinical Trial** shall mean a pivotal multi-center human clinical trial in a large number of patients to establish safety or efficacy in the particular claim and indication tested and required to obtain Regulatory Approval.

1.85 **Phase III Initiation** shall mean the date when a Licensed Product is first administered to a patient in the first Phase III Clinical Trial in the Territory.

1.86 **Publication Eligible Material** shall have the meaning set forth in Section 12.1.

1.87 **Receiver** shall have the meaning set forth in Section 11.1.

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1.88 **Regulatory Approval** shall mean any and all approvals, licenses, registrations or authorizations (including pricing and reimbursement approvals) whether or not conditional, that are granted by FDA, EMEA or other Regulatory Authority and are necessary for the commercial sale of Licensed Product in a regulatory jurisdiction in the Territory and obtained as a result of activities under this Agreement.

1.89 **Regulatory Authority** shall mean any national, supra-national (e.g., the FDA, the European Commission, the Council of the European Union, or the European Medicines Agency ("EMEA")), regional, state or local regulatory agency, department, bureau, commission, council or other governmental entity in any jurisdiction of the Territory involved in the granting of Regulatory Approval for pharmaceutical products.

1.90 **ROW** shall mean [ ]*.

1.91 **Royalty Term** shall mean for each Licensed Product and each country of the Territory, (a) the period of time commencing on the First Commercial Sale in such country of such Licensed Product and ending on the tenth (10^{th}) anniversary of such First Commercial Sale and (b) any period of time after such tenth (10^{th}) anniversary during which there is a Licensed Product Claim in such country with respect to such Licensed Product.

1.92 **Section 2.10 Negotiation Period** shall have the meaning set forth in Section 2.10.

1.93 **Sublicense Agreement** shall mean any agreement entered into with a third party whereby such third party is granted a sublicense under the Licensed Rights or such third party is granted an option to acquire a sublicense under the Licensed Rights. Notwithstanding anything express or implied in the foregoing provisions of this definition, the term "**Sublicense Agreement**" shall not include any agreement entered into with a third party whereby such third party is granted the right or option to purchase its supply of Licensed Product in finished form from Licensee, its Affiliates or Sublicensees for resale unto the market, unless, as a partial or full consideration for such purchase, such third party has a payment obligation to Licensee, its Affiliates or Sublicensees that is a percentage of such third party's net sales, including without limitation a royalty obligation.

1.94 **Sublicensee** means a third party (other than an Affiliate of Licensee) that has entered into a Sublicense Agreement.

1.95 **Sublicensing Revenue** shall mean any upfront option payments, upfront license fee payments (excluding the fair market value of equity sold, funding for the sole purpose of supporting identified and planned research and development works relating to the Licensed Products, transfer of goods and materials at cost plus an industry standard premium, bona fide loans and bona fide payments to reimburse Licensee or any of its Affiliates for patent prosecution costs incurred in connection with Licensed Products) or milestone payments (including without limitation milestone payments relating to

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research, development, regulatory or commercial events) to be paid by a Sublicensee to Licensee or any of its Affiliates pursuant to a Sublicense Agreement if and to the extent that such upfront option payments, upfront license fee payments and milestone payments are consideration for any sublicense under the Licensed Rights that is granted pursuant to such Sublicense Agreement or any option granted under such Sublicense Agreement to acquire such sublicense.

1.96 **Term** shall have the meaning set forth in Section 14.1.

1.97 **Territory** shall mean [ ]*.

1.98 **Unlicensed Product** shall mean, with respect to any Licensed Product in any given country within the Territory, any product or pharmaceutical composition that (A) contains [ ]* as such Licensed Product, and (B) is commercially available in such country other than as a result of the licenses granted by Ipsen to Licensee pursuant to this Agreement.

1.99 **Valid Claim** shall mean a claim in any (a) unexpired and issued Patent Right that has not been dedicated to the public, disclaimed, revoked or held invalid by a final unappealable decision or unappealed decision of a court of competent jurisdiction after the period for filing an appeal has expired or (b) pending patent application which patent application has been on file with the application patent office for no more than [ ]* from the earliest date from which the patent application was filed or claims earliest priority.

1.100 **Withholding Party** shall have the meaning set forth in Section 5.4.

ARTICLE 2 GRANT OF RIGHTS

2.1 License Grants. Subject to the terms of this Agreement, Ipsen, for and on behalf of itself and all of its Affiliates, hereby grants to Licensee and its Affiliates the following rights (the "**Licensed Rights**"):

- an exclusive (even as to Ipsen and its Affiliates) right and license in all countries of the Territory, under the Ipsen Technology and the Ipsen Joint Technology Rights, to research, develop, register, use, make, have made, import, export, market, distribute, offer for sale and sell Licensed Product in the Territory for any and all uses and fields of use (it being understood and agreed that, notwithstanding the foregoing exclusive grant to Licensee, Licensee hereby authorizes and consents to the exercise by Ipsen and its Affiliates of any and all rights under the Ipsen Technology and the Ipsen Joint Technology Rights if and to the extent necessary for the sole purpose of Ipsen performing its obligations under this Agreement), and

- a non-exclusive right and license in all countries of the Territory under the Ipsen [ ]* Patent Rights (to the extent that the Ipsen [ ]* Patent Rights are not included within the Ipsen Patent Rights) to research, develop, register, use,

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make, have made, import, export, market, distribute, offer for sale and sell Licensed Product in the Territory for any and all uses and fields of use, and

- a non-exclusive right and license in all countries of the Territory, under the Ipsen Future Technology, to research, develop, register, use, make, have made, import, export, market, distribute, offer for sale and sell Licensed Product in the Territory for any and all uses and fields of use.

2.2 Rights retained by Ipsen. All rights in and to the Ipsen Technology, Ipsen Joint Technology Rights, the Ipsen Future Technology and the Ipsen [ ]* Patent Rights not expressly granted to Licensee under this Agreement are reserved exclusively to Ipsen and its Affiliates.

2.3 Sublicenses. The rights and licenses granted to Licensee under Section 2.1 shall include the right to grant sublicenses under the Licensed Rights and shall also include the right to grant to a Sublicensee the right to grant further sublicenses to the extent of the Licensed Rights so sublicensed to such Sublicensee. If Licensee or any of its Affiliates enters into a Sublicense Agreement, Licensee shall ensure that all of the applicable terms and conditions of this Agreement shall apply to the applicable Sublicensee to the same extent as they apply to Licensee with respect to, and to the extent, of the Licensed Rights so sublicensed. Licensee shall assume full responsibility for the performance of all obligations so imposed on such Sublicensee and will itself account to Ipsen for all payments due under this Agreement by reason of such Sublicense Agreement. Upon execution of any Sublicense Agreement, Licensee shall provide Ipsen with the financial terms of such Sublicense Agreement for the purposes of evaluating the Share of Sublicensing Revenue owed to Ipsen as per Section 3.4 of this Agreement.

2.4 Contractors. The rights and licenses granted to Licensee under Section 2.1 shall include the right to grant rights to Contractors under Licensed Rights, in whole or in part, and shall also include the right to grant to any direct or indirect third party Contractors the right of such Contractors to further subcontract such Licensed Rights to another third party. If Licensee or any of its Affiliates enters into an agreement with a Contractor pursuant to this Section 2.4, Licensee shall ensure that all of the applicable terms and conditions of this Agreement shall apply to the Contractor to the same extent as they apply to Licensee with respect to, and to the extent, of the rights granted. Licensee shall assume full responsibility for the performance of all obligations so imposed on Contractor and will itself account to Ipsen for all payments due under this Agreement by reason of such subcontract.

2.5 Intellectual Property Rights of Ipsen Affiliates. In the event that any of the intellectual property rights granted by Ipsen and its Affiliates to Licensee and its Affiliates pursuant to Section 2.1 above are owned or Controlled by any Affiliate of Ipsen and not by Ipsen, Ipsen hereby agrees to take such action as may be required (including, without limitation, exercising control over such Affiliate) to ensure that Licensee and its Affiliates, can fully enjoy, exploit and exercise all of their respective rights under this Agreement with respect to such intellectual property rights to the same extent as if such Affiliate were a party to this Agreement.

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2.6 Prohibited Uses and Activities

2.6.1 Ipsen shall not use or practice any Licensed Rights in contravention or violation of the rights thereunder or thereto granted to Licensee pursuant to Section 2.1. Ipsen shall not grant licenses or otherwise transfer any rights to any person or entity (other than Licensee and its Affiliates) if and to the extent that any such grant or other transfer would violate, contravene, conflict with, or be inconsistent with, the rights granted to Licensee pursuant to Section 2.1 hereof.

2.6.2 During [ ]*, (i) neither Ipsen nor its Affiliates shall research, seek to discover, develop, make, have made, use, distribute, market, sell or otherwise commercialize any Licensed Product or any Unlicensed Product except if and to the extent expressly provided or permitted in this Agreement and in accordance with the terms of this Agreement and (ii) neither Ipsen nor its Affiliates shall grant to any person (other than Licensee and its Affiliates) any right or license to discover, develop, make, have made, use, distribute, market, sell or otherwise commercialize any Licensed Product or Unlicensed Product except if and to the extent expressly provided or permitted in this Agreement and in accordance with the terms of this Agreement.

2.6.3 During [ ]* (i) neither Ipsen nor its Affiliates shall research, seek to identify, develop, make, have made, use, distribute, market, sell or otherwise commercialize any Competing Product for the treatment of any of the indications for which Licensee intends to develop the relevant Licensed Product (with which such Competing Product is likely to compete) as set forth in the Initial Development Plan and (ii) neither Ipsen nor its Affiliates shall grant to any person (other than Licensee and its Affiliates) any right or license to research, seek to discover, develop, make, have made, use, distribute, market, sell or otherwise commercialize any Competing Product for the treatment of any such indications.

2.6.4 During [ ]*, (i) neither Ipsen nor its Affiliates shall use or practice any Ipsen Technology or any Ipsen Joint Technology Rights, for the purpose of, or in connection with, discovering, identifying, researching, developing, making, having made, using, distributing, marketing, selling or otherwise commercializing any Competing Product and (ii) neither Ipsen nor its Affiliates shall grant to any person (other than Licensee or any of its Affiliates) any right or license to use or practice any Ipsen Technology or any Ipsen Joint Technology Rights, for the purpose of, or in connection with, discovering, identifying, researching, developing, making, having made, using, distributing, marketing, selling or otherwise commercializing any Competing Product.

2.7 Ipsen New Formulation Technology

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2.7.1 At the written request of Licensee made at any time during [ ]* (such request being accompanied by [ ]*), Ipsen or any of its Affiliates shall undertake an evaluation of Patent Rights and Know-How owned or Controlled by Ipsen or any of its Affiliates that are not included within Ipsen Technology, Joint Patents or Joint Know-How and that the Parties, acting reasonably and in good faith, believe may be necessary or useful to the development of a new formulation for any Licensed Product that is specifically identified by Licensee (the "**Evaluation Formulation Technology**"). Any such evaluation shall be conducted by Ipsen or any of its Affiliates pursuant to an agreement to be negotiated and entered into by the Parties acting reasonably and in good faith (the "**Formulation Technology Evaluation Agreement**"). It is hereby understood and agreed by the Parties that the Formulation Evaluation Agreement shall provide that, at Ipsen's discretion, the actual activities required in connection with such evaluation may be conducted by a contract research organization mutually acceptable to the Parties. In the event that, based on the results of such evaluation, the Parties, acting reasonably and in good faith, identify any Evaluation Formulation Technology that is necessary or useful to the development of a new formulation for any such Licensed Product specifically identified by Licensee, (i) any such Evaluation Formulation Technology shall be included within the definition of, and treated for all purposes of this Agreement as, Ipsen New Formulation Technology and (ii) the Parties, acting reasonably and in good faith, shall negotiate the terms of, and execute and deliver, a license agreement pursuant to which Ipsen and its Affiliates would grant to Licensee an exclusive (even as to Ipsen and its Affiliates) right and license in all countries of the Territory, under such Ipsen New Formulation Technology, to research, develop, use, make, have made, import, export, market, distribute, offer for sale and sell Licensed Products. Such license rights shall be exclusive only with respect to Licensed Products and Ipsen shall not be prohibited from using or granting such Ipsen New Formulation Technology for any compound or product that is not a Licensed Product, a Competing Product or an Unlicensed Product. Any such exclusive license shall include the right grant sublicenses under such license rights.

2.7.2 The obligation of the Parties to negotiate a license agreement pursuant to Section 2.7.1 shall have as an objective to reach good faith agreement on terms that are scientifically and commercially reasonable. The Parties hereby acknowledge and agree that, in reaching agreement on the appropriate royalty rate applicable to such exclusive license under Ipsen New Formulation Technology, the Parties shall take into account [ ]* and [ ]*. Notwithstanding anything expressed or implied in the foregoing provisions of this Section 2.7 to the contrary, in no event shall the royalty rate applicable to Net Sales of any Licensed Product with a formulation developed with, or covered by, all or any portion of the Ipsen New Formulation Technology exceed (i) [ ]* or (ii) [ ]* in the event that (x) such Licensed Product is an Ipsen MC4 Product, (y) such Licensed Product also

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utilizes the Ipsen MC4 [ ]*, (z) the Ipsen MC4 [ ]* was accepted in writing by Licensee pursuant to Section 2.11.1 and (zz) the Ipsen MC4 [ ]* is Covered by Ipsen MC4 [ ]* Patent Rights.

2.7.3 Notwithstanding anything express or implied in the foregoing provisions of this Sections 2.7, the provisions of Section 2.7.1 and Section 2.7.2 (other than the last sentence thereof) shall not be applicable to the Ipsen MC4 [ ]* or the Ipsen MC4 [ ]* Technology.

2.8 [Intentionally Omitted.]

2.9 [Intentionally Omitted.]

2.10 Ipsen's Right of Non-Exclusive Negotiation for Licensed Product

2.10.1 Prior to Licensee entering into any Sublicense Agreement with a third party (a "**Potential Sublicensee**") pursuant to which Licensee shall grant a sublicense under the Licensed Rights to such Potential Sublicensee to develop and/or commercialize one or more Licensed Products (collectively, the "**Sublicensed Products**" and each individually a "**Sublicensed Product**") for all or part of the Territory (all or any part of the Territory covered by any such Sublicense Agreement being hereinafter referred to as the "**Sublicensed Territory**") and prior to Licensee entering into any exclusivity agreement with any Potential Sublicensee relating to the exclusive negotiation of any such Sublicense Agreement, (i) Licensee shall notify Ipsen in writing that Licensee is willing to enter into non-exclusive negotiations with Ipsen for the grant by Licensee to Ipsen of commercialization rights to such Sublicensed Products for the Sublicensed Territory and (ii) Licensee shall comply with all of the provisions set forth below in this Section 2.10.1. As soon as practicable (but in any event within [ ]* of receipt by Ipsen of such notice from Licensee), Ipsen will respond to Licensee in writing regarding Ipsen's interest in entering into such non-exclusive negotiations. If Ipsen responds to Licensee in writing that it is not interested in entering into such non-exclusive negotiations, then all obligations of the Parties under this Section 2.10 with respect to such Sublicensed Products in the Sublicensed Territory shall terminate and be of no further force or effect, both at that time and in the future, unless Licensee does not enter into a definitive Sublicense Agreement with a Potential Sublicensee within [ ]* after the date that Ipsen last delivered a written response to Licensee stating that Ipsen was not interested in entering into such non-exclusive negotiations, in which case the Party's respective rights and obligations under this Section 2.10 with respect to such Sublicensed Products in the Sublicensed Territory shall once again become applicable at that time. If Ipsen responds to Licensee in writing that it is interested in entering into such non-exclusive negotiations, the Parties will promptly commence non-exclusive, good faith negotiations through and until the earlier of (1) the [ ]* following the date that Ipsen gives such written notice to Licensee, provided that Licensee may elect, in its sole

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and absolute discretion, to have the period covered by this clause (1) be longer than [ ]* by giving written notice of such election to Ipsen (which written notice shall specify the length of such period), (2) the date that the Parties jointly determine and agree to end such negotiations and (3) the date that Ipsen notifies Licensee in writing that Ipsen does not want to continue negotiations (the period of such negotiations being hereinafter referred to as the "**Section 2.10 Negotiation Period**"). Notwithstanding anything express or implied in the foregoing provisions of this Section 2.10.1 to the contrary, (A) Licensee retains the right to terminate any such negotiations with Ipsen at any time prior to [ ]* if Licensee makes a determination, in its sole and absolute discretion, that Licensee is no longer considering granting commercialization rights to such Sublicensed Products to Ipsen and any Potential Sublicensees and (B) Licensee shall have the right to conduct discussions or negotiations with Potential Sublicensees prior to, simultaneously with, and/or after termination of, the negotiations with Ipsen, provided that Licensee shall not enter into a definitive agreement with any of such Potential Sublicensees until after [ ]*. If upon [ ]*, Licensee and Ipsen shall not have entered into a definitive agreement pursuant to which Licensee has granted to Ipsen commercialization rights to such Sublicensed Products, then Licensee will be free at any time thereafter to enter into any definitive agreement with a Potential Sublicensee pursuant to which Licensee grants to such Potential Sublicensee any commercialization rights to such Sublicensed Products in the Sublicensed Territory; provided, however, that (i) Licensee shall not enter into any such definitive agreement with a Potential Sublicensee if the terms of such definitive agreement are less favorable to Licensee and its business than the last terms with respect to such Sublicensed Products that were proposed by Ipsen in writing during the applicable Section 2.10 Negotiation Period and (ii) if Licensee does not enter into a definitive Sublicense Agreement with a Potential Sublicensee within [ ]*, the Party's respective rights and obligations under this Section 2.10 with respect to such Sublicensed Products in the Sublicensed Territory shall once again become applicable at that time.

2.10.2 Notwithstanding anything express or implied in any of the provisions of Section 2.10.1 to the contrary, this Section 2.10 shall automatically terminate upon the earlier to occur of (x) the closing of the Licensee's initial public offering or (y) the occurrence of a Change of Control of Licensee. For purposes hereof, the term "**Change of Control**" shall mean, with respect to Licensee, (i) any merger or consolidation involving Licensee or any sale of outstanding shares of capital stock of Licensee, if the stockholders of Licensee immediately prior to the consummation of such merger, consolidation or sale of outstanding shares no longer hold at least a majority of the issued and outstanding shares of capital stock of Licensee immediately after the consummation of such merger, consolidation or sale of outstanding shares and (ii) the sale of all or substantially all of the assets of Licensee. For purposes of clarification, (A) any

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equity financing or any other transaction by Licensee pursuant to which Licensee directly issues shares of its capital stock shall not be a transaction subject to clause (i) of this Section 2.10.2, and (B) neither Licensee nor Ipsen shall have any rights or obligations under Section 2.10.1 in connection with any Change of Control of Licensee (it being understood and agreed that a Change of Control of Licensee is not the type of transaction that the Parties envision as triggering the provisions of Section 2.10.1).

2.11 Ipsen MC4 [ ]*

2.11.1 **[Intentionally Ommitted.]**

2.11.2 Licensee shall evaluate any new formulation developed by Ipsen pursuant to the MC4 [ ]* Agreement and shall give written notice to Ipsen if Licensee determines, in its sole and absolute discretion, that such new formulation meets the characteristics, profile and specifications provided by Licensee therefor set forth in the MC4 [ ]* development of MC4 Products. If Licensee gives such written notice to Ipsen with respect to any such new formulation, then such new formulation shall be referred to in this Agreement as the "**Ipsen MC4 [ ]***".

2.11.3 All Patent Rights and Know-How owned or Controlled by Ipsen or any of its Affiliates that are conceived, invented, generated or reduced to practice during the conduct of the activities under the MC4 [ ]* Agreement and/or that are necessary or useful MC4 [ ]* to the development, manufacture, use or commercialization of any Licensed Product using the Ipsen MC4 [ ]* (such Patent Rights and Know-How being referred to in this Agreement as the "**Ipsen MC4 [ ]* Technology**") shall be included within the definition of, and treated for all purposes of this Agreement as, Ipsen Technology, Joint Patents or Joint Know-How, as applicable, such that the exclusive license granted by Ipsen to Licensee under Section 2.1 hereof shall include the exclusive right and license (even as to Ipsen and its Affiliates) in all countries of the Territory, under the Ipsen MC4 [ ]* Technology, to research, develop, use, make, have made, import, export, market, distribute, offer for sale and sell Licensed Products. Any such exclusive right and license shall include the right grant sublicenses under such license rights. For the avoidance of doubt and notwithstanding anything to the contrary in this Agreement, it is agreed that (x) Licensee shall have no right to practice, develop, commercialize, license or use the Ipsen MC4 [ ]* Technology except to the extent contemplated or permitted under this Agreement (including, without limitation, Section 2.1 hereof) and (y) Ipsen shall retain all rights to practice, develop, commercialize, license and otherwise use the Ipsen MC4 [ ]* Technology in connection with any product or compound that is not a Licensed Product or a Competing Product.

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2.12 Third Party Payments by Ipsen. Ipsen shall make payment of all license fees, milestone payments, royalty payments and other payments that Ipsen or any of its Affiliates is required to pay under or in connection with any agreement with a third party pursuant to which Ipsen or any of its Affiliates acquires or has acquired Patent Rights (including, without limitation, the Ipsen [ ]* Patent Rights) or Know How or other intellectual property rights licensed or sublicensed by Ipsen to License and its Affiliates pursuant to this Agreement.

ARTICLE 3 MILESTONE PAYMENTS; PAYMENT OF SHARE OF SUBLICENSING REVENUES

3.1 Subject to the provisions of this Section 3.1 and Section 3.5 below, Licensee shall pay to Ipsen the following non-refundable and non-creditable amounts upon the occurrence of the following development milestones with respect to an Ipsen MC4 Product:

Development Milestones	Amount
[ ]*	[ ]*
[ ]*	[ ]*
[ ]*	[ ]*
[ ]*	[ ]*
[ ]*	[ ]*
[ ]*	[ ]*

Each milestone payment by Licensee to Ipsen pursuant to the foregoing provisions of this Section 3.1 shall be paid only once upon the first occurrence of the applicable development milestone, regardless of how many times a particular development milestone is achieved and notwithstanding that more than one Ipsen MC4 Product achieves a given development milestone. Without limiting the generality of the foregoing sentence, in no event shall the aggregate amount of milestone payments made by Licensee to Ipsen pursuant to this Section 3.1 under any circumstances exceed [ ]*.

Licensee shall promptly inform Ipsen of the occurrence of any of the above development milestones and Licensee shall make payment of any milestone payment that Licensee is required to make pursuant to this Section 3.1 within [ ]* after the achievement of the applicable development milestone.

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3.2 Subject to the provisions of this Section 3.2 and Section 3.5 below, Licensee shall pay to Ipsen the following non-refundable and non-creditable amounts upon the occurrence of the following commercialization milestones with respect to an Ipsen MC4 Product:

Commercialization Milestones	Amount
[ ]*	[ ]*
[ ]*	[ ]*

Each milestone payment by Licensee to Ipsen pursuant to the foregoing provisions of this Section 3.2 shall be paid only once upon the first occurrence of the applicable commercialization milestone, regardless of how many times a particular commercialization milestone is achieved and notwithstanding that more than one Ipsen MC4 Product achieves a given commercialization milestone. Without limiting the generality of the foregoing sentence, in no event shall the aggregate amount of milestone payments made by Licensee to Ipsen pursuant to this Section 3.2 under any circumstances exceed [ ]*.

Licensee shall promptly inform Ipsen of the occurrence of any of the above commercialization milestones and Licensee shall make payment of any milestone payment that Licensee is required to make pursuant to this Section 3.2 within [ ]* after the end of the calendar quarter during which the applicable commercialization milestone is achieved.

3.3 Subject to the provisions of Section 3.5 below, in the event that Licensee or any of its Affiliates, on the one hand, and Sublicensee, on the other hand, execute and deliver a Sublicense Agreement, Licensee shall make payment to Ipsen of the Share (as defined in Section 3.4 below) of all Sublicensing Revenues actually received by Licensee or any of its Affiliates under such Sublicense Agreement. Licensee shall make any payment that Licensee is required to make to Ipsen pursuant to this Section 3.3 within [ ]* of the end of the Accounting Period in which Licensee or any of its Affiliates actually received any such Sublicensing Revenues.

3.4 The Share shall depend on the date of execution of the relevant Sublicense Agreement, as follows:

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Date of execution of the Sublicense Agreement	Share
[ ]*	[ ]*
[ ]*	[ ]*
[ ]*	[ ]*

For purposes of clarification, "completion" shall mean [ ]*.

Notwithstanding anything express or implied in the foregoing provisions of this Section 3.4 or elsewhere in this Agreement to the contrary, it is hereby understood and agreed that if Licensee or any of its Affiliates enters into Sublicense Agreement pursuant to which the applicable Sublicensee is granted an option that entitles such Sublicensee upon exercise of such option to obtain a sublicense under the Licensed Rights, Ipsen's Share of Sublicensing Revenues should be calculated under this Section 3.4 as follows :

(i) Ipsen's Share of any upfront option fees actually received by Licensee or any of its Affiliates in connection with the grant of such option shall be [ ]*, and

(ii) Ipsen's Share under this Section 3.4 of any upfront license fees and milestone payments actually received by Licensee or any of its Affiliates in connection with the grant of any such sublicense under the Licensed Rights upon exercise of such option shall be [ ]*.

For example, in the event that [ ]*

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[ ]*, then [ ]*.

3.5 Notwithstanding anything express or implied in the foregoing provisions of this Article 3, in the event that, but for the provisions of this Section 3.5, the same development or commercialization milestones would trigger the payment of a milestone payment pursuant to Sections 3.1 through 3.2 hereof and also the payment pursuant to Sections 3.3 and 3.4 of a Share of any Sublicensing Revenue actually received by Licensee or any of its Affiliates in connection with such development or commercialization milestones, Licensee shall pay to Ipsen [ ]*.

ARTICLE 4 PAYMENTS BASED ON SALES OF LICENSED PRODUCT

4.1 **Royalties.** In consideration for the rights and license granted under this Agreement, Licensee shall, subject to the provisions of Sections 4.2, 4.3 and 4.4 below, pay royalties to Ipsen based upon Net Sales of any given Licensed Product in any given country in the Territory during the Royalty Term applicable to sales of such Licensed Product in such country, which royalties shall be equal to [ ]* of such Net Sales; provided, however, that, subject to the provisions of Sections 4.2, 4.3 and 4.4 below, if (i) such Licensed Product is an Ipsen MC4 Product that utilizes the Ipsen MC4 [ ]*, (ii) the Ipsen MC4 [ ]* was accepted in writing by Licensee pursuant to Section 2.11.1 and (iii) the Ipsen MC4 [ ]* is Covered by Ipsen MC4 [ ]* Patent Rights, then the royalty rate applicable to Net Sales of such Ipsen MC4 Product in any given country in the Territory during the Royalty Term applicable to sales of such Ipsen MC4 Product in such country shall be (A) [ ]* if the Ipsen MC4 [ ]* is delivered by Ipsen to Licensee pursuant to Section 2.11.1 within [ ]* after the date of the MC4 [ ]* Agreement, (B) [ ]* if the Ipsen MC4 [ ]* is delivered by Ipsen to Licensee pursuant to Section 2.11.1 at any time after the [ ]* following the date of the MC4 [ ]* Agreement and such Ipsen MC4 Product in a formulation consisting of the Ipsen MC4 [ ]* is used by Licensee in [ ]* or (C) [ ]* if neither of the foregoing clauses (A) and (B) is applicable. For purposes of clarification, the determination of the amount of royalties

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due Ipsen pursuant to this Section 4.1 shall be made on a Licensed Product-by-Licensed Product basis and on a country-by-country basis. Payment of royalties due to Ipsen pursuant to this Article 4 shall be made in accordance with the provisions of Article 5 hereof.

4.2 Adjustments related to Unlicensed Products. Notwithstanding anything express or implied in Section 4.1 to the contrary and subject to Section 4.4 hereof, if, during the Royalty Term in a given country of the Territory, (i) there is no Valid Claim of an issued patent within Ipsen Patent Rights or Joint Patent Rights that Covers the sale of a Licensed Product in such country, and (ii) the aggregate sales revenue in such country of Unlicensed Products (expressed in the currency of such country) constitute more than [ ]* of the market share with respect to the aggregate sales revenue of such Unlicensed Products and such Licensed Product in such country (expressed in the currency of such country), then Licensee shall have the right to calculate royalty payments due to Ipsen pursuant to this Agreement by including only [ ]* of the amount of Net Sales that would have otherwise been included for such Licensed Product in such country to calculate such royalty payments. For the avoidance of doubt, such adjustment of royalties shall apply only if the applicable Unlicensed Products contain the same [ ]* as the applicable Licensed Product. In case of a disagreement between the Parties on the market share of one or more Unlicensed Products in any country of the Territory, the Parties agree to refer such dispute to arbitration pursuant to Article 16.

4.3 Adjustments Related to Necessary Third Party IP Rights. Subject to Section 4.4 below, on a Licensed Product-by-Licensed Product basis and on a country-by-country basis, (i) if Licensee or any of its Affiliates or Sublicensees is obligated to remit payments (the "**Necessary Third Party IP Rights Payments**") to any third party in accordance with the terms of any license entered into by Licensee or any of its Affiliates or Sublicensees with respect to Necessary Third Party IP Rights owned or controlled by such third party (and, in the case of payments required to be so remitted by any such Sublicensee, royalties otherwise due from such Sublicensee to Licensee or any of its Affiliates are reduced as a result of any such required remittance by such Sublicensee) and/or (ii) if (1) Licensee or any of its Affiliates has not obtained a license under Ipsen New Formulation Technology pursuant to Section 2.7 hereof and (2) Licensee or any of its Affiliates or Sublicensees is obligated to remit payments ("**Third Party Formulation Technology Payments**") to any third party in accordance with the terms of any license entered into by Licensee or any of its Affiliates or Sublicensees with respect to formulation technology owned or controlled by such third party and used by Licensee or any of its Affiliates and Sublicensees with any Licensed Product ("**Third Party Formulation Technology**") (and, in the case of payments required to be so remitted by a Sublicensee, royalties otherwise due from such Sublicensee to Licensee or any of its Affiliates are reduced as a result of any such required remittance by such Sublicensee), Licensee shall be permitted to offset [ ]* of Necessary Third Party IP Rights Payments and/or [ ]* of Third Party Formulation Technology Payments against royalties due to Ipsen under this Agreement with respect to sales of the applicable Licensed Product in the applicable country; provided, however, that (i) any offset of Third Party Formulation Technology Payments shall not result in a reduction of more than [ ]* of the royalty payments that would otherwise have been due to Ipsen under this

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Agreement in any calendar year with respect to sales of the applicable Licensed Product in the applicable country and (ii) any offset of Necessary Third Party IP Rights Payments shall not result in a reduction of more than [ ]* of the royalty payments that would otherwise have been due to Ipsen under this Agreement in any calendar year with respect to sales of the applicable Licensed Product in the applicable country. In case Licensee has not been able to offset any allowed amount during any relevant calendar year, no resulting payment shall be due from Ipsen to Licensee as a result of such shortfall, but Licensee shall be entitled to carry over such shortfall to one or more subsequent calendar years and seek to offset the full amount of such shortfall against payments otherwise due to Ipsen in such subsequent calendar year or calendar years (subject always to the limitation set forth in this Section 4.3 and in Section 4.4).

4.4 Total Section 4.3 and Section 4.4 Adjustments. In no event shall the adjustments provided under Sections 4.2 and 4.3 hereof, applied individually or cumulatively, result in an effective royalty rate in connection with royalty payments to Ipsen under this Agreement of less than (i) [ ]* on Net Sales of any Licensed Product in any country in any calendar year during the Royalty Term, or (ii) [ ]* on Net Sales of any Licensed Product in any country in any calendar year during the Royalty Term in the event that (w) such Licensed Product is an Ipsen MC4 Product, (x) such Licensed Product utilizes the Ipsen MC4 [ ]*, (y) the Ipsen MC4 [ ]* was accepted in writing by Licensee pursuant to Section 2.11.1 and (z) the Ipsen MC4 [ ]* is Covered by Ipsen MC4 [ ]* Patent Rights.

ARTICLE 5 PAYMENT, REPORTING, AUDITING

5.1 Currency and Conversion. Subject to the provisions set forth below in this Section 5.1, all payments under this Agreement shall be in US Dollars except for royalty payments with respect to Net Sales made in ROW, which shall be made in Euros. As regards Net Sales in United States of America, Licensee shall calculate Net Sales and calculate and pay corresponding royalties in US Dollars. Whenever calculations of Net Sales or royalties require conversion from any currency into Euros, Licensee shall convert into Euros the amount of Gross Sales and Net Sales, using the [ ]* exchange rates (as published in the Wall Street Journal European Edition or if no longer available any other sources mutually-agreed by the Parties) of the last working day of each applicable Accounting Period.

5.2 Payments and Reporting. After the First Commercial Sale of Licensed Product in the Territory, Licensee shall calculate royalties quarterly at the end of each Accounting Period [ ]* and shall pay royalties on Net Sales quarterly within [ ]* after the end of each Accounting Period.

With each such payment, Licensee shall provide in writing to Ipsen for the relevant Accounting Period at least the following information split by United States of America, and any other countries of the Territory:

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- Gross Sales (expressed in the currency in which the sale of Licensed Product is made, and, for Gross Sales achieved in the ROW, the applicable conversion rates and the resulting amount in Euros, subject to the provisions of Section 5.1 above) on a Licensed Product-by-Licensed Product basis, in unit and in value;

- Net Sales (expressed in the currency in which the sale of Licensed Product is made, and, for Net Sales achieved in the ROW, the applicable conversion rates and the resulting amount in Euros, subject to the provisions of Section 5.1 above) on a Licensed Product-by-Licensed Product basis, in unit and in value;

- Total royalty payable (expressed in USD for the USA and in Euros for ROW, subject to the provisions of Section 5.1 above) on a Licensed Product-by-Licensed Product basis.

5.3 Late payments. Any payment under Articles 3 and 4 that is not timely paid shall bear interest, to the extent permitted by applicable law, at [ ]*.

5.4 Taxes

Each Party shall pay all sales, turnover, income, revenue, value added, and other taxes levied on account of payments accruing or made to it under this Agreement. Nothing in the foregoing sentence shall be deemed to affect the definition of Manufacturing Cost and/or any right that Ipsen specifically is provided or granted under this Agreement to charge and collect from the other Party the Manufacturing Cost incurred by Ipsen in connection with Licensed Product supplied by such Party to the other Party under the terms and conditions of the Clinical Supply Agreements.

If provision is made in law or regulation of any country for withholding of taxes of any type, levies or other charges with respect to any amounts payable under this Agreement to a Party, the other Party ("**Withholding Party**") shall promptly pay such tax, levy or charge for and on behalf of the Party to the proper governmental authority, and shall promptly furnish the Party with a signed original certificate of such tax deduction. The Withholding Party shall have the right to deduct any such tax, levy or charge actually paid from payment due by the Party or be promptly reimbursed by the Party if no further payments are due by the Party. Each Party agrees to assist the other Party in claiming exemption from such deductions or withholdings under double taxation or similar agreement or treaty from time to time in force and in minimizing the amount required to be so withheld or deducted.

5.5 Blocked Countries. If by reason of law, Licensee is unable to convert to US Dollars a portion of the amount due by it under this Agreement, then Licensee shall notify Ipsen in writing and Licensee shall pay to Ipsen such portion in the currency of any other country designated by Ipsen and legally available to Licensee.

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5.5.1 **Accounting.** Licensee shall maintain and shall cause its Affiliates, Sublicensees and Contractors to maintain full, true and accurate books of account containing all particulars that may be necessary for the purpose of calculating all royalties payable under this Agreement. Such books of account shall be kept at their principal place of business. Licensee, its Affiliates, Sublicensees and Contractors shall permit Ipsen, by independent qualified public accountants selected by Ipsen, to examine such books and records at any reasonable time, but not later than [ ]* following the rendering of any corresponding reports, accountings and payments pursuant to this Agreement. The foregoing right of review may be exercised only once during each [ ]* period. Such accountants may be required by Licensee, its Affiliates, Sublicensees and Contractors to enter into a reasonably acceptable confidentiality agreement, and in no event shall such accountants disclose to Ipsen any information other than such as relates to the accuracy of reports and payments made or due hereunder. The opinion of said independent accountants regarding such reports, accountings and payments shall be binding on the parties other than in the case of manifest error. Ipsen shall bear the cost of any such examination and review; provided that if the inspection and audit shows an underpayment of royalty due to Ipsen of more than [ ]* of the amount due for the applicable Accounting Period, then Licensee shall promptly reimburse Ipsen for all costs incurred in connection with such examination and review. Licensee shall promptly pay to Ipsen the amount of any such underpayment revealed by an examination and review together with late payment interest pursuant to Section 5.3.

ARTICLE 6 DEVELOPMENT

6.1 Transfer of Ipsen Licensed Technology and Documentation to Licensee. The Parties agree that, promptly following the Effective Date, at the reasonable request from Licensee, Ipsen shall transfer:

- All research, pre-clinical and clinical data with respect to Licensed Products

- Research and development reports with respect to Licensed Products

- Any drug master files (or, at the request of Licensee, the right to reference any drug master file for any purposes, including any application for Regulatory Approval) with respect to Licensed Products

- Any copies of any correspondence in its possession or under its control with any Regulatory Authorities related to Licensed Products

· Copies of all documents in its possession or under its control relating to any Ipsen Know-How or Ipsen MC4 Compound

· Electronic copies of all patents and patent applications included within Ipsen Patent Rights

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· Assays, biological materials, research tools and research reagents used in relation to research and Development of any Ipsen MC4 Compound, provided that such items are only for use by Licensee to conduct research and Development activities pursuant to this Agreement

· Quantities of any Ipsen MC4 Compound, provided that Ipsen has sufficient inventory of such compound to transfer and supply such quantities, and provided, further, that such quantities are for use by Licensee to conduct research and Development activities pursuant to this Agreement

At least once each [ ]* during the Term and at such other times as License may reasonably request from time to time during the Term, Ipsen shall transfer to Licensee (i) any and all of the items listed above to the extent that they are in the possession or control of Ipsen and have not previously been transferred to Licensee and (ii) copies of all documents in Ipsen's possession or under its control relating to any Ipsen Licensed Know-How and electronic copies of all patents and patent applications included within Ipsen Licensed Patent Rights, in each case to the extent not previously transferred to Licensee.

The performance by Ipsen of its obligations under the foregoing provisions of this Section 6.1 shall be at no cost to Licensee.

From time to time during the applicable Initial Ipsen Support Period (as defined below), at the reasonable request of Licensee, Ipsen agrees to make available to Licensee, free of charge, those of Ipsen's employees and consultants that have knowledge and expertise in connection with researching, developing, obtaining regulatory approval for, or creating and prosecuting intellectual property with respect to, Licensed Products, or in connection with the research, development, use or practice of the Ipsen Technology, for purposes of facilitating the transfer of all Ipsen Technology to Licensee or the transfer of any of the items required to be transferred by Ipsen to Licensee pursuant to this Section 6.1. For purposes of this Agreement, the term "**Initial Ipsen Support Period**" shall mean a period of [ ]* commencing on [ ]*. Such [ ]* period may be extended by mutual agreement of the parties, acting reasonably and in good faith. Should a Licensed Product that is an Ipsen MC4 Product require the filing of the first IND or CTD substantially after the written request for the commencement of such applicable [ ]* period, then the Parties will make provisions to divide such [ ]* period to accommodate the potential need for staging the Ipsen support over this extended period. At Licensee's request made at any time during the Term following the expiration of the applicable Initial Ipsen Support Period, Ipsen may provide to Licensee, on a case-by-case basis, reasonable assistance with respect to knowledge and expertise in connection with research, developing, obtaining regulatory approval for, or creating and prosecuting intellectual property with respect to the Licensed Products, subject to the Parties agreeing on the scope of such assistance. Such assistance shall be charged to Licensee at the per diem rate of [ ]* for internal costs and at cost for external costs.

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6.2 Responsibility and Decision-Making Authority; Development Costs. Unless otherwise agreed in any definitive agreement executed by the Parties pursuant to Section 2.10, Licensee shall have the sole right, responsibility and decision-making authority for all aspects of Development of Licensed Products in the Territory, and shall bear all related costs. Notwithstanding anything express or implied in this Agreement (including, without limitation, this Section 6.2) to the contrary, Ipsen shall continue until completion certain [ ]* that are identified on Appendix C and are ongoing as of the Effective Date under its sole responsibility and decision-making authority (collectively, the "**Ipsen Ongoing Pre-Clinical Studies**").

6.3 Development Plan. The Parties have agreed upon the Initial Development Plan. Licensee shall update and modify the Development Plan from time to time to reflect all Development activities planned by Licensee to obtain Regulatory Approval for each Licensed Product in the Territory, as well as to include any changes or modifications planned by Licensee to such Development activities or to any other aspect of the Development Plan as in effect prior to such changes or modifications. Licensee shall provide to Ipsen a copy of each such update and modification of the Development Plan. The obligations of Licensee under this Section 6.3 with respect to each Licensed Product shall terminate upon the First Commercial Sale of such Licensed Product.

6.4 Reports. In addition, on [ ]* after the Effective Date and during the Term, Licensee will provide to Ipsen a written progress report that will describe the Development activities that Licensee has performed or caused to be performed during the preceding [ ]* period. The obligations of Licensee under this Section 6.4 with respect to each Licensed Product shall terminate upon the First Commercial Sale of such Licensed Product.

ARTICLE 7 REGULATORY MATTERS AND SAFETY

7.1 Responsibility and Decision-Making Authority for Regulatory Affairs. Unless otherwise agreed in any definitive agreement executed by the Parties pursuant to Section 2.10, Licensee, at its own expense, shall have the sole right, responsibility and decision-making authority for all regulatory affairs in the Territory related to Licensed Product, including the preparation and filing of applications for Regulatory Approval, as well as any or all

governmental approvals required to manufacture, or have manufactured, Licensed Product. Licensee shall file all such applications in its own name or that of its Affiliate. Licensee, at its own expense, shall have the sole right and responsibility for all communications and dealings with the Regulatory Authorities in the Territory.

7.2 Ownership of Regulatory Approvals. Unless otherwise agreed in any definitive agreement executed by the Parties pursuant to Section 2.10, Licensee shall own all Regulatory Approval files and Regulatory Approvals in the Territory.

7.3 Pharmaco-vigilance responsibility. Unless otherwise agreed in any definitive agreement executed by the Parties pursuant to Section 2.10, Licensee shall be responsible for reporting to Regulatory Authorities in the Territory any adverse

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experience and safety issues for Licensed Product in compliance with the requirements of the applicable laws, rules and regulations.

7.4 Drug Safety Database. Unless otherwise agreed in any definitive agreement executed by the Parties pursuant to Section 2.10, Licensee shall be responsible for compiling a validated global database that captures all adverse events reported to Licensee from any source and maintaining said database.

ARTICLE 8 MANUFACTURE AND SUPPLY

8.1 Supply for Development. If requested by Licensee by written notice, Ipsen shall manufacture and supply, or cause to be manufactured and supplied, [ ]* in sufficient quantities to satisfy the reasonable requirements of Licensee and its Sublicensees and Contractors for use of such [ ]* in Development activities with respect to such Licensed Product until the end of [ ]* for such Licensed Product. Ipsen's supply of [ ]* to Licensee under this Section 8.1 shall be provided at Ipsen's Manufacturing Cost. Promptly following Licensee's notice, the Parties shall enter into a clinical supply agreement and a technical agreement with respect to such clinical supplies (the "**Clinical Supply Agreements**")[(1)]. Ipsen's Manufacturing Cost will be agreed upon in the Clinical Supply Agreements (to reflect Ipsen's actual costs for manufacturing the [ ]* as well as a mechanism for adjusting such Manufacturing Cost in case of increase or decrease of any component of such Manufacturing Cost. The Clinical Supply Agreements will provide for the terms and conditions of the transfer of Ipsen's manufacturing technology at the end of [ ]*, provided, however, that the Parties agree that such transfer will be made at Licensee's cost and expense, less an amount equal to the Ipsen Manufacturing Transfer Cost, to be estimated and agreed by the parties in good faith. For the avoidance of doubt, in the event Licensee does not notify Ipsen with its request for the manufacturing by Ipsen of [ ]* pursuant to this Section 8.1, the transfer of manufacturing technology shall be made under the terms and conditions of Section 8.1. Ipsen shall not be obligated to manufacture any quantities of [ ]* pursuant to this Section 8.1 if and to the extent that such quantities will be used by Licensee or any of its Sublicensees or Contractors to make finished Licensed Product for use in [ ]*.

8.2 Transition. In the event Licensee does not notify Ipsen with its request for Ipsen manufacturing the [ ]* pursuant to Section 8.1, at the request of Licensee, Ipsen shall provide to Licensee a manufacturing transfer package relating to Ipsen's existing manufacturing technology of the Licensed Products no later than [ ]* from the date of request by Licensee, and Ipsen shall use [ ]* efforts to transfer to Licensee all Ipsen Licensed Know-How and methods pertaining to the manufacture of [ ]*

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(1) [ ]*

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[ ]* at Ipsen's cost and expense (the "**Ipsen Manufacturing Transfer Cost**") and Licensee shall use [ ]* efforts to understand and implement such Ipsen Licensed Know-How and methods pertaining to the manufacture of such Licensed Product.

8.3 Commercial Supply. Unless otherwise agreed in any definitive agreement executed by the Parties pursuant to Section 2.10, Licensee shall have the sole right, responsibility and decision-making authority for the manufacture, in accordance with good manufacturing practice, and supply of commercial quantities of Licensed Product in the Territory after receipt of Regulatory Approval therefor in the applicable jurisdiction or jurisdictions.

ARTICLE 9 COMMERCIALIZATION

9.1 Responsibility and Decision-Making Authority. Unless otherwise agreed in any definitive agreement executed by the Parties pursuant to Section 2.10, Licensee, at its own expense, shall have sole right, responsibility and decision-making authority for the marketing, promotion, sale and distribution of Licensed Product in the Territory under Licensee's Regulatory Approvals.

ARTICLE 10 INTELLECTUAL PROPERTY

10.1 Trademarks. Licensee shall identify and select one or more trademarks to be used to register, distribute and promote the Licensed Products in the Territory (collectively, **"Licensee Trademarks"** and each individually a **"Licensee Trademark"**) which shall not be the same or confusingly similar to any product of Ipsen. Unless otherwise agreed between the Parties, Ipsen shall not avail itself of any license on any Licensee Trademark, shall not register or use any Licensee Trademark and shall not license, register or use any other trademark or trade name which is the same as, or confusingly similar to, any Licensee Trademark in any country. Licensee shall own and, at its cost, shall be responsible for procurement, registration, maintenance and enforcement of all Licensee Trademarks used or registered in connection with any Licensed Product.

10.2 Infringements of Trademarks. Licensee shall have the sole right but not the obligation to initiate proceedings against, or defend claims made by, any person in connection with any Licensee Trademark. The commencement, strategies, termination, settlement or defense of any action relating to the validity or infringement of Licensee Trademarks shall be decided by Licensee. Any such proceedings shall be at the expense of Licensee. Any damages or costs recovered by Licensee as a result of any such proceedings or claims, shall be for the sole benefit and account of Licensee.

10.3 Patent Right and Know-How Ownership

10.3.1 Ipsen shall own all Ipsen Inventions, Licensee shall own all Licensee Inventions, and Ipsen and Licensee shall jointly own all Joint Inventions. Each Party promptly will notify the other Party in writing of (i) any Invention that the notifying Party believes is a Joint Invention and (ii) any

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Invention for which the notifying Party intends to file a patent application. Each Party shall require all of its employees and contractors to assign all Inventions made by them to such Party.

10.3.2 All right, title and interest in and to Ipsen Licensed Technology are and shall remain vested in Ipsen, subject only to any rights thereto granted by Ipsen to Licensee pursuant to this Agreement, including, without limitation, the Licensed Rights granted by Ipsen to Licensee pursuant to Section 2.1. Notwithstanding anything express or implied in the foregoing provisions of this Section 10.3.2 or elsewhere in this Agreement to the contrary, Ipsen and its Affiliates shall not sell, assign or otherwise transfer or dispose of all or any portion of their respective right, title and interest in and to Ipsen Licensed Technology without having obtained the prior agreement or consent of Licensee, unless (x) the proposed buyer, assignee or other transferee shall have, as a condition precedent to the effectiveness of any such sale, assignment or other transfer or disposition, executed an instrument in writing agreeing to assume all of the agreements and obligations under this Agreement of Ipsen and its Affiliates to the extent applicable to the Ipsen Licensed Technology, or the portion thereof, transferred to such buyer, assignee or other transferee, and (y) any such sale, assignment or other transfer or disposition shall not operate to release Ipsen and its Affiliates from any of its agreements or obligations under this Agreement.

10.3.3 All right, title and interest in and to Licensee Know-How, Licensee Patent Rights and Licensee Joint Technology Rights are and shall remain vested in Licensee.

10.3.4 Any and all Joint Know-How and Joint Patent Rights shall be owned by the Parties in equal undivided shares. Except to the extent otherwise provided elsewhere in this Agreement to the contrary (including, without limitation, the provisions of Section 2.1 pursuant to which Ipsen granted to Licensee an exclusive license to all of Ipsen's right, title and interest in and to all of the Joint Know-How and Joint Patent Rights for certain uses specified therein), each Party shall be free to use its undivided share of any and all Joint Inventions or any and all Joint Patent Rights without having to obtain the agreement or consent of the other Party, without having to provide notice of such use to the other Party and without having to make any accounting to the other Party for such use or any revenues or profits derived from such use. In addition, except to the extent otherwise provided elsewhere in this Agreement to the contrary, each Party shall be free to sell, assign, license and otherwise transfer or dispose of all or any portion of such Party's undivided share in any and all Joint Inventions or any and all Joint Patent Rights without having to obtain the agreement or consent of the other Party, without having to provide notice of such sale, assignment, license or other transfer or disposition to the other Party and without having to make any accounting to the other Party for such sale, assignment, license or other transfer or disposition or any revenues or profits derived from such sale, assignment, license or other transfer or disposition; provided, however, that (x) any buyer, assignee, licensee or other transferee of all or any portion of the Joint Inventions and Joint

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Patent Rights shall take all or the portion of the Joint Inventions and/or Joint Patent Rights so transferred subject to all of the agreements and obligations under this Agreement of the transferring Party (including, without limitation, the exclusive licenses granted by Ipsen to Licensee pursuant to Section 2.1 hereof with respect to certain uses of Ipsen's right, title and interest to the Joint Inventions and Joint Patent Rights), (y) such buyer, assignee, licensee or other transferee shall, as a condition precedent to the effectiveness of any such sale, assignment, license or other transfer or disposition, execute an instrument in writing agreeing to assume all of the agreements and obligations under this Agreement of the transferring Party to the extent applicable to the Joint Inventions or Joint Patent Rights, or the portion thereof, transferred to such buyer, assignee, licensee or other transferee, and (z) any such sale, assignment, license or other transfer or disposition shall not operate to release the transferring Party from any

of its agreements or obligations under this Agreement. Licensee may use during the Term any and all Joint Inventions and Joint Patent Rights for the purposes contemplated in this Agreement.

10.4 Filing — Prosecution and Maintenance of Ipsen Licensed Patent Rights and Licensee Patent Rights.

10.4.1 Ipsen shall at its own cost and expense be solely responsible for the filing, prosecution and maintenance of the Ipsen Licensed Patent Rights in the Territory, including the conduct and defense of any claims or proceedings relating to the Ipsen Licensed Patent Rights in the Territory (including but not limited to any interference, reissue or re-examination or opposition proceedings); provided, however, that Ipsen shall (i) provide Licensee with all material documentation and correspondence from, sent to or filed with patent offices in the Territory regarding the Ipsen Licensed Patent Rights, (ii) provide Licensee with a reasonable opportunity to review and comment upon all filings with such patent offices in advance of submissions to such patent offices, and (iii) shall consider, in good faith, incorporating any reasonable comments provided by Licensee with respect to any such filings. Without limiting the generality of the foregoing provisions of this Section 10.4.1, Ipsen shall at its own cost and expense file, prosecute and maintain Ipsen Licensed Patent Rights in any country in the Territory as reasonably requested by Licensee acting in a reasonable commercial manner with regards the market potential of such country, including the conduct and defense of any claims or proceedings relating to the Ipsen Licensed Patent Rights in such country (including but not limited to any interference, reissue or re-examination or opposition proceedings). If Ipsen determines in its sole discretion to abandon or not to file, prosecute or maintain any claim, patent or patent application within the Ipsen Licensed Patent Rights in any country in the Territory, including the conduct and defense of any claims or proceedings relating to such claim, patent or patent application (including but not limited to any interference, reissue or re-examination or opposition proceedings), then Ipsen shall provide Licensee with [ ]* prior written notice of such determination, and shall provide Licensee with the opportunity to file, prosecute and maintain such claim, patent or patent application in such country in the name of Licensee (or an Affiliate of

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Licensee) as assignee, including the conduct and defense of any claims or proceedings relating to such claim, patent or patent application in such country (including but not limited to any interference, reissue or re-examination or opposition proceedings), and Ipsen shall assign to Licensee its entire right in such claim, patent or patent application in such country, and thereafter Licensee shall be responsible for all costs and expenses in connection with the filing, prosecution or maintenance of any such claim, patent or patent application assigned by Ipsen to Licensee pursuant to this Section 10.4.1 and Ipsen shall not be entitled to any compensation of any kind (including, without limitation, any compensation for such assignment) in connection with any such claim, patent or patent application assigned by Ipsen to Licensee. Ipsen shall also pay for all costs and expenses in connection with any assignment by Ipsen to Licensee of any claim, patent or patent application pursuant to this Section 10.4.1. Licensee shall upon first request from Ipsen deliver to Ipsen the original of any Regulatory Approval for the purpose of applying for any supplementary protection certificates of any Ipsen Licensed Patent Rights.

10.4.2 Licensee shall at its own cost and expense be solely responsible for the filing, prosecution and maintenance of the Licensee Patent Rights, including the conduct and defense of any claims or proceedings relating to the Licensee Patent Rights in the Territory (including but not limited to any interference, reissue or re-examination or opposition proceedings).

10.4.3 Each Party will take account of the other Party's interest in the performance of its obligations under this Section 10.4. Each Party shall provide to the other all assistance reasonably requested by the other Party on all such matters (at the expense of such other Party), including agreeing to and taking all steps and executing all documents necessary to be joined as claimant or defendant in any proceedings in any country.

10.5 Filing — Prosecution and Maintenance of Joint Patent Rights. Unless the Parties otherwise mutually agree in writing, Licensee shall have the first right to file, prosecute and maintain the Joint Patent Rights in any and all countries of the world, including the conduct and defense of any claims or proceedings relating to the Joint Patent Rights in any and all countries of the world (including but not limited to any interference, reissue or re-examination or opposition proceedings), *provided however,* in the event that Licensee determines in its sole discretion to abandon or not to file, prosecute or maintain any claim, patent or patent application within the Joint Patent Rights in any country of the world, including the conduct and defense of any claims or proceedings relating to such claim, patent or patent application (including but not limited to any interference, reissue or re-examination or opposition proceedings), then Licensee shall provide Ipsen with [ ]* prior written notice of such determination, and Ipsen shall have such right and upon exercise of such right, Ipsen shall have the right to file, prosecute and maintain such claim, patent or patent application in such country, including the conduct and defense of any claims or proceedings relating to such claim, patent or patent application in such country (including but not limited to any interference, reissue or re-examination or opposition proceedings). In each case under this Section

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10.5, the filing Party (A) shall give the non-filing Party a reasonable opportunity to review the text of the application or submission before filing, (B) shall consult with the non-filing Party with respect thereto, (C) shall, prior to filing any application or submission, incorporate any reasonable comments that the non-filing Party shall make on a timely basis to such application or submission and (D) shall supply the non-filing Party with a copy of the application or submission as filed, together with notice of its filing date and serial number and all substantive prosecution. Each Party shall keep the other advised of the status of the actual and prospective patent filings described above in this Section 10.5 and, upon the request of the other, provide advance copies of any papers

related to the filing, prosecution and maintenance of such patent filings. Licensee shall promptly give notice to Ipsen of the grant, lapse, revocation, surrender, invalidation or abandonment in any country within the Territory of any Joint Patent Rights being prosecuted by Licensee. Ipsen shall promptly give notice to Licensee of the grant, lapse, revocation, surrender, invalidation or abandonment in any country within the Territory of any Joint Patent Rights being prosecuted by Ipsen. With respect to all filings under this Section 10.5, the filing Party shall be responsible for payment of all costs and expenses related to such filings (including, without limitation, fees and disbursements of outside legal counsel in connection with such filings), subject to prompt reimbursement from the non-filing Party for [ ]* of all of such costs and expenses. Either Party may disclaim its interest in any particular patent or patent application included in the Joint Patent Rights, in which case (X) the disclaiming Party shall assign its ownership interest in such patent or patent application to the other Party for no additional consideration, (Y) the Party which is then the sole owner shall be solely responsible for all future costs of such patent or patent application and (Z) the disclaiming Party shall hold no further rights thereunder.

10.6 Infringement. Each Party shall give prompt written notice to the other of any suspected or actual Infringement by a third party of all or any portion of the Ipsen Licensed Technology, Licensee Technology, Joint Inventions or Joint Patent Rights that comes to the attention of that Party during the Royalty Term with respect to any and all countries in the Territory. Licensee shall have the first right but not the obligation to initiate and pursue proceedings against such third party in connection with any such suspected or actual Infringement of all or any portion of the Ipsen Licensed Technology, Joint Inventions or Joint Patent Rights, and Licensee shall have the sole right but not the obligation to initiate and pursue proceedings against such third party in connection with any such suspected or actual Infringement of all or any portion of Licensee Technology. The commencement, strategies, termination, and settlement of any action or proceedings relating to the validity or suspected or actual Infringement of the Ipsen Licensed Technology, Joint Inventions or Joint Patent Rights, or any portion thereof, shall be decided by Licensee in consultation with Ipsen. The commencement, strategies, termination, and settlement of any action or proceedings relating to the validity or suspected or actual Infringement of Licensee Technology, or any portion thereof, shall be decided solely by Licensee without any requirement that Licensee consult with Ipsen. Any proceedings initiated and pursued by Licensee pursuant to this Section 10.6 shall be at the expense of Licensee. Nothing in this Agreement, however, shall be deemed to require Licensee to enforce all or any portion of the Ipsen Licensed Technology, Joint Inventions, Joint Patent Rights or Licensee Technology against others; provided,

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however, that if Licensee does not enforce all or any portion of the Ipsen Licensed Technology, Joint Inventions or Joint Patent Rights, Ipsen may do so at its expense and, if necessary under the relevant law of the concerned jurisdiction, in the name of Licensee as a plaintiff, unless Licensee reasonably believes that pursuit by Ipsen of any such enforcement action jeopardizes all or any portion of the Ipsen Licensed Technology, Joint Inventions or Joint Patent Rights, including the validity thereof, and sends written notice to Ipsen stating that Ipsen should not pursue any such enforcement action for this reason, in which case Ipsen shall not pursue any such enforcement action. Ipsen may not settle any proceedings or other enforcement action without the prior written consent of Licensee, which consent shall not be unreasonably withheld or delayed. At the request of the Party bringing such enforcement action or proceeding under this Section 10.6, the other Party shall cooperate reasonably with such Party, including without limitation by having such other Party agree to be named as a party if necessary to such enforcement action or proceeding, and any such reasonable cooperation by such other Party shall be at the sole cost and expense of such Party that requested such cooperation. The Party not bringing an enforcement action or proceeding under this Section 10.6 with respect to the validity or suspected or actual Infringement of Ipsen Licensed Technology, Joint Inventions or Joint Patent Rights shall be entitled to separate representation in such matter by counsel of its own choice and at its own expense. Any damages, costs or other amounts recovered in connection with any action or proceeding initiated and pursued by Licensee or Ipsen pursuant to this Section 10.6, including, without limitation, any settlement thereof, in connection with the validity or suspected or actual Infringement of Ipsen Licensed Technology, Joint Inventions or Joint Patent Rights, shall be allocated first to [ ]* and any remaining amounts shall be allocated as follows: [ ]*.

10.7 Third party intellectual property rights

10.7.1 Each Party shall give prompt written notice to the other of any intellectual property rights of any third party which could reasonably be considered as constituting impediment on the use of the Ipsen Licensed Technology, Joint Inventions or Joint Patent Rights in accordance with the provisions of this Agreement or on the research, development, manufacture, use, marketing, promotion, distribution, sale, import or export of Licensed Product, in which event the Parties shall agree on the strategy and procedural steps to be taken in respect of opposing and/or settling such potential impediment.

10.7.2 Each Party shall give prompt written notice to the other of claims or suits arising out of actual or alleged Infringement of Patent Rights, Know-How or other intellectual property owned by a third party, as a result of any use of the Ipsen Licensed Technology, Joint Inventions or Joint Patent Rights in accordance with the provisions of this Agreement or on the research, development,

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manufacture, use, marketing, promotion, distribution, sale, import or export of Licensed Product, in which event Licensee, subject to the provisions of Section 10.7.3, shall have the right to contest or defend such claim or suit on behalf of itself and on behalf of Ipsen. If Licensee elects to contest or defend such claim or suit, Licensee shall notify Ipsen of such election, and shall keep Ipsen fully informed of any development in such claim or suit, including by transmitting copies of all documents in such claim or suit. If Licensee contests or defends a claim or suit pursuant to this Section 10.7.2 and Ipsen has not elected to contest or defend such claim or suit subject to, and in accordance with, the provisions of Section 10.7.3, then (a)

Licensee shall control the defense of such claim or suit, (b) Ipsen shall provide assistance in the defense of such claim or suit in a reasonable and timely manner upon reasonable request of Licensee and at Licensee' sole cost and expense; and (c) Licensee shall have the right to compromise or settle such claim or suit; provided, however, that, if such claim or suit was originally made or filed against Ipsen or any of its Affiliates or pertains to any of the Ipsen Licensed Technology, Joint Patent Rights or Joint Know-How, any such compromise or settlement by Licensee of such claim or suit shall be subject to Ipsen's prior written approval, which shall not be unreasonably withheld or delayed. Notwithstanding Licensee's control of the defense of any claim or proceeding pursuant to this Section 10.7.2, Ipsen shall have the right to participate in such defense using counsel of its own choice and at its own expense, provided that such claim or proceeding was originally made or filed against Ipsen or any of its Affiliates or pertains to any of the Ipsen Licensed Technology, Joint Patent Rights or Joint Inventions.

10.7.3 If, within [ ]* after Licensee receives written notice of any such claim or suit, Licensee elects not to contest or defend, or fails to notify Ipsen of its intent to contest to or defend, such claim or suit, then Ipsen shall have the right to contest or defend such claim or suit on behalf of itself and Licensee and shall keep Licensee fully informed of any development in such claim or suit, including by transmitting copies of all documents submitted in such claim or suit. Notwithstanding any of the foregoing provisions of this Section 10.7.3 to the contrary, Ipsen's right under this Section 10.7.3 to contest or defend such claim or suit shall apply only if either (i) such claim or suit was originally made or brought against Ipsen or any of its Affiliates or (ii) such claim or suit pertains to any of the Ipsen Licensed Technology, Joint Patent Rights or Joint Inventions. If Ipsen contests or defends a claim or suit pursuant to this Section 10.7.3, then (a) Ipsen shall control the defense of such claim or suit, (b) Licensee shall provide assistance in the defense of such claim or suit in a reasonable and timely manner upon reasonable request of Ipsen and at Ipsen's sole cost and expense and (c) Ipsen shall have the right to compromise or settle such claim or suit; provided, however, that such compromise or settlement shall be subject to Licensee's prior written approval, which shall not be unreasonably withheld or delayed. Notwithstanding Ipsen's control of the defense of any such claim or proceeding, Licensee shall have the right to participate in such defense using counsel of its own choice and at its own expense.

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10.7.4 The defending Party shall bear its own costs and expenses (including, without limitation, attorneys fees and court costs) in connection with the defense of any claim or suit pursuant to Section 10.7.2 or Section 10.7.3, and the defending Party shall also bear the costs and expenses of the other Party if and to the extent that such costs and expenses were incurred by such other Party in connection with reasonable assistance provided by such other Party in connection with such defense at the request of the defending Party.

10.7.5 In the event that, in connection with the defense of any claim or suit pursuant to this Section 10.7 or any settlement thereof, the defending Party shall receive damages, costs or other amounts, such damages, costs or other amounts shall be treated in the manner contemplated under Section 10.6 as if they had been received by the defending Party in connection with any action or proceeding initiated and pursued by the defending Party pursuant to Section 10.6 above.

10.7.6 The provisions of this Section 10.7 and the respective rights and obligations of the Parties under this Section 10.7 shall be without prejudice to any of the provisions of Article 15 or any of the respective rights and obligations of the Parties under Article 15.

10.8 Patent Notices.

All notices provided under this Article 10 to Licensee shall be given to:

RHYTHM METABOLIC, INC.
855 Boylston Street, 11th Floor
Boston MA 02116
Attn: Bart Henderson, President

with a copy to:

Bingham McCutchen LLP
One Federal Street
Boston, Massachusetts U.S.A. 02110
Attn: Julio E. Vega, Esq.

All notices provided under this Article 10 to Ipsen shall be given to:

IPSEN PHARMA SAS.
65 Quai Georges Gorse
92100 Boulogne-Billancourt, France
Attn: Head, Patent Law

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With a copy to :

BIOMEASURE INC.
27 Maple Street
Milford, Massachussetts
01757-3650 USA
Attn : Patent Department

ARTICLE 11 CONFIDENTIAL INFORMATION

11.1 Non-Disclosure and Non-Use. In performing under this Agreement, the Parties will share proprietary information ("**Confidential Information**") with each other. For the purpose of this Section 11.1, any terms of this Agreement shall be considered as Confidential Information of both Parties. A Party receiving Confidential Information under this Agreement ("**Receiver**") from the other disclosing Party ("**Discloser**") shall maintain such Confidential Information as follows:

The Receiver of a given item of Confidential Information agrees:

· not to use such Confidential Information for any purpose other than in connection with the purpose of carrying out this Agreement;

· to treat such Confidential Information as it would for its own confidential information of the same nature and importance; and

· to take all reasonable precautions to prevent the disclosure of such Confidential Information to any third party without the prior written consent of the Discloser, except to the extent otherwise permitted pursuant to Section 11.3 below.

11.2 Exceptions. A Receiver shall be relieved of any and all obligations under Section 11.1 regarding Confidential Information which:

· was known to the Receiver or its Affiliates prior to receipt hereunder or under any confidentiality agreements signed prior to the Effective Date between the Parties; or

· as demonstrated by the Receiver by competent written proof, is independently generated by the Receiver or its Affiliates by persons who have not had access to or knowledge of the Confidential Information disclosed hereunder; or

· at the time of disclosure by the Discloser to the Receiver, was generally available to the public, or which after disclosure hereunder becomes generally available to the public through no fault attributable to the Receiver, or its Affiliates or sublicensees; or

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· is hereafter made available to the Receiver or its Affiliates for use and unrestricted disclosure by the Receiver from any third party having a right to do so.

11.3 Authorized Disclosure.

11.3.1 Nothing in this Agreement shall prohibit disclosure by a Receiver of Confidential Information to its (i) Affiliates, directors, employees, consultants, advisors or clinical investigators, (ii) potential or actual sublicensees, Contractors, assignees, lenders or investors, or (iii) other third parties, if any, but in each case only on a strict need to know basis for purposes of (x) carrying out, or causing to be carried out, any of the provisions of this Agreement, (y) the exercise or transfer by such Receiver of any of its rights under this Agreement, and (z) providing for the delegation of any of the obligations of such Receiver under this Agreement; provided, however, that any such person to whom such disclosure is made is bound by confidentiality obligations that are no less stringent than the confidentiality obligations of the Parties under this Article 11 (except that the duration of such confidentiality obligations shall be for a period not to exceed [ ]* from the time of disclosure to such person of Confidential Information).

11.3.2 The restrictions set forth in this Article 11 shall not prevent either Party from disclosing any Confidential Information to government agencies to the extent reasonably necessary to file for, prosecute or maintain Patent Rights or to seek Regulatory Approval for any Licensed Product.

The restrictions set forth in this Article 11 shall not prevent disclosure to the extent required by law or pursuant to a judicial or governmental order, provided that the Receiver makes reasonable efforts to minimize the extent of any required disclosure and gives the Discloser sufficient notice to permit the Discloser to seek a protective order or other similar order with respect to such Confidential Information, with Receiver's reasonable assistance therefor.

11.4 Survival. This Article 11 shall survive any termination or expiration of this Agreement for a period of [ ]*.

ARTICLE 12 PUBLICATION AND PRESS RELEASE

12.1 Publications. Neither Party shall publish or publicly present the results of studies carried out under this Agreement to the extent that such publication or such results include information provided to the publishing or presenting Party by the other Party, unless and until the publishing or presenting Party shall have provided the other Party with the opportunity for prior review of such publication or results in accordance with the provisions set forth below in this Section 12.1. Notwithstanding the foregoing or any other provision to the contrary in this Section 12.1, Ipsen shall not publish or publicly present the

results of studies carried out under this Agreement by Licensee, its Affiliates, Sublicensees or Contractors. For purposes of this Section 12.1, the term **"Publication Eligible Material"** shall mean any proposed abstracts, manuscripts or presentations

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(including verbal presentations) that (i) relate to any Licensed Product, (ii) are proposed to be published or publicly presented by either Party and (iii) contain information provided to the publishing or presenting Party by the other Party. Each Party agrees to provide the other Party the opportunity to review any Publication Eligible Material that such Party proposes to publish or publicly present at least [ ]* prior to their intended submission for publication and agrees, upon request, not to submit or publicly present any such Publication Eligible Material until the other Party is given a reasonable period of time (not to exceed [ ]*) to secure patent protection for any material in such publication or presentation that is owned by the non-publishing Party (either individually or jointly with the publishing Party) and which the non-publishing Party believes to be patentable. Neither Party shall have the right to publish or publicly present Confidential Information of the other Party, and each Party shall remove the Confidential Information of the other Party from any proposed publication or presentation upon request by such other Party. Nothing contained in this Section 12.1 shall prohibit the inclusion of information necessary to file a patent application with a government authority, except for Confidential Information of the non-filing Party, provided the non-filing Party is given a reasonable opportunity to review the information to be included prior to submission of such patent application. Notwithstanding the foregoing, the Parties recognize that independent investigators have been engaged, and will be engaged in the future, to conduct clinical trials of Licensed Products. Such independent investigators are understood to operate in an academic environment and shall be allowed to release information regarding such studies in a manner consistent with academic standards. In the event that either Party submits any manuscript or other publication relating to any Licensed Product, it will consider and acknowledge the contributions of the other Party, including, as appropriate, co-authorship.

12.2 Press Release; Public Disclosure of Agreement. The Parties shall issue a mutually agreed upon joint press release at an agreed date promptly following the execution of this Agreement. Ipsen and Licensee will jointly discuss and agree in writing on any statement to the public regarding this Agreement or any of its terms, subject in each case to disclosure otherwise required by law or regulation as determined in good faith by each Party. When a Party elects to make any such statement it will give the other Party at least [ ]* notice to the other Party to review and comment on such statement.

12.3 Use of Ipsen's name. Licensee shall not use Ipsen's name (or any of the names of Ipsen's Affiliates) in any communication to third parties, whether oral or written, without Ipsen's prior written approval.

12.4 Non-Disclosure of Termination Event. In the event of a termination of this Agreement by Licensee under Section 14.3, Licensee will not disclose or cause to be disclosed to any third party the facts or circumstances regarding such termination, except for any such disclosure which is required by law (including if requested by any regulatory agency, taxing authority or commission of competent jurisdiction). As part of its obligation under this Section 12.4, except as is required by law (including if requested by any regulatory agency, taxing authority or commission of competent jurisdiction), Licensee will not (i) issue any press release with respect to the facts or circumstances

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regarding termination of this Agreement under Section 14.3 or (ii) respond to press inquiries with respect to the facts or circumstances regarding such termination, other than responses which are materially consistent with public disclosure regarding the same by Ipsen. For purposes of clarity, nothing in this Section 12.4 shall prevent or restrict Licensee from disclosing or causing to be disclosed publicly or to any third party the fact that Licensee has terminated this Agreement for any reason or no reason if and when such termination has in fact occurred. In addition, notwithstanding anything express or implied in this Section 12.4 to the contrary, Licensee shall be free to disclose the facts or circumstances regarding any termination of this Agreement by Licensee under Section 14.3 to any third party to whom Licensee is entitled to disclose Confidential Information of Ipsen pursuant to Section 11.3 (it being understood that, for purposes of this sentence and the provisions of Section 11.3, such facts and circumstances shall be treated as Confidential Information of Ipsen).

ARTICLE 13 REPRESENTATIONS, WARRANTIES AND COVENANTS

13.1 Mutual Representations and Warranties. Each Party hereby represents and warrants as follows:

(a) It is a corporation duly organized, validly existing and in good standing under the laws of the jurisdiction in which it is incorporated, and has full corporate power and authority and the legal right to own and operate its property and assets and to carry on its business as it is now being conducted and as contemplated in this Agreement, including, without limitation, the right to grant the licenses it is granting hereunder.

(b) On the Effective Date, (i) it has the full right and authority to enter into this Agreement and perform its obligations hereunder, (ii) it is not aware of any impediment that would prevent it from entering into the Agreement or that would inhibit its ability to perform its obligations under this Agreement, (iii) it has taken all necessary corporate action on its part required to authorize the execution and delivery of this Agreement and the performance of its obligations hereunder, and (iv) this Agreement has been duly executed and delivered on behalf of such Party, and constitutes a legal, valid and binding obligation of such Party that is enforceable against it in accordance with its terms.

(c) It has not entered into any agreement with any third party that is in conflict with the rights granted to the other Party under this Agreement, and has not taken any action that would in any way prevent it from granting the rights granted to the other Party under this Agreement, or that would otherwise materially conflict with or materially adverse affect the rights granted to the other Party under this Agreement. Its performance and execution of this Agreement will not result in a breach of any other contract to which it is a party.

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(d) On the Effective Date, it is not aware of any action, suit, inquiry or investigation instituted by any third party that questions or threatens the validity of this Agreement.

(e) All necessary consents, approvals and authorizations of all governmental authorities and other persons or entities required to be obtained by such Party in connection with the execution, delivery and performance of this Agreement have been obtained.

(f) To the best of its knowledge, each Party has, on the Effective Date, the right to grant to the other Party the rights and licenses granted by such Party to the other Party pursuant to this Agreement.

(g) Each Party has, on the Effective Date, the necessary qualified personnel, equipment, technical know-how and other means to perform its duties under this Agreement in a timely manner in accordance with the terms hereof.

13.2 Ipsen Representations and Warranties. Ipsen warrants and represents that:

(a) Ipsen is the owner of the Ipsen Technology that exists on the Effective Date, free and clear (on the Effective Date) of all liens or security interests. On the Effective Date, neither Ipsen nor any of its Affiliates is aware of any right or license of any third party that is required and has not been obtained by Ipsen to permit Ipsen to perform its obligations under this Agreement in accordance with the terms of this Agreement or to permit Licensee to exercise its rights hereunder in accordance with the terms of this Agreement.

(b) On the Effective Date, Ipsen is the co-owner of the [ ]* Patent Application, free and clear of all liens or security interests.

(c) On the Effective Date, neither Ipsen nor any of its Affiliates owns, controls or otherwise has the right to use or practice any rights under any patent or patent application that are not included in the Ipsen Patent Rights on the Effective Date and that would be necessary to the research, Development, manufacture, marketing, promotion, use, sale, import or export of Licensed Products.

(d) On the Effective Date, neither Ipsen nor any of its Affiliates has received notice from any third party of the existence or pendency of any claims asserting that the Ipsen Licensed Technology Infringes the rights of any third party.

(e) On the Effective Date, neither Ipsen nor any of its Affiliates has given any notice to any third party asserting Infringement by such third party of all or any portion of the Ipsen Licensed Technology and neither Ipsen nor any

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of its Affiliates is not aware (without conducting any special investigation for purposes of making this representation and warranty) of any such Infringement.

(f) On the Effective Date, neither Ipsen nor any of its Affiliates is a party to any contract or agreement with a third party (other than [ ]* with respect to the Ipsen [ ]* Patent Rights) pursuant to which Ipsen or any of its Affiliates licensed-in or otherwise acquired or has the right to use the Ipsen Licensed Technology. Neither Ipsen nor any of its Affiliates is on the Effective, or will become at any time during the Term, a party to any contract or agreement with a third party pursuant to which Licensee (or any of Licensee's Affiliates, Sublicensees or Contractors) is or will be required to make payments on account of the use, practice or exploitation of all or any portion of the Ipsen Licensed Technology.

(g) Ipsen has disclosed to Licensee (i) the results of all preclinical and clinical testing in the possession or control of Ipsen or any of its Affiliates or that are known to Ipsen or any of its Affiliates on the Effective Date; and (ii) all information in the possession or control of Ipsen or any of its Affiliates or that is known to Ipsen or any of its Affiliates on the Effective Date concerning [ ]*. Ipsen has not withheld any information that, in Ipsen's reasonable judgment, is material to this transaction. All information and data disclosed by Ipsen to Licensee are complete and accurate in all material respects.

(h) On the Effective Date, there is no litigation pending or, to the knowledge of Ipsen and its Affiliates, threatened against Ipsen or any of its Affiliates with respect to all or any portion of the Ipsen Licensed Technology.

(i) On or prior to the Effective Date, neither Ipsen nor any of its Affiliates has entered into any agreement with a third party pursuant to which Ipsen or any of its Affiliates shall have agreed not to enforce any right of Ipsen or any of its Affiliates to preclude such third party from using or practicing any or all of the Ipsen Licensed Technology.

(j) Except for the Patent Rights set forth on Appendix A, as of the date of this Agreement, neither Ipsen nor any of its Affiliates own or Control as of the date of this Agreement, or will own or Control at any time after the date of this Agreement, any Patents Rights that claim any Ipsen MC4 Program Invention.

(k) That the representation set forth in Section 13.2(k) of the Original Agreement was true and correct as of the Effective Date.

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13.3 Licensee Representations and Warranties. Licensee warrants and represents that as of the Effective Date, Licensee did not knowingly withhold any material information related to the Ipsen Patent Rights with regards to third party intellectual property rights.

13.4 No Other Representations or Warranties. EXCEPT AS EXPRESSLY PROVIDED IN THIS AGREEMENT OR IN ANY OTHER WRITTEN AGREEMENT BETWEEN THE PARTIES, THE FOREGOING REPRESENTATIONS AND WARRANTIES ARE IN LIEU OF, AND EACH PARTY EXPRESSLY DISCLAIMS, ANY AND ALL REPRESENTATIONS AND WARRANTIES OF ANY KIND, EXPRESS OR IMPLIED, INCLUDING, WITHOUT LIMITATION, WARRANTIES OF DESIGN, MERCHANTABILITY, AND FITNESS FOR A PARTICULAR PURPOSE.

13.5 Mutual Covenants. Each Party covenants the following:

(a) That it shall comply in all material respects with all federal, state, provincial, territorial, governmental and local laws, rules and regulations applicable to the development, manufacture and commercialization of Licensed Products by such Party.

(b) That it shall disclose immediately to the other Party all information in its possession or control and as to which it becomes aware concerning side effects, injury, toxicity or sensitivity reaction and incidents or severity thereof with respect to Licensed Products.

ARTICLE 14 TERM AND TERMINATION

14.1 Term.

This Agreement is entered into for a period commencing on the Effective Date and, unless this Agreement is terminated sooner as provided in this Article 14, ending, on a country-by-country basis and on a Licensed Product-by-Licensed Product basis, on the expiration of the applicable Royalty Term (the "**Term**"). Upon expiration of the Term of this Agreement, the Licensed Rights granted by Ipsen to Licensee pursuant to Section 2.1 hereof, to the extent they remain in full force and effect at the time of such expiration, shall thereafter become irrevocable, perpetual and fully paid-up exclusive licenses and shall survive such expiration of the Term of this Agreement.

14.2 Breach. A Party ("**Non-Breaching Party**") shall have the right, in addition to any other rights and remedies, to terminate this Agreement in the event the other Party ("**Breaching Party**") is in breach of any of its material obligations under this Agreement. The Non-Breaching Party shall provide written notice to the Breaching Party, which notice shall identify the breach. The Breaching Party shall have a period of [ ]* after such written notice is provided to cure such breach. If such breach is not cured within the relevant period, this Agreement shall terminate. The waiver by either Party of any breach of any term or condition of this Agreement shall not be deemed a waiver as to any subsequent or similar breach. The right to terminate this Agreement

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under this Section 14.2 is in addition to any other right and protection that may otherwise be available as a result of a breach, including, without limitation, the right to damages.

14.3 Voluntary Termination. Licensee may terminate the Agreement for any reason or no reason (including, without limitation, any decision by Licensee to discontinue Development) and at any time by giving Ipsen one hundred eighty (180) days prior written notice. Such 180 day notice period may be reduced by Ipsen, on a Licensed Product-by Licensed Product basis, in the event Ipsen has identified a new licensee for one or more Licensed Products before the expiration of such 180 day notice period.

14.4 Ipsen Right to Voluntarily Terminate.

14.4.1 Ipsen shall have the unilateral right to terminate this Agreement in its entirety, upon written notice to Licensee with immediate effect, if Licensee, its Affiliates or Sublicensees in any country of the world brings an action or proceeding seeking to have an Ipsen License Patent Right declared invalid or unenforceable.

14.4.2 In case that Licensee does not Develop a Licensed Product or does not continue the Development of a Licensed Product already in Development, in either case both directly and indirectly (through an Affiliate, Sublicensee or Contractor), then Licensee shall so inform Ipsen and Ipsen shall have the unilateral right to terminate this Agreement with respect to such Licensed Product upon written notice to Licensee with immediate effect. In the event of early termination of this Agreement with respect to any Licensed Product pursuant to this Section 14.4.2, (A) all Licensed Rights granted by Ipsen to Licensee pursuant to Section 2.1 hereof with respect to such Licensed Product shall terminate and Ipsen Licensed Know-How and Ipsen Licensed Patent Rights with respect to such Licensed Product shall revert back to Ipsen at no cost to Ipsen and (B) all Licensee IP (as defined in Section 14.6 hereof) with respect, and to the extent it pertains, to such Licensed Product shall be licensed to Ipsen or its designee, at Ipsen's request, pursuant to a written agreement to be negotiated in good faith by the Parties whereby Ipsen will compensate Licensee for such license of Licensee IP. Any such written agreement shall also provide that Ipsen will assume any and all obligations of Licensee to third parties relating to such Licensee IP. In the event the Parties cannot reach an agreement on the terms of such written agreement, the Parties agree to refer this matter to arbitration as per Article 16. Notwithstanding anything express or implied in this Section 14.4.2 to the contrary, the parties agree that, so long as Licensee is actively engaged in finding a partner or Sublicensee to Develop any Licensed Product or to continue Development of any Licensed Product already in Development and can make the reasonable demonstration of such active out-licensing activities, the provisions of this Section 14.4.2 shall not be applicable to such Licensed Product.

14.5 Bankruptcy. Except if and to the extent otherwise provided under applicable law, either Party shall have the right to terminate this Agreement upon written notice to the other Party if such other Party is generally unable to meet its debts when

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due, or makes a general assignment for the benefit of its creditors, or there shall have been appointed a receiver, trustee or other custodian for such other Party for all or a substantial part of its assets, or any case or proceeding shall have been commenced or other action taken by or against such other Party in bankruptcy or seeking the reorganization, liquidation, dissolution or winding-up of such other Party or any other relief under any bankruptcy, insolvency, reorganization or other similar act or law, and any such event shall have continued for sixty (60) days undismissed, unstayed, unbonded and undischarged. Any termination of this Agreement pursuant to this Section 14.5 shall be effective immediately upon the delivery by the terminating Party of the written notice of termination contemplated above in this Section 14.5.

14.6 Consequences of Early Termination. In any event of early termination of this Agreement other than due to early termination by Licensee on account of material breach by Ipsen of any of its obligations under this Agreement, (A) all Licensed Rights granted by Ipsen to Licensee pursuant to Section 2.1 hereof shall terminate and Ipsen Licensed Know-How and Ipsen Licensed Patent Rights shall revert back to Ipsen at no cost for Ipsen and (B) all Licensee Know-How, Licensee Patent Rights and Licensee Joint Technology including without limitation preclinical, clinical and manufacturing data and improvements of Licensee with respect to Licensed Products, as well as all of the then ongoing development activities and manufacturing Know-How with respect to any Licensed Product ("**Licensee IP**"), shall be licensed to Ipsen or its designee, at Ipsen's request, pursuant to a written agreement to be negotiated in good faith by the Parties whereby Ipsen will compensate Licensee for such license of Licensee IP. Any such written agreement shall also provide that Ipsen will assume any and all obligations of Licensee to third parties relating to such Licensee IP. In the event the Parties cannot reach an agreement on the terms of such written agreement, the Parties agree to refer this matter to arbitration as per Article 16.

14.7 Other Consequences of Early Termination. Upon termination of this Agreement:

14.7.1 Licensee shall:

14.7.1.1 make its personnel reasonably available to Ipsen as necessary to effect an orderly transition of development and commercial responsibilities, with the reasonable cost of such personnel to be borne by Ipsen for such services; and

14.7.1.2 assign and transfer to Ipsen, and execute all such documents as may be reasonably required to transfer hereunder, all of Licensee's right, title and interest in the following to the extent they pertain to Licensed Products:

- all regulatory filings (such as INDs), Regulatory Approvals, clinical trial agreements (to the extent assignable and not cancelled), provided however that the responsibility for interacting with the applicable regulatory authorities in connection with the assignment and transfer

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of such regulatory filings, Regulatory Approvals and clinical trial agreements and the preparation of the documentation necessary to such assignment and transfer shall be Ipsen's; and

- all customer lists, marketing and promotional material, and all other documentation related to marketing, sale, and promotion of the Licensed Product in the Territory, and

- all trademarks used for Licensed Product, provided however that the responsibility of preparing and filing of the documents for the recordation of the assignments with the competent authorities in each applicable country and any action required ancillary, shall be borne by Ipsen and that each Party shall bear its expenses caused by its activities in connection with the assignments and transfer of the trademarks.

14.7.1.3 subject to, and in accordance with, the provisions of Section 14.6 hereof regarding Licensee IP, assign and transfer to Ipsen, and execute all such documents as may be reasonably required to transfer hereunder, all of Licensee's right, title and interest in the following to the extent they pertain to Licensed Product:

· all drug master files and related manufacturing data in connection with Licensed Product; and

· all data, including formulation data, results, clinical trial data, support documentation having arisen out of the materials and other information, in Licensee's possession and control related to Licensed Product in the Territory.

14.7.2 subject to, and in accordance with, the provisions of Section 14.6 hereof regarding Licensee IP, Licensee shall initiate transfer (and complete the same in a timely manner), to Ipsen of all technical and industrial know how related to the manufacturing of Licensed Product for use by Ipsen and shall provide reasonable assistance and support (up to a reasonable number of person-days of qualified personnel) as may be reasonably required by Ipsen to be in a position to make Licensed Product itself. Any such transfer under this Section 14.7.2 shall be at Ipsen's expense except in the case of early termination of this Agreement resulting from Licensee's material breach in which case any such transfer shall be at Licensee's sole cost and expense.

14.7.3 All licenses granted by Ipsen to Licensee under this Agreement shall terminate on the effective date of termination. Notwithstanding anything in this Section 10.7.3 or elsewhere in this Agreement to the contrary, Ipsen may authorize Licensee for a period not exceeding [ ]* to continue making, marketing, promoting and selling Licensed Product in the Territory after the termination of such licenses.

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14.7.4 No compensation or refund shall be due by either Party to the other Party, otherwise than damages as determined by a court of competent jurisdiction and compensation that may be due by Ipsen to Licensee as contemplated under Section 14.6.

14.7.5 Licensee shall agree to take such actions and execute such instruments, agreements and documents as are necessary to effect the foregoing.

14.7.6 Unless otherwise agreed by the Parties, the termination of this Agreement shall cause the automatic termination of all ancillary agreements related hereto, including, but not limited to, the Clinical Supply Agreements.

14.8 Survival of Sublicenses. Notwithstanding anything express or implied in this Article 14 or elsewhere in this Agreement to the contrary, each Sublicense Agreement shall survive any termination of this Agreement and shall continue in full force and effect in accordance with the respective terms thereof, provided that (i) the applicable Sublicensee shall not be in material breach of such Sublicense Agreement and (ii) the terms of such Sublicense Agreement permit Ipsen to replace Licensee as a party under such Sublicense Agreement upon any such termination of this Agreement and that such Sublicense Agreement and its terms conform with all of the requirements therefor set forth in this Agreement.

14.9 Accrued Rights; Surviving Rights and Obligations. Expiration or termination of this Agreement, for any reason, will not relieve either Party of any obligation accruing prior to such expiration or termination. Articles 1, 11, 12, 13, 14, 15, 16 and 17 and Section 5.5.1 shall survive expiration or termination of this Agreement. In addition, the obligations and rights of any other provisions of this Agreement, which by their nature of the provision and the nature of the termination or expiration, are intended to survive, shall survive and continue to be enforceable.

ARTICLE 15 INDEMNIFICATION

15.1 Indemnification by Ipsen. Ipsen agrees to indemnify, hold harmless and defend Licensee and its Affiliates and their respective directors, officers, employees and agents (collectively, the **"Licensee Indemnitees"**) from and against any and all suits, claims, actions, demands, liabilities, expenses and/or loss, cost of defense (including without limitation reasonable attorneys' fees, court costs, witness fees, damages, judgements, fines and amounts paid in settlement) and any other amounts (collectively, **"Losses"**) that any Licensee Indemnitee becomes legally obligated to pay to a third party, because of any claim or claims against such Licensee Indemnitee to the extent that such claim or claims arise out of or resulted from (i) a material breach of a representation or warranty or covenant by Ipsen under Article 13; (ii) a material breach by Ipsen of any of its obligations under this Agreement or the Clinical Supply Agreements; (iii) the manufacture by or on behalf of Ipsen of any Licensed Product and the supply thereof to Licensee or any of its Affiliates, Sublicensees or Contractors pursuant to this Agreement or the Clinical Supply Agreements; (iv) the use, research, or handling of any Licensed Product, by or on behalf of Ipsen or any of its Affiliates, licensees, sublicensees,

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distributors or contractors, or any of their respective employees or agents; or (iv) the gross negligence or willful misconduct of Ipsen or any of its Affiliates or contractors, or any of their respective employees or agents; provided, however, that Ipsen shall not be required to indemnify the Licensee Indemnitees for any Losses pursuant to this Section 15.1 to the extent that (1) such Losses arise from Licensee's material breach of any of its obligations under this Agreement or the Clinical Supply Agreements, (2) such Losses arise or result from the gross negligence or willful misconduct of Licensee or any of its Affiliates or Contractors, or any of their respective employees or agents, or (3) Ipsen's liability for such Losses is limited pursuant to Section 5.4.

15.2 Indemnification by Licensee. Licensee agrees to indemnify, hold harmless and defend Ipsen and its Affiliates and their respective directors, officers, employees and agents (collectively, the **"Ipsen Indemnitees"**) from and against any and all Losses that any Ipsen Indemnitee becomes legally obligated to pay to a third party, because of any claim or claims against such Ipsen Indemnitee to the extent that such claim or claims arise out of or resulted from (i) a material breach of a representation or warranty or covenant by Licensee under Article 13, (ii) a material breach by Licensee of any of its obligations under this Agreement or the Clinical Supply Agreements, (iii) the making, use, research, development, handling or commercialization of any Licensed Product by or on behalf of Licensee or any of its Affiliates, Sublicensees or Contractors, or any of their respective employees or agents or (v) the gross negligence or willful misconduct of Licensee or its Affiliates or Contractors, or any of their respective employees or agents; *provided, however,* that Licensee shall not be required to indemnify the Ipsen Indemnitees for any Losses pursuant to this Section 15.2 to the extent that (1) such Losses arise from Ipsen's material breach of any of its obligations under this Agreement or the Clinical Supply Agreements, (2) such Losses arise or result from the gross negligence or willful misconduct of Ipsen or any of its Affiliates or contractors, or any of their respective agents or employees, (3) such Losses arise or result from the manufacture and supply of Licensed Product by or on behalf of Ipsen pursuant to this Agreement or the Clinical Supply Agreements, (4) such Losses arise or result from any Infringement of the patent rights or other intellectual property rights of any third party as a result of the use or practice of Ipsen Licensed Technology by Licensee or any of its Affiliates, Sublicensees or Contractors in accordance with the provisions of this Agreement or (5) Licensee's liability for such Losses is limited pursuant to Section 15.4.

15.3 Procedure. In the event of a claim by a third party against any person entitled to indemnification under this Agreement ("**Indemnified Person**"), the Indemnified Person shall promptly notify the Party having the indemnification obligation under this Agreement with respect to such claim (such Party, the "**Indemnifying Party**") in writing of the claim. The indemnifying Party shall have the right to assume the defense of any such third party claim for which it is obligated to indemnify the Indemnified Person under this Article 15. The Indemnified Person shall cooperate with the Indemnifying Party (and its insurer) as the Indemnifying Party may reasonably request, and at the Indemnifying Party's sole cost and expense. The Indemnified Person shall have the right to participate, at its own expense and with counsel of its choice, in the defense of any claim or suit that has been assumed by the Indemnifying Party. The Indemnifying Party shall have no obligation to indemnify an Indemnified Person in

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connection with any settlement made without the Indemnifying Party's prior written consent. If the Parties cannot agree as to the application of this Article 15 to any third party claim, the Parties may conduct separate defenses of such claims, with each Party retaining the right to claim indemnification from the other in accordance with this Article 15 upon resolution of the underlying claim.

15.4 NOTWITHSTANDING ANYTHING EXPRESS OR IMPLIED IN THIS AGREEMENT TO THE CONTRARY, IN NO EVENT SHALL EITHER PARTY BE LIABLE TO THE OTHER PARTY FOR [ ]* ARISING OUT OF THIS AGREEMENT.

ARTICLE 16 DISPUTE RESOLUTION AND GOVERNING LAW

16.1 Disputes. Unless otherwise set forth in this Agreement, in the event of a dispute arising under this Agreement between the Parties, the Parties shall remain bound by the terms of this Agreement and each Party shall refer such dispute to one executive officer, and such executive officer shall attempt in good faith to resolve such dispute.

16.2 Arbitration. If the Parties are unable to resolve a given dispute pursuant to Section 16.1 within [ ]* of referring such dispute to the executive officers, the Parties shall remain bound by the terms of this Agreement and either Party may have the given dispute settled by binding arbitration in the manner described below:

16.3 Arbitration Request. If a Party intends to begin an arbitration to resolve a dispute arising under this Agreement, such Party shall provide written notice (the "**Arbitration Request**") to the other Party of such intention and the issues for resolution.

16.4 Additional Issues. Within [ ]* after the receipt of the Arbitration Request, the other Party may, by written notice, add additional issues for resolution.

16.5 Arbitration Procedure. Any arbitration to resolve a dispute arising under this Agreement shall be a final and binding arbitration pursuant to the then-current Rules of Arbitration of the International Chamber of Commerce as hereinafter provided:

16.5.1 The Arbitration Tribunal shall consist of three (3) arbitrators. Each party shall nominate one (1) arbitrator and the two (2) arbitrators so named will then jointly appoint the third arbitrator as chairman of the Arbitration Tribunal. If one Party fails to nominate its arbitrator or, if the parties' arbitrators cannot agree on the person to be named as chairman within [ ]*, the International Chamber of Commerce shall make the necessary appointments for arbitrator or chairman in accordance with the Rules of Arbitration of the International Chamber of Commerce.

16.5.2 The place of arbitration shall be in London, England, and the arbitration proceedings shall be held in English. The procedural law of the place of arbitration shall apply where the said Rules are silent.

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16.5.3 The award of the Arbitration Tribunal shall be final and judgment upon such an award may be entered in any competent court or application may be made to any competent court for juridical acceptance of such an award and order of enforcement.

16.5.4 Notwithstanding the referral of any dispute, controversy or claim arising out of or in connection with this Agreement to arbitration pursuant to this Section 16.5, both Parties shall remain free to seek interim, injunctive or conservatory relief, provided that the order of the relevant judicial authority shall not in any way prejudice the above tribunals' power to settle the dispute referred to them in accordance with the Rules of Arbitration of the International Chamber of Commerce.

16.6 Governing Law. This Agreement shall be governed by and construed in accordance with the laws of the State of New York, U.S.A., without reference to its choice of laws principles, and shall not be governed by the United Nations Convention of International Contracts on the Sale of Goods (the Vienna Convention).

ARTICLE 17 MISCELLANEOUS

17.1 Agency - Independent Contractor. Neither Party is an employee, agent or representative of the other Party for any purpose, and this Agreement shall not create or establish an employment, agency or any other relationship. Except as may be specifically provided herein, neither Party shall have any right, power, or authority, nor shall they represent themselves as having authority to assume, create or incur any expense, liability or obligation, express or implied, on behalf of the other Party, or otherwise act as an agent for the other Party for any purpose. The Parties agree that the relationship of Ipsen and Licensee established by this Agreement is that of independent licensee and licensor. This Agreement does not, is not intended to, and shall not be construed to, establish a partnership or joint venture.

17.2 Entire Agreement. This Agreement, including all appendices, schedules and attachments, embodies the entire understanding of the Parties with respect to the subject matter hereof and supersedes all previous communications, representations or understandings, and agreements, whether oral or written, between the Parties relating to the subject matter hereof.

17.3 Assignment. Except to the extent otherwise expressly provided elsewhere in this Agreement, either Party may assign this Agreement or any of such Party's rights and obligations under this Agreement to any of its Affiliates or any third party, provided that the rights and obligations of the Parties under this Agreement shall be binding upon and inure to the benefit of the successors and assigns of the Parties and that an assignment or delegation of this Agreement by a Party or of any of a Party's obligations under this Agreement shall not operate to release such Party from any of its obligations under this Agreement or from the specific obligation assigned or delegated by such Party. Any assignment not in accordance with this Agreement shall be void.

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17.4 Notices. Any notice or other communication under this Agreement, unless otherwise specified, shall be in writing and provided when delivered to the addressee at the address listed below (a) on the date of delivery if delivered in person or (b) three (3) days after mailing to the other Party by express mail or overnight delivery service, which obtains a signed receipt:

In the case of Ipsen:

IPSEN PHARMA SAS
65 Quai Georges Gorse
92100 Boulogne Billancourt - FRANCE
Attn.: General Counsel

In the case of Licensee:

RHYTHM METABOLIC, INC.
855 Boylston Street, 11th Floor,
Boston MA 02116
Attn: M. Bart Henderson – President

with a copy to:

Bingham McCutchen LLP

One Federal Street
Boston, Massachusetts U.S.A. 02110
Attn: Julio E. Vega, Esq.

Either Party may change its address for communications by a notice in writing to the other Party in accordance with this Section.

17.5 Force Majeure. Any prevention, delay or interruption of performance (collectively "**Delay**") by any Party under this Agreement shall not be a breach of this Agreement if and to the extent caused by occurrences beyond the reasonable control of the Party affected by the force majeure, including but not limited to acts of God, embargoes, governmental restrictions, terrorism, general strike, fire, flood, earthquake, explosion, riots, wars (declared or undeclared), civil disorder, rebellion or sabotage. The affected Party shall immediately notify the other Party upon the commencement and end of the Delay. During the Delay, any time for performance hereunder by either Party shall be extended by the actual time of Delay. If the Delay resulting from the force majeure exceeds [ ]*, the other Party, upon written notice to the affected Party, may elect to (a) treat such Delay as a material breach solely for purposes of exercising the right to terminate this Agreement for material breach pursuant to, and in accordance with, Section 14.2, or (b) extend the term of this Agreement for an amount of time equal to the Delay.

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17.6 Severability. If any of the provisions of this Agreement are held to be void or unenforceable by a court of competent jurisdiction, then such void or unenforceable provisions shall be replaced by valid and enforceable provisions which will achieve as far as possible the economic business intentions of the Parties. However the remainder of this Agreement will remain in full force and effect, provided that the material interests of the Parties are not affected, i.e. the Parties would presumably have concluded this Agreement without the unenforceable provisions.

17.7 No Right to Use Names. Except as otherwise expressly provided herein, this Agreement provides no grant of right to a Party, express or implied, to use in any manner the housemarks or trademarks of the other Party or its Affiliates.

17.8 Bankruptcy. All rights and licenses granted under or pursuant to this Agreement by Ipsen are, and will otherwise be deemed to be, for purposes of Section 365(n) of the U.S. Bankruptcy Code (or the equivalent provisions, if any, in the bankruptcy laws of the applicable jurisdiction) licenses of rights to "intellectual property" as defined under Section 101 of the U.S. Bankruptcy Code.

17.9 Legal and Administrative Obligations. In conducting its obligations under this Agreement, each Party shall observe any and all applicable laws and regulations of the Territory, with respect to the development, manufacture, warehousing, promotion, distribution and sale of [ ]*, and undertakes to make and fulfill any and all formalities in connection with all such activities which may be required under applicable laws and regulations of the Territory. In conducting its obligations under this Agreement, each party further agrees to comply in all means with the current applicable Good Clinical Practices, Good Manufacturing Practices and Good Distribution Practices and apply a high standard of ethics. In particular, each Party undertakes to comply with the principles set forth in the OECD (Organization for Economic Co-operation and Development) Convention on Combating Bribery of Foreign Public Officials in International Business Transactions while performing its activities within the scope of this Agreement.

17.10 Performance by Affiliates. Each of Licensee and Ipsen acknowledge that obligations under this Agreement may be performed by Affiliates of Licensee and Ipsen. Each of Licensee and Ipsen guarantee and warrant any performance of this Agreement by its Affiliates. Wherever in this Agreement the Parties delegate responsibility to Affiliates, the Parties agree that such entities may not make decisions inconsistent with this Agreement, amend the terms of this Agreement or act contrary to its terms in any way.

17.11 Counterparts. The Parties may execute this Agreement in counterparts, each of which the Parties shall deem an original, but all of which together shall constitute one and the same instrument.

17.12 Waiver. A waiver of any default, breach or non-compliance under this Agreement is not effective unless signed by the Party to be bound by the waiver. No waiver will be inferred from or implied by any failure to act or delay in acting by a Party

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in respect of any default, breach, non-observance or by anything done or omitted to be done by the other Party. The waiver by a Party of any default, breach or non-compliance under this Agreement will not operate as a waiver of that Party's rights under this Agreement in respect of any continuing or subsequent default, breach or non-compliance (whether of the same or any other nature).

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CONFIDENTIAL

IN WITNESS WHEREOF, the Parties have executed this Agreement by their proper officers as of the date and year first above written.

IPSEN PHARMA S.A.S.		**RHYTHM METABOLIC, INC.**	
By:	/s/ Pierre Boulud	By:	
Name:	Pierre Boulud	Name:	
Title:	EVP Corporate Strategy and Managing Director	Title:	

[Signature Page to Ipsen/Metabolic License Agreement]

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CONFIDENTIAL

IN WITNESS WHEREOF, the Parties have executed this Agreement by their proper officers as of the date and year first above written.

IPSEN PHARMA S.A.S.		**RHYTHM METABOLIC, INC.**	
By:		By:	/s/ Keith Gottesdiener
Name:		Name:	Keith Gottesdiener
Title:		Title:	CEO

[Signature Page to Ipsen/Metabolic License Agreement]

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APPENDIX A — IPSEN [ ]* Patent Rights as of January 30, 2013

[ ]*

First Priority Country	Filing Date	Application Number	Publication Date	Publication Number	Grant Date	Grant Number	Expiration Date
[ ]*							

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APPENDIX B — IPSEN ONGOING PRE-CLINICAL STUDIES

[ ]*

Study	Study no.	Status 22/12/09	Final

[ ]*

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Appendix C — INITIAL DEVELOPMENT PLAN

Rhythm Metabolic, Inc.

Clinical Development Plan

[ ]*

[ ]*

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DEVELOPMENT AND MANUFACTURING SERVICES AGREEMENT

THIS DEVELOPMENT AND MANUFACTURING SERVICES AGREEMENT is made as of July 17, 2013 (the "Effective Date") by and between **RHYTHM METABOLIC, INC.,** a Delaware corporation with offices at 855 Boylston Street, 11th Floor, Boston, MA 02116, USA ("Rhythm") and **PEPTISYNTHA Inc.**, a US company incorporated under the laws of the state of Delaware with its registered office at 3333 Richmond Avenue, Houston Texas 77098, USA ("Manufacturer").

RECITALS:

WHEREAS, Rhythm desires to engage Manufacturer to perform certain Development and/or Manufacturing Services (as those terms are defined below), on the terms and conditions set forth below, and Manufacturer desires to perform such Services for Rhythm.

AGREEMENT:

NOW, THEREFORE, in consideration of the foregoing premises and the covenants of the parties set forth in this Agreement, the parties hereto agree as follows:

1. Definitions. Unless this Agreement expressly provides to the contrary, the following terms, whether used in the singular or plural, have the respective meanings set forth below:

1.1 "Affiliate" means, with respect to either Rhythm or Manufacturer, any corporation, company, partnership, joint venture and/or firm which controls, is controlled by or is under common control with Rhythm or Manufacturer, as the case may be. As used in the definition of Affiliate, "control" means (a) in the case of corporate entities, direct or indirect ownership of at least fifty percent (50%) of the stock or shares having the right to vote for the election of directors (or such lesser percentage that is the maximum allowed to be owned by a foreign corporation in a particular jurisdiction), and (b) in the case of non-corporate entities, the direct or indirect power to manage, direct or cause the direction of the management and policies of the non-corporate entity or the power to elect at least fifty percent (50%) of the members of the governing body of such non-corporate entity.

1.2 "Agreement" means this Development and Manufacturing Services Agreement, together with all Appendices attached hereto, as amended from time to time by the parties in accordance with Section 15.6, and all fully signed Work Orders entered into by the parties.

1.3 "API/Drug Substance" means the active pharmaceutical ingredient or drug substance identified on the applicable Work Order, or any intermediate or component of such active pharmaceutical ingredient or drug substance.

1.4 "Applicable Law" means all applicable ordinances, rules, regulations, laws, guidelines, guidances, requirements and court orders of any kind whatsoever of any Authority, as amended from time to time including, without limitation, cGMP (if applicable).

1.5 "Authority" means any government regulatory authority responsible for granting approvals for the performance of Services under this Agreement or for issuing regulations

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pertaining to the Manufacture and/or use of Product in the intended country of use, including, without limitation, the FDA.

1.6 "Batch" means a specific quantity of Product that is intended to be of uniform character and quality, within specified limits, and is produced during the same cycle of Manufacture as defined by the applicable Batch record.

1.7 "Batch Documentation" has the meaning set forth in Section 6.2.

1.8 "Certificate of Analysis" means a document signed by an authorized representative of Manufacturer, describing Specifications for, and testing methods applied to, Product, and the results of testing.

1.9 "Certificate of Compliance" means a document, signed by an authorized representative of Manufacturer, certifying that a particular Batch was Manufactured in accordance with cGMP (if applicable), all other Applicable Law, and the Specifications.

1.10 "cGMP" means current good manufacturing practices and regulations applicable to the Manufacture of Product that are promulgated by any Authority.

1.11 "Change Order" has the meaning set forth in Section 5.3.

1.12 "Confidential Information" has the meaning set forth in Section 10.

1.13 "Develop" or "Development" means the studies and other activities conducted by Manufacturer under this Agreement to develop and/or validate all or any part of a Manufacturing Process including, without limitation, analytical tests and methods, formulations and dosage forms and stability.

1.14 "Equipment" means any equipment or machinery, including Rhythm Equipment, used by Manufacturer in the Development and/or Manufacturing of Product, or the holding, processing, testing, or release of Product.

1.15 "Facility" means the facilities of Manufacturer identified in the applicable Work Order, or facilities of an Affiliate of Manufacturer acting as a subcontractor as permitted herein.

1.16 "FDA" means the United States Food and Drug Administration, and any successor agency having substantially the same functions.

1.17 "FDCA" means the United States Federal Food, Drug and Cosmetic Act, 21 U.S.C. §321 et seq., as amended from time to time.

1.18 "*force majeure*" has the meaning set forth in Section 15.2.

1.19 "Improvements" means all Technology, discoveries, inventions, developments, modifications, innovations, updates, enhancements, improvements, writings or rights (whether or not protectable under patent, trademark, copyright or similar laws) that are conceived, discovered, invented, developed, created, made or reduced to practice in the performance of Services under this Agreement.

1.20 "IND" means an Investigational New Drug application filed with the FDA in accordance with Applicable Law.

1.21 "Manufacture" and "Manufacturing" means any steps, processes and activities necessary to produce Product including, without limitation, the manufacturing, processing, packaging, labeling, quality control testing, stability testing, release, storage or supply of Product.

1.22 "Manufacturer Indemnitees" has the meaning set forth in Section 12.2.

1.23 "Manufacturer Technology" means (a) the Technology of Manufacturer (a) existing prior to the Effective Date, or (b) developed or obtained by or on behalf of Manufacturer independent of this Agreement and without reliance upon the Confidential Information of Rhythm.

1.24 "Manufacturing Process" means any and all processes, methods, procedures and activities (or any step in any process or activity) used or planned to be used by Manufacturer to Manufacture Product, as evidenced in the Batch Documentation or master Batch Documentation.

1.25 "New Drug Application" means a New Drug Application filed with the FDA in accordance with Applicable Law.

1.26 "Product" means any API/Drug Substance, or drug product comprised of API/Drug Substance in each case as specified in the applicable Work Order, including, if applicable, bulk packaging and/or labeling as provided in such Work Order.

1.27 "Quality Agreement" has the meaning set forth in Section 2.2.

1.28 "Records" has the meaning set forth in Section 5.4(a).

1.29 "Representative" has the meaning set forth in Section 3.1.

1.30 "Reprocess" and "Reprocessing" means introducing a Product back into the process and repeating appropriate manipulation steps that are part of the established Manufacturing Process. Continuation of a process step after an in-process control test show the process to be incomplete is not considered reprocessing.

1.31 "Rework" and "Reworking" means subjecting a Product to one or more processing steps that are different from the established Manufacturing Process.

1.32 "Rhythm Equipment" means the Equipment, if any, identified on the applicable Work Order as being provided by Rhythm or purchased or otherwise acquired by Manufacturer at Rhythm's expense.

1.33 "Rhythm Indemnitees" has the meaning set forth in Section 12.1.

1.34 "Rhythm Materials" means the materials identified in the applicable Work Order as being provided by Rhythm, including labels (if any) for Product.

1.35 "Rhythm Technology" means (a) Rhythm Materials and any intermediates, components, or derivatives of Rhythm Materials, (b) Product and any intermediates, components, or derivatives of Product, (c) Specifications, and (d) the Technology of Rhythm or its Affiliates

existing prior to the Effective Date, or (ii) developed or obtained by or on behalf of Rhythm or its Affiliates independent of this Agreement and without reliance upon the Confidential Information of Manufacturer.

1.36 "Services" means the Development, Manufacturing and/or other services described in a Work Order entered into by the parties.

1.37 "Specifications" means the list of tests, references to any analytical procedures and appropriate acceptance criteria which are numerical limits, ranges or other criteria for tests described in order to establish a set of criteria to which Product at any stage of Manufacture should conform to be considered acceptable for its intended use that are provided by or approved by Rhythm, as such specifications are amended or supplemented from time to time by Rhythm in writing.

1.38 "Technology" means all inventions, technology, compositions of matter, methods, processes, techniques, trade secrets, copyrights, know-how, data, documentation, regulatory submissions, specifications and other intellectual property of any kind (whether or not protectable under patent, trademark, copyright or similar laws).

1.39 "Work Order" means a written work order referencing this Agreement, substantially in the form attached hereto as Appendix A, for the performance of Services by Manufacturer under this Agreement.

2. Engagement of Manufacturer.

2.1 Services and Work Orders. From time to time, Rhythm may wish to engage Manufacturer to perform Services for Rhythm. Such Services will be set forth in a Work Order. Each Work Order will be appended to this Agreement, will include the material terms for the project, and may include the scope of work, specified Services, Specifications, deliverables, timelines, milestones (if any), quantity, budget, payment schedule and such other details and special arrangements as are agreed to by the parties with respect to the activities to be performed under such Work Order. No Work Order will be effective unless and until it has been agreed to and signed by authorized representatives of both parties. Documents relating to the relevant project, including without limitation Specifications, proposals, quotations and any other relevant documentation, will only be effective if attached to the applicable Work Order and incorporated in the Work Order by reference. Each fully signed Work Order will be subject to the terms of this Agreement and will be incorporated herein and form part of this Agreement. Manufacturer will perform the Services specified in each fully signed Work Order, as amended by any applicable Change Order(s), and in accordance with the terms and conditions of such Work Order and this Agreement. Notwithstanding the foregoing, nothing in this Agreement will obligate either party to enter into any Work Order under this Agreement.

2.2 Quality Agreement. If appropriate or if required by Applicable Law, the parties will also agree upon a Quality Agreement containing quality assurance provisions for the Manufacture of Product ("Quality Agreement"), which agreement will also be attached to the applicable Work Order and incorporated by reference in the Work Order.

2.3 Conflict Between Documents. If there is any conflict, discrepancy, or inconsistency between the terms of this Agreement and any Work Order, Quality Agreement, purchase order, or other document or form used by the parties, the terms of this Agreement will control.

3. Project Performance.

3.1 Representatives. Each party will appoint a representative having primary responsibility for day-to-day interactions with the other party for the Services (each, a "Representative"), who will be identified in the applicable Work Order. Each party may change its Representative by providing written notice to the other party in accordance with Section 15.3; provided that Manufacturer will use reasonable efforts to provide Rhythm with at least forty-five (45) days prior written notice of any change in its Representative for the Services. Except for notices or communications required or permitted under this Agreement, which will be subject to Section 15.3, or unless otherwise mutually agreed by the parties in writing, all communications between Manufacturer and Rhythm regarding the conduct of the Services pursuant to such Work Order will be addressed to or routed directly through the parties' respective Representatives.

3.2 Communications. The parties will hold project team meetings via teleconference or in person, on a periodic basis as agreed upon by the Representatives. Manufacturer will make written reports to Rhythm as specified in the applicable Work Order.

3.3 Subcontracting. Manufacturer may not subcontract with any third party to perform any of its obligations under this Agreement without the prior written consent of Rhythm, except that Manufacturer may subcontract to any Affiliate of Manufacturer without the prior written consent of Rhythm if, but only if, Manufacturer provides at least 30 days advance written notice to Rhythm of any such subcontracting to any such Affiliate of Manufacturer. Manufacturer shall promptly provide to Rhythm any information that Rhythm reasonably requests concerning any permitted subcontractor, including, without limitation, any permitted subcontractor that is an Affiliate of Manufacturer. Manufacturer will be solely responsible for the performance of any permitted subcontractor, and for costs, expenses, damages, or losses of any nature arising out of such performance as if such performance had been provided by Manufacturer itself under this Agreement. Manufacturer will cause any such permitted subcontractor to be bound by, and to comply with, the terms of this Agreement, as applicable, including without limitation, all confidentiality, quality assurance, regulatory and other obligations and requirements of Manufacturer set forth in this Agreement.

3.4 Duty to Notify. Manufacturer will promptly notify Rhythm if at any time during the term of this Agreement Manufacturer has reason to believe that it will be unable to perform or complete the Services in a timely manner. Compliance by Manufacturer with this Section 3.4 will not relieve Manufacturer of any other obligation or liability under this Agreement.

4. Materials and Equipment.

4.1 Supply of Materials. Unless the parties otherwise agree in a Work Order, Manufacturer will supply, in accordance with the relevant approved raw material specifications, all materials to be used by Manufacturer in the performance of Services under a Work Order other than the Rhythm Materials specified in such Work Order. Rhythm or its designees will provide Manufacturer with the Rhythm Materials. Manufacturer agrees (a) to account for all Rhythm Materials, (b) not to provide Rhythm Materials to any third party (other than an Affiliate acting as a permitted subcontractor) without the express prior written consent of Rhythm, (c) not to use Rhythm Materials for any purpose other than conducting the Services, including, without limitation, not to analyze, characterize, modify or reverse engineer any Rhythm Materials or take any action to determine the structure or composition of any Rhythm Materials unless required

pursuant to a signed Work Order, and (d) to destroy or return to Rhythm all unused quantities of Rhythm Materials according to Rhythm's written directions.

4.2 Ownership of Materials. Rhythm will at all times retain title to and ownership of the Rhythm. Materials, Product, any intermediates and components of Rhythm Materials or Product, and any work in process at each and every stage of the Manufacturing Process. Manufacturer will provide within the Facility an area or areas where the Rhythm Materials, Product, any intermediates and components of Rhythm Materials or Product, and any work in process are segregated and stored in accordance with the Specifications and cGMP (if applicable), and in such a way as to be able at all times to clearly distinguish such materials from products and materials belonging to Manufacturer, or held by it for a third party's account. Manufacturer will ensure that Rhythm Materials, Product, any intermediates and components of any Rhythm Materials or Product, and any work in process are free and clear of any liens or encumbrances. Manufacturer will at all times take such measures as are required to protect the Rhythm Materials, Product, any intermediates and components of any Rhythm Materials or Product, and any work in process from risk of loss or damage at all stages of the Manufacturing Process. Manufacturer will immediately notify Rhythm if at any time it believes any Product or Rhythm Materials, or any intermediates and components of any Rhythm Materials or Product, have been damaged, lost or stolen.

4.3 Supply of Equipment. Unless otherwise agreed in a Work Order, Manufacturer will supply all Equipment necessary to perform the Services, except that Rhythm will supply the Rhythm Equipment, if any. The Rhythm Equipment will not be used by Manufacturer except in performance of Services under the applicable Work Order. Title to the Rhythm Equipment will remain with Rhythm and Manufacturer will ensure that the Rhythm Equipment is properly labeled as Rhythm property and remains free and clear of any liens or encumbrances. At Rhythm's written request, the Rhythm Equipment will be returned to Rhythm, or to Rhythm's designee. Manufacturer will be responsible, at its own cost, for maintenance of the Rhythm Equipment. To the extent Rhythm provides spare parts for the Rhythm Equipment, such spare parts will remain the property of Rhythm and will be used by Manufacturer only for maintenance of the Rhythm Equipment. Manufacturer will immediately notify Rhythm if at any time it believes any Rhythm Equipment has been damaged, lost or stolen.

5. Development and Manufacture of Product.

5.1 Resources: Applicable Law. Manufacturer will comply with all Applicable Law in performing Services.

5.2 Facility.

(a) Performance of Services. Manufacturer will perform all Services at the Facility, provide all staff necessary to perform the Services in accordance with the terms of the applicable Work Order and this Agreement, and hold at such Facility all Equipment, Rhythm Equipment, Rhythm Materials and other items used in the Services. Manufacturer will not change the location of such Facility or use any additional facility for the performance of Services under this Agreement without at least one hundred fifty (150) days prior written notice to, and prior written consent from, Rhythm, which consent will not be unreasonably withheld or delayed (it being understood and agreed that Rhythm may withhold consent pending satisfactory completion of a quality assurance audit and/or regulatory impact assessment of the new location or additional facility, as the case may be). Manufacturer will maintain, at its own expense, the Facility and all Equipment required for the Manufacture of Product in a state of repair and

operating efficiency consistent with the requirements of cGMP (if applicable) and all Applicable Law.

(b) Validation. Manufacturer will be responsible for performing all validation of the Facility, Equipment and cleaning and maintenance processes employed in the Manufacturing Process in accordance with cGMP (if applicable), Manufacturer's SOPs, the applicable Quality Agreement, Applicable Law, and in accordance with any other validation procedures established by Rhythm and made known in writing to Manufacturer. Manufacturer will also be responsible for ensuring that all such validated processes are carried out in accordance with their terms.

(c) Licenses and Permits. Manufacturer will be responsible for obtaining, at its expense, any Facility or other licenses or permits, and any regulatory and government approvals necessary for the performance of Services by Manufacturer under this Agreement. At Rhythm's request, Manufacturer will provide Rhythm with copies of all such approvals and submissions to Authorities, and Rhythm will have the right to use any and all information contained in such approvals or submissions in connection with regulatory approval and/or commercial development of Product.

(d) Access to Facility. Manufacturer will permit Rhythm or its duly authorized representatives to observe and consult with Manufacturer during the performance of Services under this Agreement, including without limitation the Manufacturing of any Batch of Product. Manufacturer also agrees that Rhythm and its duly authorized agents will have continuous access upon reasonable notice, during operational hours and during active Manufacturing, to inspect the Facility and Manufacturing Process to ascertain compliance by Manufacturer with the terms of this Agreement, including, without limitation, inspection of (i) the Equipment and materials used in the performance of Services, (ii) the holding facilities for such materials and Equipment, and (iii) all Records relating to such Services and the Facility. Rhythm will also have the right, at its expense, to conduct "mock" pre-approval audits upon reasonable notice to Manufacturer, and Manufacturer agrees to cooperate with Rhythm in such "mock audits."

5.3 Changes to Work Orders, Manufacturing Process and Specifications.

(a) Changes to Work Orders. If the scope of work of a Work Order changes, then the applicable Work Order may be amended as provided in this Section 5.3(a). If a required modification to a Work Order is identified by Rhythm or by Manufacturer, the identifying party will notify the other party in writing as soon as reasonably possible. Manufacturer will provide Rhythm with a change order containing a description of the required modifications and their effect on the scope, fees and timelines specified in the Work Order ("Change Order"), and will use reasonable efforts to do so within ten (10) business days of receiving or providing such notice, as the case may be. No Change Order will be effective unless and until it has been signed by authorized representatives of both parties. If Rhythm does not approve such Change Order, and has not terminated the Work Order, but requests the Work Order to be amended to take into account the modification, then the parties will use reasonable efforts to agree on a Change Order that is mutually acceptable. If practicable, Manufacturer will continue to work under the existing Work Order during any such negotiations, provided such efforts would facilitate the completion of the work envisioned in the proposed Change Order, but will not commence work in accordance with the Change Order until it is authorized in writing by Rhythm.

(b) Process/Specifications Changes. Any change or modification to the Manufacturing Process or Specifications for any Product must be approved in advance by Rhythm and will be made in accordance with the change control provisions of the applicable Quality Agreement. With timely notice, Rhythm shall grant such approval for any such change or modification to the Manufacturing Process, unless such change or modification is material in which case the granting of such approval shall be at Rhythm's sole and absolute discretion.

5.4 Record and Sample Retention.

(a) Records. Manufacturer will keep complete and accurate records (including, without limitation, reports, accounts, notes, data, and records of all information and results obtained from performance of Services) of all work done by it under this Agreement, in form and substance as specified in the applicable Work Order, the applicable Quality Agreement, and this Agreement (collectively, the "Records"). All such Records will be the property of Rhythm. Manufacturer will not transfer, deliver or otherwise provide any such Records to any party other than Rhythm, without the prior written approval of Rhythm. Records will be available at reasonable times for inspection, examination and copying by or on behalf of Rhythm All original Records of the Development and Manufacture of Product under this Agreement will be retained and archived by Manufacturer in accordance with cGMP (if applicable) and Applicable Law, but in no case for less than a period of five (5) years following completion of the applicable Work Order. Upon Rhythm's request, Manufacturer will promptly provide Rhythm with copies of such Records. Five (5) years after completion of a Work Order, all of the aforementioned records will be sent to Rhythm or Rhythm's designee; provided, however, that Rhythm may elect to have such records retained in Manufacturer's archives for an additional period of time at a reasonable charge to Rhythm.

(b) Sample Retention. Manufacturer will take and retain, for such period and in such quantities as may be required by cGMP (if applicable) and the applicable Quality Agreement, samples of Product from the Manufacturing Process produced under this Agreement. Further, upon Rhythm's written request, Manufacturer will submit such samples to Rhythm.

5.5 Regulatory Matters.

(a) Regulatory Approvals. Rhythm will be responsible for obtaining, at its expense, all regulatory and governmental approvals and permits necessary for Rhythm's use of any Product Developed and/or Manufactured under this Agreement, including, without limitation, IND, ANDA, and NDA submissions and any analogous submissions filed with the appropriate Authority of a country other than the United States. Manufacturer will be responsible for providing Rhythm with all supporting data and information relating to the Development and/or Manufacture of Product necessary for obtaining such approvals, including, without limitation, all Records, raw data, reports, authorizations, certificates, methodologies, Batch Documentation, raw material specifications, SOPs, standard test methods, Certificates of Analysis, Certificates of Compliance and other documentation in the possession or under the control of Manufacturer relating to the Development and Manufacture of Product (or any intermediate, or component of Product).

(b) Regulatory Inspections. Manufacturer will permit Rhythm or its agents to be present and participate in any visit or inspection by any Authority of the Facility (to the extent it relates in any way to any Product) or the Manufacturing Process. Manufacturer will give as much advance notice as reasonably possible to Rhythm of any such visit or inspection. Manufacturer will provide Rhythm with a copy of any report or other written communication

received from such Authority in connection with such visit or inspection, and any written communication received from any Authority relating to any Product, the Facility (if it relates to or affects the Development and/or Manufacture of Product) or the Manufacturing Process, within two (2) business days after receipt, and will consult with, and require approval from, Rhythm before responding to each such communication. Manufacturer will provide Rhythm with a copy of its final responses within five (5) business days after submission.

5.6 Waste Disposal. The generation, collection, storage, handling, transportation, movement and release of hazardous materials and waste generated in connection with the Services will be the responsibility of Manufacturer at Manufacturer's sole cost and expense. Without limiting other applicable requirements, Manufacturer will prepare, execute and maintain, as the generator of waste, all licenses, registrations, approvals, authorizations, notices, shipping documents and waste manifests required under Applicable Law.

5.7 Safety Procedures. Manufacturer will be solely responsible for implementing and maintaining health and safety procedures for the performance of Services and for the handling of any materials or hazardous waste used in or generated by the Services. Manufacturer, in consultation with Rhythm, will develop safety and handling procedures for API/Drug Substance and Product; provided, however, that Rhythm will have no responsibility for Manufacturer's health and safety program.

6. Testing and Acceptance Process.

6.1 Testing by Manufacturer. The Product Manufactured under this Agreement will be Manufactured in accordance with the Manufacturing Process approved by Rhythm, and with cGMP (unless otherwise expressly stated in the applicable Work Order) and will conform to the Specifications. Each Batch of Product will be sampled and tested by Manufacturer against the Specifications, and the quality assurance department of Manufacturer will review the documentation relating to the Manufacture of the Batch and will assess if the Manufacture has taken place in compliance with cGMP (if applicable) and the Manufacturing Process.

6.2 Provision of Records. If, based upon such tests and documentation review, a Batch of Product conforms to the Specifications and was Manufactured according to cGMP (if applicable) and the Manufacturing Process, then a Certificate of Compliance will be completed and approved by the quality assurance department of Manufacturer. Manufacturer shall maintain full Batch records that will be accessible to Rhythm on the premises of the Manufacturer. Batch excerpts shall be made available to Rhythm or its nominee within twenty (20) working days at Rhythm's request. Those Batch excerpts consist of (i) a flow chart of synthesis performed (batch history), including summary of investigation reports, significant deviation reports, planned changes or OOS results generated during manufacture of the Product, (ii) a Certificate of Analysis (CoA), and (iii) a Certificate of Compliance (CoC) (collectively, "Batch Documentation"). For each Batch of Product, Batch Documentation will be delivered at no cost to Rhythm by a reputable overnight courier or by registered or certified mail, postage prepaid, return receipt required to verify delivery date.

Upon request Manufacturer will deliver to Rhythm a complete and accurate copy of the Batch records for each Batch of Product. Upon request, Manufacturer will also deliver to Rhythm all raw data, reports, authorizations, certificates, methodologies, raw material specifications, SOPs, standard test methods, and other documentation in the possession or under the control of Manufacturer relating to the Manufacture of each Batch of Product. Such information (apart from Batch Documentation) requested by Rhythm from Manufacturer will be delivered at cost. If

Rhythm requires additional copies of such information, these will also be provided by Manufacturer to Rhythm at cost.

6.3 Review of Batch Documentation; Acceptance. Rhythm will review the Batch Documentation for each Batch of Product and may test samples of the Batch of Product against the Specifications. Rhythm will notify Manufacturer in writing of its acceptance or rejection of such Batch within six (6) weeks of receipt of the complete Batch Documentation relating to such Batch. During this review period, the parties agree to respond promptly, but in any event within ten (10) days, to any reasonable inquiry or request for a correction or change by the other party with respect to such Batch Documentation. Rhythm has no obligation to accept a Batch if such Batch does not comply with the Specifications and/or was not Manufactured in compliance with cGMP (if applicable) and the Manufacturing Process.

6.4 Disputes. In case of any disagreement between the parties as to whether Product conforms to the applicable Specifications or cGMP (if applicable), the quality assurance representatives of the parties will attempt in good faith to resolve any such disagreement and Rhythm and Manufacturer will follow their respective SOPs to determine the conformity of the Product to the Specifications and cGMP (if applicable). If the foregoing discussions do not resolve the disagreement in a reasonable time (which will not exceed thirty (30) days), a representative sample of such Product will be submitted to an independent testing laboratory mutually agreed upon by the parties for tests and final determination of whether such Product conforms with such Specifications. The laboratory must meet cGMP (if applicable), be of recognized standing in the industry, and consent to the appointment of such laboratory will not be unreasonably withheld or delayed by either party. Such laboratory will use the test methods contained in the applicable Specifications. The determination of conformance by such laboratory with respect to all or part of such Product will be final and binding on the parties absent manifest error. The fees and expenses of the laboratory incurred in making such determination will be paid by the party against whom the determination is made.

6.5 Product Non-Compliance and Remedies. If a Batch of Product fails to conform to the Specifications or was not Manufactured in compliance with cGMP (if applicable) and the Manufacturing Process, then Manufacturer will, as Rhythms' sole and exclusive remedy and in lieu of other remedies available at law or in equity (except for any right of Rhythm to indemnification pursuant to Section 12.1 hereof in connection with third party claims), at Rhythm's sole option:

(a) refund in full the fees and expenses paid by Rhythm for such Batch, including, but not limited to, the cost of Rhythm Materials used in the Manufacture of such Batch; or

(b) at Manufacturer's cost and expense, including, but not limited to, the cost of Rhythm Materials used in the Manufacture of such Batch, Manufacture a new Batch of Product as soon as reasonably possible; or

(c) Rework or Reprocess the Product, at Manufacturer's cost and expense, so that the Batch can be deemed to have been Manufactured in compliance with cGMP (if applicable) and the Manufacturing Process, and to conform to Specifications.

Moreover, the parties will meet to discuss, evaluate and analyze the reasons for and implications of the failure to comply with cGMP (if applicable) and/or the Manufacturing Process and will

decide whether to proceed with or to amend the applicable Work Order via a Change Order, or to terminate such Work Order.

6.6 Disposition of Non-Conforming Product. The ultimate disposition of non-conforming Product will be the responsibility of Rhythm's quality assurance department.

7. Shipping and Delivery. Manufacturer agrees not to ship Product to Rhythm or its designee until it has received a written approval from Rhythm or Rhythm's designee to release and ship. Manufacturer will ensure that each Batch will be delivered to Rhythm or Rhythm's designee, (a) on the delivery date and to the destination designated by Rhythm in writing, and (b) in accordance with the instructions for shipping and packaging specified by Rhythm in the applicable Work Order or as otherwise agreed to by the parties in writing. Delivery terms will be FCA (Incoterms 2000), or as specified in the applicable Work Order. A bill of lading will be furnished to Rhythm with respect to each shipment.

8. Fees and Payments.

8.1 Price. The price of Product and/or the fees and expenses for the performance of Services will be set forth in the applicable Work Order.

8.2 Invoice. Manufacturer will invoice Rhythm according to the invoice schedule in the applicable Work Order, referencing in each such invoice the Work Order(s) to which such invoice relates. Notwithstanding the foregoing, Manufacturer will not issue a final invoice for a Batch of Product until such time as such Batch has been shipped to Rhythm. Payment of undisputed invoices will be due sixty (60) days after receipt of the invoice and reasonable supporting documentation by Rhythm.

8.3 Payments. Rhythm will make all payments pursuant to this Agreement by check or wire transfer to a bank account designated in writing by Manufacturer. All payments under this Agreement will be made in United States Dollars.

8.4 Financial Records. Manufacturer will keep accurate records of all Services performed and invoice calculations, and, upon the request of Rhythm, will permit Rhythm or its duly authorized agents to examine such records upon prior notice during normal business hours for the purpose of verifying the correctness of all such calculations.

8.5 Taxes. Duty, sales, use or excise taxes imposed by any governmental entity that apply to the provision of Services will be borne by Rhythm (other than taxes based upon the income of Manufacturer).

9. Intellectual Property Rights.

9.1 Rhythm Technology. All rights to and interests in Rhythm Technology will remain solely in Rhythm and no right or interest therein is transferred or granted to Manufacturer under this Agreement. Manufacturer acknowledges and agrees that it does not acquire a license or any other right to Rhythm Technology except for the limited purpose of carrying out its duties and obligations under this Agreement and that such limited, non-exclusive, license will expire upon the completion of such duties and obligations or the termination or expiration of this Agreement, whichever is the first to occur.

9.2 Manufacturer Technology.

9.2.1 All rights to and interests in Manufacturer Technology will remain solely in Manufacturer and, except as otherwise set forth in this Section 9, no right or interest therein is transferred or granted to Rhythm under this Agreement.

9.2.2 Manufacturer hereby grants to Rhythm and its Affiliates a non-exclusive, worldwide, perpetual, irrevocable (subject to Section 14.3 (a), (b) and (c)), royalty-free and transferable (subject to the provisions of Section 9.2.4) license to use and modify Manufacturer Technology to develop, Manufacture, have Manufactured, distribute, offer for sale, sell, and otherwise dispose of Product. Rhythm and its Affiliates shall have the right, subject to Section 9.2.3, to grant sublicenses in respect of such license to any person to whom Rhythm (and/or its Affiliates, licensees, sublicensees, successors or assigns) has licensed or otherwise granted the right to develop, Manufacture, have Manufactured or commercialize Product. For and in consideration of such non-exclusive license granted by Manufacturer to Rhythm and its Affiliates, Rhythm hereby agrees that, during the period commencing on the launch date of a Product and ending on the [ ]* anniversary of the launch date of such Product, Rhythm (and/or its Affiliates, licensees, sublicensees, successors or assigns) shall source from Manufacturer at least [ ]* of that portion of its requirements for such Product that Rhythm (and/or its Affiliates,

licensees, sublicensees, successors or assigns) is sourcing from all third party contract manufacturers that are not Affiliates, subject to, and in accordance with, the terms and conditions set forth in this Agreement; provided, however, that the foregoing provisions of this sentence shall apply only if (i) Manufacturer can Manufacture at least [ ]* of the requirements of Rhythm (and/or its Affiliates, licensees, sublicensees, successors or assigns) for such Product in accordance with the terms of this Agreement and the quality and cost to Rhythm (and/or its Affiliates, licensees, sublicensees, successors or assigns) of such quantities of such Product to be Manufactured by Manufacturer for Rhythm (and/or its Affiliates, licensees, sublicensees, successors or assigns) shall be no less favorable to Rhythm (and/or its Affiliates, licensees, sublicensees, successors or assigns) than if such Product was Manufactured by any other third party contract manufacturer offering comparable services and quality standards, and for the same quantities of Product, (ii) Manufacturer shall not have breached in any material respect any of its obligations under this Agreement unless Manufacturer has remedied such breach within thirty (30) days after receiving written notice from Rhythm of such breach, and (iii) Rhythm (and/or its Affiliates, licensees, sublicensees, successors or assigns) continue(s) to practice Manufacturer Technology to Manufacture or have Manufactured commercial quantities of such Product.

9.2.3 For each sublicense granted by Rhythm pursuant to the provisions of Section 9.2.2, Rhythm (a) shall inform Manufacturer thereof and ensure that such sublicense shall be consistent with the terms of this Agreement, and shall for such purpose enter into the appropriate agreement with the concerned sublicensee, and (b) be responsible for any failure by such sublicensee to abide by any of its undertakings and obligations under such agreement.

9.2.4 The rights granted by Manufacturer under Section 9.2.2 are transferable to any person to whom Rhythm (and/or its Affiliates, licensees, sublicensees, successors or assigns) has licensed or otherwise granted the right to develop, Manufacture, have Manufactured or commercialize Product, provided, however that Rhythm (a) shall, prior to any such transfer, inform Manufacturer thereof in writing, (b) shall ensure that such transfer shall be consistent with the terms of this Agreement, and (c) shall for such purpose enter into the appropriate agreement with the concerned company.

9.3 Improvements.

9.3.1 Manufacturer agrees (a) to promptly disclose to Rhythm all patentable Improvements, and (b) that all Improvements will be the sole and exclusive property of Rhythm, and are hereby assigned to Rhythm (or its designee), and (c) that any such assignment to Rhythm (or its designee) shall be made without additional compensation to Manufacturer. Manufacturer will take such steps as Rhythm may reasonably request (at Rhythm's expense) to vest in Rhythm (or its designee) ownership of the Improvements.

9.3.2 Rhythm hereby grants to Manufacturer and its Affiliates a non-exclusive, worldwide, perpetual, irrevocable (subject to Section 14.3 (a), (b) and (0) and royalty-free license, with the right to sublicense, under the Improvements assigned by Manufacturer to Rhythm pursuant to Section 9.3.1, to manufacture, distribute, offer for sale, sell, and otherwise dispose of any product other than a compound or product targeting the [ ]*.

9.4 Patent Filings. Rhythm will have the exclusive right and option, but not the obligation, to prepare, file, prosecute, maintain and defend, at its sole expense, any patents that claim or cover the Improvements.

9.5 Technology Transfer. If Rhythm elects to Manufacture Product, or to have Product Manufactured by a third party, then Manufacturer will provide to Rhythm or its designee, all Manufacturing information, including, without limitation, documentation, technical assistance, materials and cooperation by appropriate employees of Manufacturer as Rhythm or its designee may reasonably require in order to Manufacture Product. Rhythm will compensate Manufacturer and/or its Affiliates, for such assistance at the hourly-rate(s) set forth in the applicable Work Order, or such other reasonable rate(s) as the parties may agree in writing, and shall reimburse to Manufacturer and/or its Affiliates all travel and lodging expenses incurred for the same provided that they have been approved in advance by Rhythm.

10. Confidentiality.

10.1 Confidential Information. During the Term and continuing thereafter, each party will keep confidential and not disclose to others or use for any purpose other than as necessary to fulfill its obligations or in the reasonable exercise of rights granted to it under this Agreement, all "Confidential Information" of the other party. As used in this Agreement, "Confidential Information" of either party means any scientific, technical, trade or business information which (x) is given by such party or its Affiliates or their respective employees or representatives to the other and which is treated by the disclosing party as confidential or proprietary or a trade secret and is not within the scope of clause (y) or clause (z) below, (y) is developed by the other party for such party under the terms of this Agreement or (z) is owned by such party by virtue of any provision of this Agreement that assigns or transfers ownership thereof to such party from the other party. Confidential Information of Manufacturer includes, but is not limited to, Manufacturer Technology, including any Manufacturer Technology embodied in any Batch Record or Batch Documentation. Confidential Information of Rhythm includes, but is not limited to, Rhythm Technology and Improvements. The restrictions of this Section will not apply to any portion of the Confidential Information which (a) is known to the recipient at the time of disclosure and is not subject to another confidentiality obligation to the discloser or its Affiliates, as reasonably documented by recipient's written records; (b) later becomes available to the public through no fault of the recipient; (c) is received from a third party having the lawful right to disclose the information; or (d) is independently developed by or on behalf of recipient without

use of or reliance upon discloser's Confidential Information. Any information which is specific, shall not be deemed to be within any of the foregoing exceptions, merely because it is embraced by more general information which falls within any one or more of the foregoing exceptions. In addition, information will not be deemed to be available to the public by reason solely that it is accessible to only a few of those people to whom it might be of commercial interest, and any combination of two (2) or more portions of the Confidential Information shall not be deemed to be generally available to the public by reason solely of each separate portion being so available.

10.2 Permitted Disclosure. A party may disclose Confidential Information of the other party to (a) its Affiliates, and to its and their directors, employees, consultants, and agents in each case who have a specific need to know such Confidential Information and who are bound by a like obligation of confidentiality and restriction on use and (b) the extent such disclosure is required to comply with Applicable Law, the rules of any stock exchange or listing entity, or to defend or prosecute litigation; provided, however, that the recipient provides prior written notice of such disclosure to the discloser and takes reasonable and lawful actions to avoid or minimize the degree of such disclosure, including upon the discloser's request, seeking confidential treatment of such Confidential Information. Moreover, Rhythm may disclose Confidential Information of Manufacturer relating to the Development and/or Manufacture of Product to entities with whom Rhythm has (or may have) a marketing and/or development collaboration for the Product or to whom Rhythm has (or may have) granted a license or sublicense to develop, manufacture or commercialize the Product or to *bona fide* actual or prospective underwriters, investors, lenders or other financing sources or to potential acquirors of the business to which this Agreement relates, and who in each case have a specific need to know such Confidential Information and who are bound by a like obligation of confidentiality and restrictions on use.

10.3 Return of Confidential Information. This Agreement does not constitute the conveyance of ownership with respect to or a license to any Confidential Information, except as otherwise provided in this Agreement. Upon the expiration or termination of this Agreement for any reason, each party agrees, except as otherwise provided in this Agreement, to return to the other party all documentation or other tangible evidence or embodiment of Confidential Information belonging to the other party and not to use such Confidential Information, unless otherwise agreed. Notwithstanding the foregoing, one archival copy may be maintained by the recipient and kept confidential and segregated from the recipient's regular files.

10.4 Public Statements. Except to the extent otherwise required in order to comply with any Applicable Law, neither party will make any public statements or releases concerning this Agreement or the transactions contemplated by this Agreement, or use the other party's name in any form of advertising, promotion or publicity, without obtaining the prior written consent of the other party.

11. Representations and Warranties.

11.1 Manufacturer's Representations and Warranties. Manufacturer represents and warrants to Rhythm that:

(a) it has the full power and right to enter into this Agreement and that there are no outstanding agreements, assignments, licenses, encumbrances or rights of any kind held by other parties, private or public, that are inconsistent with the provisions of this Agreement;

(b) the execution and delivery of this Agreement by Manufacturer has been authorized by all requisite corporate action and this Agreement is and will remain a valid and

binding obligation of Manufacturer, enforceable in accordance with its terms, subject to laws of general application relating to bankruptcy, insolvency and the relief of debtors;

(c) the Services will be performed with requisite care, skill and diligence, in accordance with Applicable Law and industry standards, and by individuals who are appropriately trained and qualified;

(d) it has and shall continue to have written agreements with its directors, officers, employees, agents, permitted subcontractors and representatives to effectuate the terms of this Agreement, including without limitation Sections 9 and 10 hereof, and shall enforce such agreements to provide Rhythm with the benefits thereof;

(e) the conduct and the provision of the Services will not violate any patent, trade secret or other proprietary or intellectual property rights of any third party and it will promptly notify Rhythm in writing should it become aware of any claims asserting such violation;

(f) it shall not knowingly use or incorporate any invention, discovery, technology, know-how and/or other intellectual property that is not owned by, or otherwise assignable, licensable or sublicensensable by, Manufacturer in the performance of the Services without the prior written consent of Rhythm;

(g) at the time of delivery to Rhythm, the Product Manufactured under this Agreement (i) will have been Manufactured in accordance with cGMP (if applicable) and all other Applicable Law, the Manufacturing Process, the applicable Quality Agreement, and Specifications, and (ii) will not be adulterated or misbranded under the FDCA or other Applicable Law; and

(h) Manufacturer, its Affiliates, approved subcontractors, and each of their respective officers and directors, as applicable, and any person used by Manufacturer, its Affiliates or approved subcontractors to perform Services under this Agreement (i) have not been debarred and are not subject to a pending debarment, and will not use in any capacity in connection with the Services any person who has been debarred or is subject to a pending debarment pursuant to Section 306 of the FDCA, 21 U.S.C. § 335a, (ii) are not ineligible to participate in any federal and/or state healthcare programs or federal procurement or non-procurement programs (as that term is defined in 42 U.S.C. 1320a-7b(f)), (iii) are not disqualified by any government or regulatory agencies from performing specific services, and are not subject to a pending disqualification proceeding, and (iv) have not been convicted of a criminal offense related to the provision of healthcare items or services and are not subject to any such pending action. Manufacturer will notify Rhythm immediately if Manufacturer, its Affiliates, approved subcontractors, or any of their respective officers or directors, as applicable, or any person used by

Manufacturer, its Affiliates or approved subcontractors to perform Services under this Agreement is subject to any of the foregoing, or if any action, suit, claim, investigation, or proceeding relating to the foregoing is pending, or to the best of Manufacturer's knowledge, is threatened.

11.2 Rhythm Representations and Warranties. Rhythm represents and warrants to Manufacturer that:

(a) it has the full power and right to enter into this Agreement and that there are no outstanding agreements, assignments, licenses, encumbrances or rights held by other parties, private or public, that are inconsistent with the provisions of this Agreement; and

(b) the execution and delivery of this Agreement by Rhythm has been authorized by all requisite corporate action and this Agreement is and will remain a valid and binding obligation of Rhythm, enforceable in accordance with its terms, subject to laws of general application relating to bankruptcy, insolvency and the relief of debtors.

11.3 Disclaimer of Other Representations and Warranties. EXCEPT AS EXPRESSLY SET FORTH IN THIS AGREEMENT OR IN ANY WORK ORDER, NEITHER PARTY MAKES ANY REPRESENTATIONS OR EXTENDS ANY WARRANTIES OF ANY KIND, EITHER EXPRESS OR IMPLIED, INCLUDING, BUT NOT LIMITED TO, WARRANTIES OF MERCHANTABILITY, FITNESS FOR A PARTICULAR PURPOSE, OR NON-INFRINGEMENT.

12. Indemnification.

12.1 Indemnification by Manufacturer. Manufacturer agrees to indemnify Rhythm, its Affiliates and its and their respective officers, directors, employees, subcontractors, and agents (collectively, the "Rhythm Indemnitees") against any and all losses, damages, liabilities or expenses (including reasonable attorneys fees and other costs of defense) (collectively, "Losses") in connection with any and all actions, suits, claims or demands that may be brought or instituted against any Rhythm Indemnitee by any third party to the extent they arise out of or relate to (a) breach of this Agreement by Manufacturer, or (b) Manufacturer Indemnitees' negligence or willful misconduct in performing obligations under this Agreement.

12.2 Indemnification by Rhythm. Rhythm agrees to indemnify Manufacturer, its Affiliates and its and their respective officers, directors, employees, subcontractors, and agents (collectively, the "Manufacturer Indemnitees") against any and all Losses in connection with any and all actions, suits, claims or demands that may be brought or instituted against any Manufacturer Indemnitee by any third party to the extent they arise out of or relate to (a) the use of the Product (except to the extent that such Losses are within the scope of the indemnification obligation of Manufacturer under Section 12.1), (b) any breach of this Agreement by Rhythm, or any Rhythm Indemnitees' negligence or willful misconduct in performing obligations under this Agreement.

12.3 Indemnification Procedures. Each party agrees to notify the other party within thirty (30) days of receipt of any claims made for which the other party might be liable under Section 12.1 or 12.2, as the case may be. Subject to Section 12.4, the indemnifying party will have the right, but not the obligation, to defend, negotiate, and settle such claims. The indemnified party will be entitled to participate in the defense of such matter and to employ counsel at its expense to assist therein; provided, however, that if the indemnifying party elects to defend the indemnified party, the indemnifying party will have final decision-making authority regarding all aspects of the defense of any claim, subject to Section 12.4. The party seeking indemnification will provide the indemnifying party with such information and assistance as the indemnifying party may reasonably request, at the expense of the indemnifying party. The parties understand that no insurance deductible will be credited against losses for which a party is responsible under this Section 12.

12.4 Settlement. Neither party will be responsible or bound by any settlement of any claim or suit made without its prior written consent; provided, however, that the indemnified party will not unreasonably withhold or delay such consent. If a settlement contains an absolute waiver of liability for the indemnified party, and each party has acted in compliance with the requirements of Section 12.3, then the indemnified party's consent will be deemed given. Notwithstanding the foregoing, (i) Manufacturer will not agree to settle any claim on such terms or conditions as would impair Rhythm's ability or right to manufacture, market, sell or otherwise use Product, or as would impair Manufacturer's ability, right or obligation to perform its obligations under this Agreement, and (ii) Rhythm will not agree to settle any claim on such terms or conditions as would impair Manufacturer's ability, right or obligation to perform its obligations under this Agreement.

12.5 Limitation of Liability. NEITHER PARTY WILL BE LIABLE UNDER ANY LEGAL THEORY (WHETHER TORT, CONTRACT OR OTHERWISE) FOR SPECIAL, INDIRECT, INCIDENTAL, CONSEQUENTIAL OR PUNITIVE DAMAGES ARISING OUT OF OR RELATED TO THIS AGREEMENT OR THE EXERCISE OF ITS RIGHTS HEREUNDER, INCLUDING LOST PROFITS ARISING FROM OR RELATING TO ANY BREACH OF THIS AGREEMENT, HOWEVER CAUSED, EVEN IF THE PARTY HAS BEEN ADVISED OF THE POSSIBILITY OF SUCH DAMAGES, EXCEPT AS A RESULT OF A BREACH OF THE CONFIDENTIALITY AND NON-USE OBLIGATIONS IN SECTION 10. NOTHING IN THIS SECTION 12.5 IS INTENDED TO LIMIT OR RESTRICT THE INDEMNIFICATION RIGHTS OR OBLIGATIONS OF EITHER PARTY.

13. Insurance.

13.1 Manufacturer Insurance. Manufacturer will secure and maintain in full force and effect throughout the term of this Agreement (and for at least three (3) years thereafter for claims made coverage), insurance with coverage and minimum policy limits set forth as follows:

(a) *Worker's Compensation*, including coverage for occupational disease, with benefits determined by statute;

(b) *Comprehensive General Liability and Personal/Advertising Injury*, including coverage for contractual liability assumed by Manufacturer and coverage for Manufacturer's independent contractor(s), with at least [ ]* United States Dollars ($[ ]*) combined single limit for bodily injury and property damage per occurrence, and a general aggregate limit of [ ]* United States Dollars ($[ ]*);

(c) *Products Liability*, exclusive of the coverage provided by the Comprehensive General Liability policy, with at least [ ]* United States Dollars ($[ ]*) per occurrence and an aggregate limit of [ ]* United States Dollars ($[ ]*);

(d) *"All Risk" Property*, valued at replacement cost, covering loss or damage to the Facility and Rhythm's property and materials in the care, custody, and control of Manufacturer; and

(e) *Comprehensive Automobile Liability, Employer's Liability, and Umbrella Liability*, in such amounts and under such terms as are customary for similar companies providing like services.

13.2 Evidence of Insurance. Manufacturer will furnish to Rhythm a certificate from an insurance carrier (having a minimum AM Best rating of A and financial strength of VIII) demonstrating the insurance requirements set forth above. The insurance certificate will confirm each of the following:

(a) excluding Manufacturer's Worker's Compensation policy, Rhythm and its Affiliates are named as an additional insured with respect to matters arising from this Agreement;

(b) such insurance is primary and non-contributing to any liability insurance carried by Rhythm; and

(c) thirty (30) days prior written notice will be given to Rhythm of cancellation or any material change in the policies.

13.3 Insurance Information. Manufacturer will comply, at Rhythm's expense, with reasonable requests for information made by Rhythm's insurance provider representative(s), including permitting such representative(s) to inspect the Facility during operational hours and upon reasonable notice to Manufacturer. In regard to such inspections, the representative(s) will adhere to such guidelines and policies pertaining to safety and non-disclosure as Manufacturer may reasonably require.

14. Term and Termination.

14.1 Term. This Agreement will take effect as of the Effective Date and, unless earlier terminated pursuant to this Section 14, will expire on the later of (a) six (6) years from the Effective Date, or (b) the completion of Services under all Work Orders executed by the parties prior to the sixth anniversary of the Effective Date. The term of this Agreement may be extended by Rhythm continuously for additional two (2) year periods upon written notice to Manufacturer at least thirty (30) days prior to the expiration of the then current term.

14.2 Termination by Rhythm. Rhythm will have the right, in its sole discretion, to terminate this Agreement or any Work Order (a) upon thirty (30) days prior written notice to Manufacturer(in which case Rhythm shall reimburse Manufacturer for the expenses accrued against any pending Work Order), or (b) immediately upon written notice if (i) in Rhythm's reasonable judgment, Manufacturer is or will be unable to perform the Services in accordance with the agreed upon timeframe and/or budget set forth in the applicable Work Order and after discussion the Parties have not been able to find common ground in relation thereto, or (ii) Manufacturer fails to obtain or maintain any material governmental licenses or approvals required in connection with the Services.

14.3 Termination by Either Party. Either party will have the right to terminate this Agreement or any signed Work Orders that are pending by written notice to the other party, upon the occurrence of any of the following:

(a) the other party files a petition in bankruptcy, or enters into an agreement with its creditors, or applies for or consents to the appointment of a receiver or trustee, or makes an assignment for the benefit of creditors, or becomes subject to involuntary proceedings under any bankruptcy or insolvency law (which proceedings remain undismissed for sixty (60) days);

(b) the other party fails to start and diligently pursue the cure of a material breach of this Agreement within thirty (30) days after receiving written notice from the other party of such breach;

(c) the other party challenges the validity of the Rhythm Technology, the Improvements, or the Manufacturer Technology, as the case may be; or

(d) a *force majeure* event that will, or continues to, prevent performance (in whole or substantial part) of this Agreement or any pending Work Order for a period of at least ninety (90) days, In the case of a *force majeure* event relating solely to a pending Work Order, the right to terminate will be limited to such Work Order.

14.4 Effect of Termination. Manufacturer will, upon receipt of a termination notice from Rhythm, promptly cease performance of the applicable Services and will take all reasonable steps to mitigate the out-of-pocket expenses incurred in connection therewith. In particular, Manufacturer will use its best efforts to:

(a) immediately cancel, to the greatest extent possible, any third party obligations;

(b) promptly inform Rhythm of any irrevocable commitments made in connection with any pending Work Order(s) prior to termination;

(c) promptly return to the vendor for a refund all unused, unopened materials in Manufacturer's possession that are related to any pending Work Order; provided, that Rhythm will have the option, but not the obligation, to take possession of any such materials;

(d) promptly inform Rhythm of the cost of any remaining unused, unreturnable materials ordered pursuant to any pending Work Order(s), and either deliver such materials to Rhythm (or its designee) or properly dispose of them, as instructed by Rhythm; and

(e) perform only those services and activities mutually agreed upon by Rhythm and Manufacturer as being necessary or advisable in connection with the close-out of any pending Work Order(s).

14.5 Return of Materials/Confidential Information. Upon the expiration or termination of this Agreement, each party will promptly return all Confidential Information of the other party that it has received pursuant to this Agreement as required by Section 10.3 and otherwise comply with the obligations set forth in Section 10.3. Manufacturer will also promptly return all Rhythm Materials, Rhythm Equipment, retained samples, data, reports and other property, information and know-how in recorded form that was provided by Rhythm, or developed in the performance of the Services, that are owned by or licensed to Rhythm.

14.6 Inventories. Upon expiration or termination of this Agreement or a pending Work Order, Rhythm at its discretion (a) may purchase from Manufacturer any existing inventories of Product ordered under this Agreement that conforms to the Specifications and is Manufactured in accordance with cGMP (if applicable) and the Manufacturing Process, at the price for such Product set forth in the applicable Work Order, and (b) may either (i) purchase any such Product in process held by Manufacturer as of the date of the termination, at a price to be mutually agreed (it being understood that such price will reflect, on a pro rata basis, work performed and non-cancelable out-of-pocket expenses actually incurred by Manufacturer with

respect to the Manufacture of such in-process Product), or (ii) direct Manufacturer to dispose of such material at Rhythm's cost.

14.7 Payment Reconciliation. Within thirty (30) days after the close-out of a Work Order, Manufacturer will provide to Rhythm a written itemized statement of all work performed by it in connection with the terminated Work Order, an itemized breakdown of the costs associated with that work, and a final invoice for that Work Order. If Rhythm has pre-paid to Manufacturer more than the amount in a final invoice then Manufacturer agrees to promptly refund that money to Rhythm, or to credit the excess payment toward another existing or future Work Order, at the election of Rhythm.

14.8 Survival. Expiration or termination of this Agreement for any reason will not relieve either party of any obligation accruing prior to such expiration or termination. Further, the provisions of Sections 1, 2.3, 4, 5.2(c), 5.2(d), 5.4 through 5.7, 6, 9, 11 through 13, 14.4 through 14.8 and 15, and the provisions of any applicable Quality Agreement, will survive any termination or expiration of this Agreement. The provisions of Section 10 shall survive for a period of ten (10) years after the expiration or termination, of this Agreement.

15. Miscellaneous.

15.1 Independent Contractor. All Services will be rendered by Manufacturer as an independent contractor for federal, state and local income tax purposes and for all other purposes. Manufacturer will not in any way represent itself to be a partner or joint venturer of or with Rhythm. This Agreement does not create an employer-employee relationship between Rhythm on the one hand and Manufacturer or any employee, subcontractors, Affiliate of Manufacturer, or any Manufacturer personnel on the other. Manufacturer is acting under this Agreement as an independent contractor with full power and authority to determine the means, manner and method of performance of Manufacturer's duties. Manufacturer shall be responsible for and shall withhold and/or pay any and all applicable federal, state or local taxes, payroll taxes, workers' compensation contributions, unemployment insurance contributions, or other payroll deductions from the compensation of Manufacturer's employees and other Manufacturer personnel. Manufacturer understands and agrees that it is solely responsible for such matters and that it will indemnify Rhythm and hold Rhythm harmless from all claims and demands in connection with such matters.

15.2 *Force Majeure*. Except as otherwise expressly set forth in this Agreement, neither party will have breached this Agreement for failure or delay in fulfilling or performing any term of this Agreement when such failure or delay is caused by or results from causes beyond the reasonable control of the affected party, including, without limitation, fire, floods, embargoes, shortages, epidemics, quarantines, war, acts of war (whether war be declared or not), insurrections, riots, civil commotion, strikes, acts of God or acts, omissions, or delays in acting, by any governmental authority ("*force majeure*"). The party affected by any event of *force majeure* will promptly notify the other party, explaining the nature, details and expected duration of the *force majeure* event. Such party will also notify the other party from time to time as to when the affected party reasonably expects to resume performance in whole or in part of its

obligations under this Agreement, and to notify the other party of the cessation of any such event. A party affected by an event of *force majeure* will use its reasonable efforts to remedy, remove, or mitigate such event and the effects of it with all reasonable dispatch. If a party anticipates that an event of *force majeure* may occur, such party will notify the other party of the nature, details and expected duration of the *force majeure* event. Upon termination of the event of force majeure, the performance of any suspended obligation or duty will promptly recommence.

Notwithstanding the foregoing, in no case shall an event of force majeure excuse timely payment of amounts due hereunder for Services rendered by Manufacturer.

15.3 Notices. All notices must be in writing and sent to the address for the recipient set forth in this Agreement below or in a subsequent notice as the recipient may specify in writing under this procedure. All notices must be given (a) by personal delivery, with receipt acknowledged, or (b) by first class, prepaid certified or registered mail, return receipt requested, or (c) by prepaid international express delivery service. Notices will be effective upon receipt or at a later date stated in the notice.

If to Manufacturer, to:

Managing Director
Peptisyntha SA
Rue de Ransbeek 310
1120 Brussels
Belgium

If to Rhythm, to:

Rhythm Metabolic, Inc.
855 Boylston Street, 11th Floor
Boston, MA 02116
USA
Attention: President

15.4 Assignment. This Agreement may not be assigned or otherwise transferred by either party without the prior written consent of the other party; provided, however, that either party may, without such consent, but with notice to the other party, assign this Agreement, in whole or in part, (a) in connection with the transfer or sale of all or substantially all of its assets or the line of business or Product to which this Agreement relates, (b) to a successor entity or acquirer in the event of a merger, consolidation or change of control, or (c) to any Affiliate. Any purported assignment in violation of the preceding sentence will be void. Any permitted assignee will assume the rights and obligations of its assignor under this Agreement and any permitted assignment shall not release the assigning party from its obligations under this Agreement.

15.5 Entire Agreement. This Agreement, including the attached Appendices and any fully-signed Work Orders, each of which are incorporated herein, constitute the entire agreement between the parties with respect to the specific subject matter of this Agreement and all prior agreements with respect thereto are superseded. For clarity, this Agreement shall not affect or modify, and is separate and distinct from, the existing Development and Manufacturing Services Agreement, effective as of July 2, 2010, as amended, by and between Rhythm Pharmaceuticals, Inc., and PEPTISYNTHA Inc., which shall continue in force and effect in accordance with its terms.

15.6 No Modification. This Agreement and and/or any Work Order or Quality Agreement may be changed only by a writing signed by authorized representatives of both parties.

15.7 Severability; Reformation. If for any reason a court of competent jurisdiction finds any provision of this Agreement or any portion of such a provision to be invalid or unenforceable, such provision will be reformed to the extent required to make the provision valid and enforceable to the maximum extent permitted by law.

15.8 Governing Law. The validity, interpretation, and enforcement of this Agreement, matters arising out of or related to this Agreement or its making, performance or breach, and related matters shall be governed by the laws of the state of New York, excluding its conflict of laws and principles.

All disputes arising out or in connection with the interpretation, performance and/or termination of this Agreement, which cannot be amicably settled between the parties, shall be finally settled under the Rules of Conciliation and Arbitration of the International Chamber of Commerce by one or more arbitrators appointed in accordance with such Rules. Arbitration proceedings shall take place in New York, and shall be conducted in the English language. The award rendered therein shall be final and binding upon the parties. The foregoing is without prejudice to each party's right to seek injunctions and other relief in any appropriate court, to the extent such relief is not available in arbitration.

No term of this Agreement shall be enforceable under the Contracts (Rights of Third Parties) Act 1999 by a person who is not a party to this Agreement, but this shall not affect any right or remedy of any third party which exists or is available other than under that Act. The parties expressly reject any application to this Agreement of (a) the United Nations Convention on Contracts for the International Sale of Goods, and (b) the 1974 Convention on the Limitation Period in the International Sale of Goods, as amended by that certain Protocol, done at Vienna on April 11, 1980.

15.9 Waiver. No waiver of any term, provision or condition of this Agreement in any one or more instances will be deemed to be or construed as a further or continuing waiver of any other term, provision or condition of this Agreement. Any such waiver, extension or amendment will be evidenced by an instrument in writing executed by an officer authorized to execute waivers, extensions or amendments.

15.10 Counterparts. This Agreement may be executed in any number of counterparts, each of which will be deemed an original and all of which together will constitute one and the same instrument.

15.11 Headings. This Agreement contains headings only for convenience and the headings do not constitute or form a part of this Agreement, and should not be used in the construction of this Agreement.

15.12 No Benefit to Third Parties. The representations, warranties, covenants and agreements set forth in this Agreement are for the sole benefit of the parties hereto and their successors and permitted assigns, and they will not be construed as conferring any rights on any other persons.

[Signature page follows]

IN WITNESS WHEREOF, the parties hereto have caused this Agreement to be executed by their duly authorized representatives as of the date first above written.

RHYTHM METABOLIC, INC.		**PEPTISYNTHA, INC.**	
By	/s/ Bart Henderson	By	/s/ Vincent Wilmet
Print Name	Bart Henderson	Print Name	Vincent Wilmet
Title	President	Title	General Manager [illegible]
Date	7/23/13	Date	July 17, 2013

APPENDIX A
SAMPLE WORK ORDER

THIS WORK ORDER is by and between **RHYTHM METABOLIC, INC.**, ("Rhythm") and PEPTISYNTIIA, Inc ("Manufacturer"), and upon execution will be incorporated into the Development and Manufacturing Services Agreement between Rhythm and Manufacturer dated as of July , 2013 (the "Agreement"). Capitalized terms in this Work Order will have the same meanings as set forth in the Agreement.

Rhythm hereby engages Manufacturer to provide Services, as follows:

1. API/Drug Substance and Product.

Describe the specific API/Drug Substance(s) and Product(s).

2. Services. Manufacturer will render to Rhythm the following Services:

Describe the specific Services to be conducted by Manufacturer or attach Manufacturer's proposal.

3. Facilit(ies). The Services described above will be rendered at the following facilities of Manufacturer:

Include Facility address(es).

4. Rhythm Materials. Rhythm will provide to Manufacturer the following materials to be used by Manufacturer to perform the Services:

Describe specific materials being provided by Rhythm to Manufacturer.

5. Rhythm Equipment.

Include any equipment that will be provided by Rhythm to Manufacturer to be used by Manufacturer in performance of the Services.

6. Manufacturer Representative. *Name and Title*

7. Rhythm Representative. *Name and Title*

8. **Compensation.** The total compensation due Manufacturer for Services under this Work Order is **[INSERT WRITTEN AMOUNT (INSERT NUMERICAL AMOUNT]**. Manufacturer will invoice Rhythm for all amounts due under this Work Order. Such amounts will be invoiced in United States Dollars to the attention of **[INSERT NAME]** as follows: **[INSERT INVOICE SCHEDULE]**. All undisputed payments will be made by Rhythm within ninety (90) days of its receipt of an invoice and reasonable supporting documentation. Payments will be made in United States Dollars.

9. **[Quality Agreement.** The provisions of the Quality Agreement, attached hereto as Attachment 1, are incorporated herein by reference.]

All other terms and conditions of the Agreement will apply to this Work Order.

WORK ORDER AGREED TO AND ACCEPTED BY:

RHYTHM METABOLIC, INC.		**PEPTISYNTHA, INC.**	
By		By	/s/ Vincent Wilmet
Print Name		Print Name	Vincent Wilmet
Title		Title	General Manager [illegible]
Date		Date	July 18, 2013

EXHIBIT 10.8

RHYTHM PHARMACEUTICALS, INC. REQUESTS THAT THE MARKED PORTIONS OF THIS EXHIBIT BE GRANTED CONFIDENTIAL TREATMENT UNDER RULE 406 OF THE SECURITIES ACT OF 1933, AS AMENDED

EXECUTION VERSION

LICENSE AGREEMENT

BY AND BETWEEN

CAMURUS AB

AND

RHYTHM PHARMACEUTICALS, INC.

CONFIDENTIAL

* CONFIDENTIAL TREATMENT REQUESTED. OMITTED PORTIONS FILED WITH THE SECURITIES AND EXCHANGE COMMISSION PURSUANT TO RULE 406 PROMULGATED UNDER THE SECURITIES ACT OF 1933, AS AMENDED

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CONFIDENTIAL

* CONFIDENTIAL TREATMENT REQUESTED. OMITTED PORTIONS FILED WITH THE SECURITIES AND EXCHANGE COMMISSION PURSUANT TO RULE 406 PROMULGATED UNDER THE SECURITIES ACT OF 1933, AS AMENDED

LICENSE AGREEMENT

This License Agreement is made as off the Effective Date (hereinafter defined) between **Camurus AB**, a limited liability company organized and existing under the laws of Sweden and having its principal place of business at Ideon Science Park, Sölvegatan 41, SE-223 70 Lund, Sweden (**"Camurus"**) and **Rhythm Pharmaceuticals, Inc.**, a corporation organized and existing under the laws of Delaware and having its principal place of business at 855 Boylston Street, 11th Floor, Boston, MA 02116 USA (**"Rhythm"**) (each a **"Party"** and collectively, the **"Parties"**)

WITNESSETH

WHEREAS, Camurus is the owner of all right, title and interest in and to certain patents and know-how relating to the FC Technology (as defined below) which delivers therapeutic levels of drug substance over extended periods by offering a lipid based injectable liquid solution that, within minutes after

injection, forms a controlled release liquid crystal gel matrix in situ on contact with body fluids at site of injection;

WHEREAS, Rhythm has capabilities in the development, manufacture, promotion, marketing, sales and life cycle management of pharmaceutical products and is the owner of all right, title and interest in and to a drug compound known as RM-493;

WHEREAS, Rhythm wishes to obtain an exclusive world-wide license to the FC technology to formulate RM-493 and to develop, manufacture, promote, market, distribute and sell the Product (as defined below) in the Territory (as defined below); and

WHEREAS, Camurus is willing to grant such world-wide exclusive rights to Rhythm in respect of the Product upon the terms and conditions hereinafter set forth.

NOW, THEREFORE, in consideration of the covenants and obligations expressed herein, and intending to be legally bound, the Parties agree as follows:

1 DEFINITIONS

1.1 **"Adverse Events"** has the meaning ascribed to it in Section 3.8.

1.2 **"Affiliate"** means, with respect to a Party, any entity or person that controls, is controlled by, or is under common control with that Party. For the purpose of this definition, "control" or "controlled" means, direct or indirect, ownership of fifty percent (50%) or more of the shares of stock entitled to vote for the election of directors in the case of a corporation or fifty percent (50%) or more of the equity interest in the case of any other type of legal entity; status as a general partner in any partnership; or any other arrangement whereby the entity or person controls or has the right to control the board of directors or equivalent governing body of a corporation or other entity or the ability to cause the direction of the management or policies of a corporation or other entity. The Parties acknowledge that in the case of entities organized under the laws of certain countries where the maximum percentage ownership permitted by law for a foreign investor is less than fifty

percent (50%), such lower percentage shall be substituted in the preceding sentence, provided that such foreign investor has the power to direct the management and policies of such entity.

1.3 "**Business Day**" means Monday through Friday, other than holidays observed by Camurus or Rhythm.

1.4 **"Camurus IP"** means (a) the Camurus Platform IP and (b) Camurus' interest in any Joint IP.

1.5 **"Camurus Platform IP"** means (a) all Patent Rights listed in Exhibit 1.5 and (b) all other Intellectual Property Controlled by Camurus or any of its Affiliates during the Term hereof that covers the FC Technology.

1.6 **"Camurus Platform Patents"** has the meaning ascribed to it in Section 7.3.

1.7 **"Camurus Trademark"** means Trademarks Controlled by Camurus, including FluidCrystal® and other Trademarks described in Exhibit 1.7, that relate to the FC Technology.

1.8 **"GCP"** means Good Clinical Practices, as set forth in the ICH Harmonized Guidance on Good Clinical Practice (CPMP/ICH/135/95).

1.9 **"GMP"** means Good Manufacturing Practices, as set forth in the Rules Governing Medicinal Product in the European Union volume 4 and the equivalent requirements and/or applicable guidance in any other jurisdiction in the Territory.

1.10 **"Clinical Trials"** means human clinical trials conducted on healthy volunteers or patients to provide data supporting Regulatory Approval of such drug or label expansion of such drug,

1.11 **CMO"** means one or more Third Party contract manufacturing organization(s) that may be used to source ingredients, components, packaging materials and the like and to manufacture, package, label and quality release Rhythm's requirements for Product for use and/or sale in the Territory, all pursuant to the Rhythm Supply Agreement.

1.12 **"Collaboration Inventions"** means all Intellectual Property conceived and reduced to practice by a Party or any of its Affiliates or by a Third Party on behalf of such Party in the course of performing activities under this Agreement or any of Rhythm's licensees or Sub-licensees.

1.13 **"Collaboration Product Patents"** has the meaning ascribed to it in Section 7.3(b) hereof.

1.14 **"Commercially Reasonable Efforts"** means the level of effort and resources required to develop the Product in a sustained manner consistent with the efforts an international specialty pharmaceutical company of similar size and resources would typically devote to a product owned by such entity which is of similar market potential, at a similar stage in the development or life of such product, taking into account issues of safety, efficacy, product profile, the competitiveness of the

marketplace, the proprietary position of the product, the regulatory structure involved, profitability of the product and other relevant commercial factors.

1.15 **"Competing Product"** means any pharmaceutical product comprising [ ]*.

1.16 **"Confidential Information"** means the following, subject to the exceptions set forth in Section 8.1:

(i) the terms and conditions of this Agreement, for which each Party will be considered a Disclosing Party and a Recipient;

(ii) Know-How within Camurus IP for which Camurus will be considered the Disclosing Party and Rhythm shall be the Recipient;

(iii) Know-How within Rhythm IP for which Rhythm will be considered the Disclosing Party and Camurus shall be the Recipient; and

(iv) any other non-public information, whether or not patentable, disclosed or provided by one Party to the other Party in connection with this Agreement, including, without limitation, information regarding such Party's strategy, business plans, objectives, research, technology, products, IP strategy, business affairs or finances including information of the type that is customarily considered to be confidential information by parties engaged in activities that are substantially similar to the activities being engaged in by the Parties under this Agreement, for which the Party making such disclosure will be considered the Disclosing Party and the receiver will be the Recipient.

1.17 **"Control" or "Controlled"** means possession by a Party of the right to grant to the other Party a license, sublicense or other right to use, of the scope provided for in this Agreement, to Intellectual Property and rights to access or cross-reference regulatory filings without violating the terms of any agreement or other arrangement with any Third Party.

1.18 **"Development Data"** means all chemistry, manufacturing and control, preclinical and clinical data including, without limitation, pharmacological, pharmacokinetic, pharmaceutical development and toxicological data, on the Product (including placebo), including any of the foregoing arising from post registration studies, that is generated at any time during the Term of this Agreement by or for either Party and their Affiliates or any of Rhythm's licensees or sub-licensees.

1.19 **"Development Plan"** means Rhythm's plan for pre-clinical and clinical development of the Product together with associated budget through the Ph1B PK/POC Study. The Development Plan as in effect as of the Effective Date is attached hereto as Exhibit 1.19. The Development Plan is subject to update in accordance with Section 3.1 hereof.

1.20 **"Disclosing Party"** means the Party which discloses Confidential Information to the other Party.

1.21 **"Drug"** means Setmelanotide (also known as RM-493) with the chemical structure described in Exhibit 1.19, and its salts.

1.22 **"Effective Date"** means the date of the signature of the last Party to execute this Agreement.

1.23 **"EMA"** means the European Medicines Agency and/or the Committee for Human Medicinal Product or any successor agency thereof or, to the extent the mutual recognition or decentralized procedure is used for a Product in the EU, any national governmental authority having the authority to regulate the sale of medicinal of pharmaceutical products in any country in the EU.

1.24 **"FC Technology"** means (i) Camurus' proprietary formulation technology that is referred to as FluidCrystal® injection depot technology, comprising a lipid based injectable liquid solution that, within minutes after injection, forms a controlled release liquid crystal gel matrix in situ on contact with body fluids at the site of injection, including modifications and improvements to such proprietary formulation technology, and (ii) any other controlled release lipid formulation for injection that is conceived and reduced to practice by, or on behalf of, Camurus and that incorporates any active pharmaceutical ingredient without relating specifically to the Drug, Product or Competing Product excluding for the avoidance of doubt controlled release lipid formulations for injection that are developed by a Third Party and acquired by Camurus through licensing, acquisition, merger or otherwise..

1.25 **"First Commercial Sale"** means the date on which a Product is first sold following Regulatory Approval in the Territory by Rhythm or any of its Affiliates or Sublicensees to a Third Party (other than sales by Rhythm to its Affiliates or Sublicensees) in a commercial arm's length transaction.

1.26 "**First Product Patent Application**" means a patent application filed by Rhythm with the United States Patent and Trademark Office pursuant to Section 7.3(d) hereof that specifically claims the Product.

1.27 **"FTE"** means a full time equivalent person year equal to at least 1,650 hours per year of work carried out by an employee.

1.28 **"FTE Costs"** means the cost of FTEs at the FTE Rate.

1.29 **"FTE Rate"** means the price of a single FTE per Calendar Year. The FTE Rate shall be US$[ ]* per hour for all staff. The FTE Rate reflects the fully burdened internal costs of an FTE including all employee-related compensation, including but not limited to, salaries, wages, bonuses, benefits, profit sharing, share option grants, and any other employment costs, including travel and associated subsistence costs (but excluding travel and subsistence costs incurred in any travel) and professional dues and allocable overhead. On the 1 January each Calendar Year, commencing with 1 January 2016, the FTE Rate will be increased by the percentage (%) increase in inflation as measured by the Swedish Consumer Price Index

published by the Statistiska Centralbyrån of Sweden on each 1 January of each Calendar Year. Camurus shall provide Rhythm with the revised FTE Rate by 1 February of each Calendar Year.

1.30 **"GAAP"** means U.S. Generally Accepted Accounting Principles, consistently applied.

1.31 **"Generic Product"** means a product approved under an Abbreviated New Drug Application, or ANDA, or any non-United States equivalent filing, with the Product as the reference product, that is "therapeutically equivalent" as evidenced by the assignment of any 'A' level therapeutic equivalence rating by the FDA, or any non-United States equivalent rating, such that the product is therapeutically equivalent to the Product, or otherwise is generally substitutable by the pharmacist for the Product when filling a prescription written for the Product without having to seek authorization to do so from the physician writing such prescription.

1.32 **"IND"** means an Investigational New Drug application (together with all subsequent submissions, supplements and amendments thereto, and any materials, documents or information referred to or relied upon thereby) filed with the FDA in conformance with applicable laws and regulations, and the equivalent thereof (or other right to commence clinical testing in humans), as applicable, in jurisdictions outside the United States.

1.33 **"Intellectual Property" or "IP"** means any Patent Rights, Trademarks, Know-How, Confidential Information, and any other intellectual property rights.

1.34 **"Joint Invention"** shall have the meaning defined in Section 7.2(c).

1.35 **"Joint IP"** means any Joint Invention and any Patent Rights claiming any Joint Invention.

1.36 **"Joint Patents"** has the meaning ascribed to it in Section 7.3 (c).

1.37 **"JDC"** means the Joint Development Committee referred to in Section 3.3.

1.38 **"Know-How"** means technical and other information which is not in the public domain, including information comprising or relating to concepts, trade secrets, data, designs, discoveries, formulae, ideas, inventions, materials, methods, models, research plans, procedures, designs for experiments and tests and results of experimentation and testing (including results of research or development), processes (including manufacturing processes, specifications and techniques), laboratory records, chemical, pharmacological, toxicological, clinical, analytical and quality control data, clinical and non-clinical trial data, case report forms, data analyses, reports, manufacturing data or summaries and information contained in submissions to and information from ethical committees and regulatory authorities. Know-How includes documents containing Know-How, including any rights including trade secrets, copyright, database or design rights protecting such Know-How. The fact that an item is known to the public shall not be taken to preclude the possibility that a compilation including the item, and/or a development relating to the item, is not known to the public.

1.39 **"LIBOR"** has the meaning ascribed to it in Section 5.8.

1.40 **"Licensed Field"** means any and all uses including, but not limited to, the treatment, prevention or diagnosis of any disease, disorder or condition.

1.41 **"Manufacturing Costs"** means all [ ]*.

1.42 **"NDA"** means a new drug, biologic or other application, health registration, marketing authorization application, common technical document, regulatory submission, notice of compliance or equivalent application to the FDA or other applicable Regulatory Authority (excluding local and general business licenses and permits) required to be approved before commercial sale or use of the Product as a pharmaceutical or medicinal product in any formulation or dosage form (excluding any pricing and reimbursement approvals), together with all subsequent submissions, supplements and amendments thereto.

1.43 **"NDA Approval"** means approval of an NDA by the FDA or other applicable Regulatory Authority.

1.44 **"Net Sales"** means, with respect to any Product, the gross amount invoiced by Rhythm, its Affiliates or Sublicensees to unrelated Third Party distributors or agents (in each case, who are not sublicensees), or end users in the Territory for the sale or transfer for value of the applicable Product, less deductions for: (i) trade, quantity and cash discounts and rebates actually given to and taken by customers; (ii) refunds, chargebacks and any other allowances actually paid to or taken by customers, including those granted to managed care entities; (iii) amounts separately and actually credited to customers for Product returns, credits or allowances; (iv) rebates actually paid or credited to any governmental agency (or branch thereof) or to any Third Party payor, administrator or contractee (such as those in respect of any state or federal Medicare, Medicaid or similar programs); (v) discounts mandated by, or granted to meet the requirements of, applicable state, provincial or federal law, paid or credited to a wholesaler, purchaser, Third Party or other contractee including required chargebacks and retroactive price reductions; (vi) special outbound packing, freight, shipping insurance and other transportation expenses that are separately billed to the customer or prepaid; (vii) sales, value-added,

excise and turnover taxes, tariffs and duties, and other taxes directly related to the sale of the Product (but excluding net income taxes); and (viii) the actual amount of any write-offs for bad debt relating to such sales, provided when paid the amount shall be added to the Net Sales.

The amounts of any deductions taken pursuant to clauses (i)-(viii) shall be determined from books and records maintained in accordance with GAAP. This definition of Net Sales shall be updated as needed from time to time as appropriate to reflect changes required by (i) the adoption by Rhythm, as part of its ordinary business practices, consistently applied, of accounting standards other than GAAP or as required by law, or (ii) GAAP so long as Rhythm is utilizing GAAP as its accounting standard. Net Sales shall not include revenue received by Rhythm or any of its Affiliates from transactions with an Affiliate, where the Product in question will be resold to an independent third-party distributor or agent (in each case, who is not a Sublicensee) or end user by the Affiliate where such revenue received by the Affiliate from such resale is included in Net Sales. Revenue received by Rhythm (or any of its Affiliates) from transactions with an Affiliate, where the Product in question is used by the Affiliate solely for such Affiliate's internal purposes shall also be included in Net Sales at a price equal to the fair market value of such transfer(s).

If the Product is sold in a bundled manner with other products or services of Rhythm then all such deductions shall be fairly and equitably allocated to the Product and other products or services of Rhythm, its Affiliates and Sublicensees, such that the Product does not bear a disproportionate portion of such deductions. The transfer of Product by Rhythm to an Affiliate or Sublicensee shall not be deemed a sale. Net Sales shall be calculated in accordance with generally accepted accounting principles in the United States (US GAAP), consistently applied.

1.45 **"Patent Right"** means (a) all national, regional and international patents and patent applications, including provisional patent applications; (b) all patent applications filed either from such patents, patent applications or provisional applications or from an application claiming priority from any of these, including utility applications, divisionals, continuations, continuations-in-part, provisionals, converted provisionals, and continued prosecution applications, and reissue applications; (c) any and all patents that have issued or in the future issue from the foregoing patent applications described in clauses (a) and (b), including author certificates, inventor certificates, utility models, petty patents and design patents and certificates of invention; (d) any and all extensions or restorations by existing or future extension or restoration mechanisms, including revalidations, reissues, re-examinations and extensions (including any supplementary protection certificates and the like) of the foregoing patents or patent applications described in clauses (a), (b) and (c); and (e) any similar rights, including so-called pipeline protection (where the subject matter previously disclosed was not previously patentable in a particular jurisdiction but subsequently becomes patentable subject matter in such jurisdiction), or any importation, revalidation, confirmation or introduction patent or registration patent or patent of additions to any such foregoing patent applications and patents.

1.46 **"Payment Report"** has the meaning ascribed to it in Section 5.7.

1.47 **"Ph1B PK/POC Study"** has the meaning ascribed to it in Section 3.6.

1.48 **"Product(s)"** means the Drug as sole active pharmaceutical ingredient formulated with the FC Technology for injection. For clarity, Products comprised of the same active pharmaceutical ingredient and delivered by similar drug administration methods (e.g., injection, such as by pen, syringe and needle, or needle-free) for same or different duration, or different doses of the same or different formulations of the FC Technology, shall be considered the same Product.

1.49 **"Prosecute" or "Prosecuting"** means with regard to specified Patent Rights, preparing, filing, prosecuting, validating, maintaining and defending such Patent Rights, including with respect to any re-examination, reissue, revocation, interference or opposition proceedings including any appeal therefrom. For the avoidance of doubt, "**Prosecuting"** excludes any infringement suits or other legal proceedings to enforce the specified Patent Rights, regardless of whether or not such proceedings involve the defense of the Patent Rights in suit.

1.50 **"Recipient"** means the Party, which receives Confidential Information from the other Party.

1.51 **"Regulatory Approvals"** means any NDA Approvals and other approvals, licenses, registrations, or authorizations granted or issued by any Regulatory Authority necessary for the manufacture, packaging, labeling, use, storage, transport, export, import, clinical testing, promotion or sale of the Product in a country, including pricing and reimbursement approvals to the extent the applicable Regulatory Authority in such country require a pricing or reimbursement approval prior to commercialization of a Product in such country.

1.52 **"Regulatory Authority"** means any national, supranational, regional, state or local regulatory agency, department, bureau, commission, council or other governmental entity, including the FDA, in any country involved in the granting or receipt as the case may be of INDs, NDAs or Regulatory Approvals.

1.53 **"Rhythm Collaboration IP"** means all Collaboration Inventions owned by Rhythm pursuant to Section 7.2, 7.3 (d) or Section 7.4, including Rhythm's interest in any Joint IP.

1.54 **"Rhythm IP"** means the Rhythm Collaboration IP and the Rhythm Product IP.

1.55 **"Rhythm Product IP"** means (a) all Patent Rights; (b) all Know-How and all other Intellectual Property; in each of (a) and (b) that (1) are Controlled by Rhythm or any of its Affiliates as of the Effective Date or become Controlled by Rhythm or its Affiliates during the term hereof and (2) are necessary or useful to make or have made, use, offer to sell, sell, have sold, import, or otherwise exploit the Product. Notwithstanding the foregoing, Rhythm Product IP shall not include any Rhythm Collaboration IP.

1.56 **"Rhythm Product Patents"** means all Patent Rights within Rhythm Product IP.

1.57 **"Rhythm Supply Agreement"** means supply agreement between Rhythm and CMO governing the supply of the Product to Rhythm by CMO for the Territory.

1.58 **"Rhythm Trademarks"** means any Trademark owned or registered by Rhythm or that may be granted to Rhythm in the Territory to be used on the Product in the Territory and excluding any Camurus Trademarks.

1.59 **"Royalty Term"** has the meaning ascribed to it in Section 5.3.

1.60 **"Sublicensee"** shall have the meaning defined in Section 2.3.

1.61 **"Term"** shall have the meaning defined in Section 11.1.

1.62 **"Territory"** means the entire world.

1.63 **"Third Party"** means any entity other than Camurus or Rhythm or their respective Affiliates.

1.64 **"Trademarks"** means registered trademarks and applications therefor, unregistered trade or service marks and company names in each case with any and all associated

goodwill and all rights or forms of protection of a similar or analogous nature including rights which protect goodwill whether arising or granted under the laws of any jurisdiction and, for purposes of this definition, trade dress.

1.65 **"Valid Claim"** means a claim of a (i) granted patent which has not been revoked or held unenforceable or invalid by a decision of a court or other governmental agency of competent jurisdiction, which is not appealable or has not been appealed within the time allowed for appeal, and which has not been abandoned, disclaimed or surrendered, or (ii) an unissued published patent application that has not been formally terminated, abandoned, denied or admitted to be invalid or unenforceable through reissue, re-examination or disclaimer and which claim has been pending no longer than the earlier of (a) the date that is ten (10) years after the earliest priority date of the earliest application in which the claim could have been presented or (b) the date that is ten (10) years after the Effective Date, wherein after such earlier date such claim is expired and not a Valid Claim until the date that such a claim is granted or accepted for grant; provided, however, that if the holding of such court or agency with respect to a patent application is later reversed by a court or agency with overriding authority, the claim shall be reinstated as a Valid Claim with respect to Net Sales made after the date of such reversal.

1.66 Interpretation.

· Whenever any provision of this Agreement uses the term "including" (or "includes"), such term shall be deemed to mean "including without limitation" and "including but not limited to" (or "includes without limitations" and "includes but is not limited to") regardless of whether the words "without limitation" or "but not limited to" actually follow the term "including" (or "includes");

· "Herein", "hereby", "hereunder", "hereof" and other equivalent words shall refer to this Agreement in its entirety and not solely to the particular portion of this Agreement in which any such word I used;

· All definitions set forth herein shall be deemed applicable whether the words defined are used herein in the singular or the plural;

· Wherever used herein, any pronoun or pronouns shall be deemed to include both the singular and plural and to cover all genders;

· The recitals set forth at the start of this Agreement, along with the Exhibits to this Agreement, and the terms and conditions incorporated in such recital, Exhibits shall be deemed integral parts of this Agreement and all references in this Agreement to this Agreement shall encompass such recitals, Exhibits and the terms and conditions incorporated in such recitals, Exhibits, *provided*, that in the event of any conflict between the terms and conditions of this Agreement and any terms and conditions set forth in the Exhibits the terms of this Agreement shall control;

· In the event of any conflict between the terms and conditions of this Agreement and any terms and conditions that may be set forth on any order, invoice, verbal agreement or otherwise, the terms and conditions of this Agreement shall govern;

· The Agreement shall be construed as if both Parties drafted it jointly, and shall not be construed against either Party as principal drafter;

· Unless otherwise provided, all references to Sections and Exhibits in this Agreement are to Sections and Exhibits of and to this Agreement;

· Unless otherwise provided, all references to days, months, quarters or years are references to calendar days, calendar months, calendar quarters or calendar years;

· Any reference to any federal, national, state, local or foreign statute or law shall be deemed to also refer to all rules and regulations promulgated thereunder, unless to context requires otherwise; and

· Wherever used, the word "shall" and the word "will" are each understood to be imperative or mandatory in nature and are interchangeable with one another.

2 LICENSE GRANT TO RHYTHM

2.1 License Grant. Camurus hereby grants to Rhythm, and Rhythm hereby accepts, the exclusive royalty bearing license under the Camurus IP to develop, make or have made, use, sell, offer for sale, market and promote the Product in the Licensed Field in the Territory. The exclusive rights of Rhythm granted herein are subject to the rights required for Camurus to perform its obligations and exercise its rights under this Agreement.

2.2 Subcontracting. Subject to the terms of Section 2.3, Rhythm and its Affiliates shall have the right, without obtaining the written consent of Camurus, (i) to subcontract its development and manufacturing responsibilities under this Agreement (and grant any necessary sublicenses in connection therewith), and (ii) to engage contract sales organizations to supplement or complement Rhythm's own sales force. Rhythm shall at all times be liable for all such activities as if such activities had been undertaken by Rhythm hereunder.

2.3 Sublicenses. Subject to Section 2.2 Rhythm may not grant sublicenses under the licenses granted under Section 2.1, except as follows.

(a) Rhythm may grant sublicenses to Camurus IP as required to make and have made the Product;

(b) Rhythm may grant sublicenses to the Camurus IP to any of its Affiliates or Third Parties to develop, make, have made, use, sell, offer for sale, market and promote the Product in the Licensed Field in the Territory,

provided, that in each such case, (i) Rhythm shall be liable to Camurus as if Rhythm is exercising such sublicensed rights itself under this Agreement, (ii) the Sublicensee shall be permitted to grant further sublicenses, (iii) Rhythm shall provide upon written request by Camurus reasonable assurance that its Sublicensees are required to comply with confidentiality, indemnity, reporting, audit rights, access to Development Data, and information obligations owed by such Sublicensees to Rhythm that correspond and are no less stringent than the confidentiality, indemnity,

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reporting, audit rights, access to Development Data, and information obligations owed by Rhythm to Camurus as set forth in this Agreement. Rhythm shall promptly provide notice to Camurus of any sublicense granted pursuant to this Section 2.3. Any person or entity that receives a sublicense or is otherwise granted the right to promote and sell the Product as permitted hereunder is a "**Sublicensee**".

2.4 Grant Back to Camurus. Subject to and upon the terms and conditions set forth in this Agreement, Rhythm hereby grants to Camurus, and Camurus hereby accepts, a world-wide, paid up, non-exclusive, perpetual license, with the right to sublicense, under Rhythm Collaboration IP (but excluding Rhythm's Development Data and regulatory filings, including INDs, NDAs and Regulatory Approvals, which are addressed in Section 3.7), to develop, make or have made, use, sell, offer for sale, market and promote products that are not the Product or a Competing Product, in the Territory. Notwithstanding anything express or implied in the foregoing provisions of this Section 2.4 to the contrary, such license by Rhythm to and/or under Rhythm Collaboration IP shall only include those portions of any Rhythm Collaboration IP that are directly related to the FC Technology and that do not include information concerning the Drug, the Product or any Competing Product or any method of making or using the same. In the event that Camurus sublicenses any of its rights under this Section 2.4, (i) Camurus shall be liable to Rhythm as if Camurus were exercising such sublicensed rights itself under this Agreement and (ii) Camurus shall provide upon written request by Rhythm reasonable assurance that any sublicensee of Camurus' rights under this Section 2.4 is required to comply with obligations with respect to confidentiality and indemnity owed by such sublicensee to Camurus that correspond and are no less stringent than the obligations owed by Camurus to Rhythm pursuant to this Agreement with respect to confidentiality and indemnity.

3 DEVELOPMENT OF PRODUCT

3.1 Rhythm Development Responsibility and Diligence. Rhythm shall have the responsibility for, and have final decision-making authority with respect to, development of the Product at its own cost and Rhythm shall in doing so at all times exercise Commercially Reasonable Efforts to develop the Product through completion of the Ph1B PK/POC Study. If Rhythm elects to continue development of the Product following successful completion of the Ph1B PK/POC Study in accordance with Section 3.6, then Rhythm shall be deemed to have satisfied Rhythm's obligation to use Commercially Reasonable Efforts to develop the Product. Rhythm shall keep the JDC regularly apprised of the progress of the execution of the Development Plan(s). Both parties recognize that, in general, the Development Plans represent projections only and may be subject to change during the development process. Both Parties also recognize that the development of the Product is being undertaken as a bridge of Rhythm's efforts to develop the Drug and secure its approval by Regulatory Authorities; accordingly, in the event and to the extent that the primary Drug development program suffers delays or set-backs, those events will have a corresponding effect on efforts under this Agreement with respect to the Product. Rhythm may decide from time to time to update to the Development Plan(s) as necessary to reflect changes in the progress of development

for the Product. Any proposed change to the Development Plan shall set forth a summary anticipated development activities and timelines for the Product, and propose any responsibility of Rhythm or Camurus (if any) for carrying out any such activities. Rhythm shall also provide to Camurus draft forms of Product protocols for the purpose of obtaining comments. Rhythm shall consider in good faith all comments provided by Camurus within the thirty (30) day period following Camurus receipt of such protocols. Any Clinical Trials shall be conducted by Rhythm in accordance with GCP. If Rhythm elects to continue development of the Product following successful completion of the Ph1B PK/POC Study in accordance with Section 3.6, then Rhythm shall thereafter provide Camurus within sixty (60) days after the end of every second calendar quarter, a reasonably detailed report on progress made toward the development of the Product during such preceding 6-month period, including the status of applications for regulatory approvals until such time as Rhythm becomes obligated to provide Payment Reports pursuant to Section 5.7 in the U.S. or one or more countries within the EU. Rhythm shall be deemed to have satisfied such obligation to provide such reasonably detailed in any calendar year if Rhythm complies with its obligations under Section 3.4(d) hereof with respect to any meeting of the JDC that takes place on any date during such calendar year that is on or prior to the 60th day after the end of the second calendar quarter of such calendar year.

3.2 Camurus Services. Rhythm may utilize Camurus to perform certain agreed development activities as shall be specified in a separate written agreed addendum to the Development Plan. Rhythm shall reimburse Camurus for its costs and expenses incurred in providing such services pursuant to a budget for such costs and expenses, including FTE Costs, which shall be set forth in the addendum to the Development Plan. Such costs and expenses incurred by Camurus may be invoiced to Rhythm on a monthly basis. Rhythm shall effect payment of all invoices to Camurus' designated bank account within thirty (30) days after the date of Camurus' invoice. Camurus shall together with such invoices provide reasonable available supporting documentation of such costs and expenses (including relevant Third Party invoice and specification of hours worked by Camurus and a summary of the work performed). Rhythm agrees not to withhold payment in respect of any Third Party costs that are within an agreed budget, although Rhythm may dispute the same. For clarity, Camurus shall not be obliged to carry out any activities unless Rhythm has agreed to reimburse Camurus the associated costs and expenses.

3.3 Joint Development Committee. Within ten (10) days of the Effective Date, the Parties shall appoint a Joint Development Committee (the **"JDC"**) of four (4) members. Subject to this Section 3.3 and Section 3.4 below, the JDC shall be the primary forum for exchange of information and review of Rhythm's progress in the development and registration of the Product and the JDC shall have the following responsibilities;

(i) reviewing the progress and results of Rhythm's development efforts;

(ii) reviewing material amendments or updates to the Development Plan;

(iii) agreeing procedure for filing of Joint Patents;

(iv) reviewing the progress of Camurus' technology transfer activities in respect of the Product as detailed in Section 6.2,

* CONFIDENTIAL TREATMENT REQUESTED. OMITTED PORTIONS FILED WITH THE SECURITIES AND EXCHANGE COMMISSION PURSUANT TO RULE 406 PROMULGATED UNDER THE SECURITIES ACT OF 1933, AS AMENDED

(v) discuss publications regarding Product (such as abstract presentations at conferences, symposiums), and

(vi) Camurus will advise the JDC of any material issues that it is observing with respect to the characteristics of its FC Technology that are of potential utility to Rhythm in its development efforts with respect to its clinical and regulatory approach for the Product all to the extent covered by Rhythm's license rights in Section 2.1.

3.4 Meetings of the JDC:

(a) The JDC shall consist of an equal number of representatives appointed by each of Camurus and Rhythm. Each Party may, with notice to the other, substitute any of its members serving on the JDC and may invite ad hoc non-voting members as desired. The Parties may also, by mutual agreement, increase or decrease the number of members serving on the JDC; provided that the number of members representing each Party remains equal. Rhythm shall have the right to appoint one of its members to be the chairperson of the JDC, whose term shall run for so long as the JDC is in existence.

(b) The JDC shall meet as necessary but in any event no less frequently than semi-annually. Meetings of the JDC may take place by telephonic or video conference unless otherwise agreed. Minutes from the meetings of the JDC shall be kept by the Chairman of the JDC and circulated to Camurus members within a reasonable time for comments and approval. Minutes shall not become official until approved by both Parties in writing; minutes shall be presented for approval as the first order of business at the subsequent JDC meeting, or if it is necessary to approve the minutes prior to such subsequent meeting, then the Parties shall approve the minutes within thirty (30) days of receipt thereof.

(c) Each Party shall bear its own costs, including travel and lodging for its personnel serving on the JDC or attending meeting of the JDC.

(d) Each Party shall submit to the JDC members ten (10) days in advance of each JDC meeting reasonably detailed progress and other reports to keep the JDC informed of the current progress and status of the conduct of its respective activities.

(e) The quorum for JDC meetings shall be two (2) members, provided there are at least one (1) member from each of Camurus and Rhythm present.

(f) Information that otherwise falls under the definition of Confidential Information contained in reports made pursuant to Section 3.3 or Section 3.4 will be subject to the confidentiality provisions of Section 8.

(g) The term for the JDC shall commence on the date it is established by the Parties and continue until the Product receives regulatory approval in the United States or the EU.

3.5 Regulatory Filings and Approvals in the Territory. Rhythm shall have the responsibility for, and have final decision-making authority with respect to applying for and obtaining Regulatory Approvals for each Product in the Territory

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which applications and approvals shall be held by and in the name of Rhythm. Camurus shall provide assistance as reasonably requested in (i) compiling an IND and NDA; (ii) providing support for meetings with Regulatory Authorities and (iii) responding to questions from the Regulatory Authorities on technical (as opposed to pricing) questions on the Product and Camurus shall be reimbursed for such work at Camurus FTE Costs and reimbursement of documented expenses. Rhythm shall pay all user fees and other costs required to obtain and maintain such Regulatory Approvals.

3.6 Decision Not To Proceed After Ph1B PK/POC Clinical Trial. Without limiting the generality of the foregoing, on a Product-by-Product basis, Rhythm shall use Commercially Reasonable Efforts to perform the development activities through the completion of the first Ph1B PK/POC Clinical Trial with the Product as set forth in the Development Plan (the **"Ph1B PK/POC Study"**). Within ninety (90) days following receipt of the final report from the Ph1B PK/POC Study Rhythm shall make a determination whether or not to proceed with development. If Rhythm elects to proceed with further development following a successful Ph1B PK/POC Study then Rhythm shall thereafter provide Camurus with the semi-annual reports described in Section 3.1 (last sentence). If Rhythm elects to proceed with further development that constitutes re-performance of a Ph1B PK/POC Study on an alternative formulation of the Product that was the subject of an unsuccessful Ph1B PK/POC Study then Rhythm shall provide Camurus with an updated Development Plan covering subsequent development activities through the re-performance of such Ph1B PK/POC Study within sixty (60) days of the date it notifies Camurus of its decision to re-perform a Ph1B PK/POC Study. If Rhythm elects not to proceed with any additional development then Rhythm shall notify Camurus of such decision and terminate this Agreement in accordance with Section 11.3(e). If Rhythm fails to deliver notice to Camurus of Rhythm's decision to proceed with development or to terminate development within the 90-day period specified above then Camurus may terminate this Agreement as set forth in Section 11.3(e). Notwithstanding anything to the contrary herein, if Rhythm has not initiated dosing in the first Phase III study with the Product within [ ]* from the completion of the Ph1B PK/POC Study then Rhythm shall be required to terminate the Agreement in accordance with Section 11.3(e) and if Rhythm fails to terminate the Agreement then Camurus may terminate this Agreement as set forth in Section 11.3(e); provided, however that where Rhythm's failure to meet the foregoing [ ]* deadline results from any documented safety issues, manufacturing process issues, changes to legal requirements or requests from a Regulatory Authority, in each case to the extent outside Rhythm's control, then as long as Rhythm uses commercially reasonable efforts to overcome such issues, Rhythm shall not be required to terminate the Agreement as provided above in this Section 3.6 and Camurus shall not have the right to terminate the Agreement as provided above in this Section 3.6.

3.7 Development Data. To the extent permitted by law and subject to the terms and conditions set forth in this Section 3.7, Rhythm grants Camurus, its Affiliates and licensees the right to cross-reference those portions of any Development Data and regulatory filings, including INDs, NDAs and Regulatory Approvals, Controlled by Rhythm or its Affiliates that are directly related to safety and CMC aspects of the FC Technology and do not include information concerning the Drug and that have

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been submitted to the FDA or any other applicable Regulatory Authorities, in each case only to the extent that such right to cross-reference, is necessary or useful for Camurus', its Affiliates' and licensees' regulatory filings for other products that utilize the FC Technology, provided that such other products do not consist of a Product or a Competing Product. Camurus shall provide Rhythm with at least thirty (30) days advanced written notice of the regulatory agency and division which is receiving the cross-reference filing, before Camurus or any of its Affiliates or licensees exercises any right of cross-reference as contemplated under the foregoing provisions of this paragraph. Rhythm shall give Camurus, its Affiliates and licensees reasonable access and right to use (including the right to copy where reasonably required) to a copy of those portions of the Development Data, IND, NDA or Regulatory Approvals Controlled by Rhythm, its Affiliates or its Sublicensees that are directly related to safety and CMC aspects of the FC Technology and do not include information concerning the Drug , in each case only to the extent that such right of reasonable access and use is necessary or useful for development or regulatory filings for products that utilize the FC Technology and do not consist of a Product or a Competing Product. Camurus shall be responsible for reimbursement to Rhythm of any costs on an hourly fee basis incurred in connection with the provision of access to any data by Rhythm pursuant to this Section 3.7, including the costs of segregating data that relates solely to the FC Technology. Such costs shall be calculated on an hourly fee basis.

Camurus shall provide Rhythm, its Affiliates, Sublicensees with a right of cross-reference, a right of reasonable access and a right to use the development data and regulatory filings and regulatory approvals that Camurus or its Affiliates Control that are directly related to the FC Technology and that do not include information concerning any active pharmaceutical ingredient under development by Camurus or its Affiliates or licensees or sublicensees, in each case only to the extent that such right to cross-reference, such right of reasonable access and such right of use is necessary or useful for regulatory filings for the Product made or to be made by Rhythm, its Affiliates or Sublicensees. Rhythm shall provide Camurus with at least thirty (30) days advanced written notice of the regulatory agency and division which is receiving the cross-reference filing,

before Rhythm or any of its Affiliates or Sublicensees exercises any right of cross-reference as contemplated under the foregoing provisions of this paragraph. Rhythm shall be responsible for reimbursement to Camurus of any costs incurred in connection with the provision of access to any data by Camurus pursuant to this Section 3.7, including the costs of segregating data that relates solely to the FC Technology. Such costs shall be calculated on an hourly fee basis. It is noted that Camurus is currently negotiating sublicensing rights under its license agreement with [ ]* to [ ]* generated know-how pertaining to the FC Technology and that do not include information concerning any active pharmaceutical ingredient under development by [ ]* or its Affiliates. The Parties agree that until Camurus succeeds in securing such sublicensing rights from [ ]* under such license agreement that would permit Camurus to grant to Rhythm rights to such know-how as provided in Section 3.7, Camurus shall not sublicense or otherwise grant or provide the rights granted by Rhythm to Camurus in this Section 3.7 or Section 2.4 to [ ]* or its Affiliates.

3.8 Reporting Adverse Events: Rhythm shall be responsible for reporting all adverse events (as defined in the then current edition of ICH Guidelines and any other relevant regulations or regulatory guidelines or any other safety problem of any significance, hereafter "Adverse Events") relating to the Product to the appropriate regulatory authorities in the countries in the Territory in accordance with the appropriate laws and regulations of the relevant countries and authorities. Rhythm shall ensure that its Affiliates and Sublicensees comply with all such reporting obligations. In the event that Rhythm knows or acquires knowledge that any Adverse Event relating to the Product is attributable to the FC Technology and is not attributable to the Drug, then Rhythm shall provide prompt written notice of such Adverse Event to Camurus. In addition, at each meeting of the JDC, a representative of Rhythm shall present to the JDC, and the JDC shall review, all Adverse Event relating to the Product that have occurred since the last meeting of the JDC

4 COMMERCIALIZATION

4.1 Responsibility. Rhythm shall have responsibility for, and final decision-making authority with respect to, commercialization of Products in the Territory at its own cost.

4.2 **Reserved**.

4.3 **Reserved**.

4.4 **Reserved**.

4.5 **Reserved**.

5 PAYMENT OBLIGATIONS

5.1 Signing Fee. Within the later to occur of (i) five (5) Business Days of the Effective Date and (ii) five (5) Business Days after receipt of an invoice from Camurus, Rhythm shall pay Camurus a non-refundable and non-creditable signing fee of [ ]* US Dollars (US$[ ]* payable by wire transfer of immediately available funds to an account designated in writing by Camurus.

5.2 Milestone Payments. On a Product-by-Product basis, Rhythm shall pay the following non-refundable, non-creditable amounts upon the achievement of the following events, within the later to occur of (i) sixty (60) calendar days after each such event and (ii) ten (10) Business Days after receipt of an invoice from Camurus for the milestone payment due with respect to each such event:

MILESTONE EVENT	MILESTONE PAYMENT
Upon completion (i.e. release of first eGMP batch of Product) of tech transfer and IND support for the filing of the first IND for the Ph1B PK/POC Study but in no event later than upon filing of said IND.	US$ [ ]*.
Successful completion of the Ph1B PK/POC Study. Successful completion shall be deemed to have occurred if, after completion of the Ph1B PK/POC Study, Rhythm pursues additional development activities in preparation for the commencement of a Phase II Study. If, after completion of the Ph1B PK/POC Study, Rhythm does not pursue development activities in preparation for the commencement of a Phase II Study, Rhythm must within 90 days from completion of the Ph1B PK/POC Study (i) treat the Ph1B PK/POC Study as successfully completed and pay the associated $[ ]* Milestone Payment to Camurus, (ii) renegotiate and agree with Camurus as to the extent of Rhythm's obligation, if any, to have to pay	US$ [ ]*.

the $[ ]* Milestone Payment Milestone Payment associated with successful completion of the Ph1B PK/POC Study or (iii) terminate this Agreement as set forth in Section 11.3(e). Nothing in this paragraph shall be construed as requiring that any Milestone Payment be paid or payable more than once upon the first achievement of the applicable Milestone and any renegotiated Milestone Payment under this paragraph shall be in lieu of the $[ ]* Milestone Payment payable by Rhythm to Camurus upon successful completion of the Ph1B PK/POC Study with the Product.	
First dosing of the Product in the first Phase III Clinical Trial.	US$ [ ]*.
Filing of the first NDA for the Product in the United States.	US$ [ ]*.
First NDA Approval for the Product in the United States.	US$ [ ]*.

Filing of the first NDA for the Product in the EU.	US$ [ ]*.
First NDA Approval for the Product in the EU.	US$ [ ]*.

In no event shall any development or approval milestone payment be payable more than once for each Product and in no event shall the aggregate amount of all development and approval milestone payments payable with respect to each Product exceed US$[ ]*.

5.3 Royalties.

On a Product-by-Product basis, Rhythm shall pay to Camurus royalties (**"Royalties"**) equal to the percentages on the below annual Net Sales of Product in the Territory as described below.

Product Net Sales Tier	**Royalty**
For the portion of aggregate annual Net Sales of Product of less than [ ]* in the Territory	[ ]*%
For the portion of aggregate annual Net Sales of Product equal to or greater than [ ]* and less than [ ]* in the Territory	[ ]*%
For the portion of aggregate annual Net Sales of Product equal to or greater than [ ]* and less than [ ]* in the Territory	[ ]*%
For the portion of aggregate annual Net Sales of Product equal to or greater than [ ]* in the Territory	[ ]*%

Royalties shall be payable for a time period calculated on a Product-by-Product and country-by-country basis in respect of the licenses granted to Rhythm by Camurus hereunder beginning on the First Commercial Sale of such Product in such country and ending on the later of (a) [ ]* after the date of such First Commercial Sale of such Product in such country and (b) the expiration of the last to expire Valid Claim covering such Product within (i) Camurus Platform Patents or (ii) Patent Rights claiming Collaboration Inventions, in such country. The period during which Royalties are payable in respect of a Product in any country is referred to as the **"Royalty Term"**. Notwithstanding the foregoing, royalty rates shall be reduced by [ ]*% with respect to sales of a Product in any country of the Territory during the Royalty Term if the sale, manufacture or use of the Product in such country is not covered by any Valid Claim within (1) the Camurus Platform Patents or (2) Patent Rights covering Collaboration Inventions and in each case there is a Generic

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Product sold in such country. In no event may the Royalties set forth first above in this Section 5.3 be reduced by more than [ ]*% by application of one or more royalty reduction provisions in this Agreement.

5.4 Sales Milestones. Rhythm shall pay the following non-refundable, non-creditable sales milestones upon the achievement of the following sales levels for all Products in the Territory. Payment for any such milestones shall be made within the later to occur of (i) sixty (60) calendar days after the achievement of the applicable milestone and (ii) ten (10) Business Days of receipt of appropriate original invoice from Camurus. Sales milestones will be paid in accordance with the schedule below, with each milestone paid only once and on the first occurrence of the event, as set forth below. In the event more than one sales milestone is reached in the same year, then each such milestone shall be due that year.

Product Event	**Amount**

When Net Sales of a Product in the Territory first exceed US$[	]* in a calendar year	US$[	]*
When Net Sales of a Product in the Territory first exceed US$[	]* in a calendar year	US$[	]*
When Net Sales of a Product in the Territory first exceed US$[	]* in a calendar year	US$[	]*
When Net Sales of a Product in the Territory first exceed US$[	]* in a calendar year	US$[	]*

In no event shall sales milestone payments be payable in excess of US$[ ]*.

5.5 Third Party Licenses. If Rhythm, to avoid infringement of Third Party Patent Rights in connection with the Product, to the extent such infringement relates the use of Camurus IP, obtains a license under an issued patent(s) from such Third Party in any country in the Territory to make or have made, use, offer to sell, sell, have sold, import, or otherwise exploit a Product pursuant to the licenses granted hereunder, then Royalties calculated on Net Sales of such Product in such country shall, subject to Section 5.3, be offset by [ ]* of any royalties paid by Rhythm as and when paid to such Third Party under such Third Party license. For the avoidance of doubt, payments to such Third Party that may be offset shall be limited to such payments allocable to the license of such technology (excluding, for example, any payments in respect of development services or the supply of products) and allocable to the Product (excluding, for example, other uses of such technology by Rhythm). Rhythm shall provide Camurus with copies of the relevant terms of such license agreement with such Third Party and other material information in its possession in respect of such technology subject to Camurus undertaking confidentiality in respect of such disclosures by Rhythm. Rhythm shall consult with Camurus prior to entering into any such license agreement and provide Camurus a reasonable opportunity to provide its views on the need or benefit to obtain such license and the financial and other terms thereof. If Rhythm exercises

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its right in Section 5.6 to buy down Royalties, then Rhythm's rights to offset future royalties paid to Third Parties as provided in this Section 5.5 shall cease.

5.6 Royalty Buy-Down. Rhythm shall have the right on a Product-by-Product basis, exercisable at any time during a period beginning on the First Commercial of the applicable Product and ending on the [ ]* anniversary thereof, to buy down the Royalties to a flat rate of [ ]* on Net Sales of such Product by making payment to Camurus of a one-time non-refundable and non-creditable amount of [ ]*. The reduced royalty rate shall apply to all Net Sales of such Product from the calendar quarter following the calendar quarter in which said lump-sum payment is received by Camurus. Any sales milestones that would otherwise become due pursuant to Section 5.4 after the calendar quarter in which said payment was received by Camurus, shall no longer be payable.

5.7 Royalty and Milestone Reports. Royalty payments shall be paid within sixty (60) calendar days after the first day of January, April, July and October of each year following the First Commercial Sale of a Product, and shall include a written report with respect to the preceding quarter (the **"Payment Report"**) stating: (a) the gross sales and number of units sold of each presentation of the Product sold by Rhythm, its Affiliates and Sublicensees in each country in the Territory; (b) Net Sales of the Product sold by Rhythm, its Affiliates and Sublicensees, during such quarter on a country-by-country basis; (c) the date of any First Commercial Sale of the Product in each country during such quarter, (d) currency exchange rates used in determining the Royalties and (e) a calculation of the amounts due to Camurus. Rhythm shall notify Camurus in writing within sixty (60) calendar days after the achievement of any milestone described in Section 5.2 or Section 5.4.

5.8 Payments.

(a) All payments due under this Agreement shall be paid in immediately available funds in US Dollar to the bank account designated in writing by Camurus, as the case may be. To the extent Net Sales are accrued in currencies other than US Dollar, Net Sales shall be converted to US Dollar, as the case may be, at the average daily rate of exchange for the applicable calendar quarter as published by Financial Times (UK edition). The calculation of the average rate of exchange shall be stated in terms of US Dollar per foreign currency units.

(b) All payments hereunder are exclusive of any taxes, fees or charges imposed by any local or national authority. In the event that Rhythm reasonably determines that any tax, duty or other levy is required to be paid or withheld on account of Royalties or other payments payable to Camurus under this Agreement, Rhythm shall make such withholding payments as required and subtract such withholding payments from the payments to be made to Camurus as set forth in this Section 5, or, if applicable, Camurus will reimburse Rhythm or its designee(s) for the amount of such required withholding payments that are not subtracted from the payments made to Camurus as set forth in this Section 5, within fifteen (15) days of notice to Camurus. Rhythm shall provide Camurus with documentation of such withholding and payment in a manner that is satisfactory for purposes of reporting to the U.S. Internal Revenue Service. Any withholdings paid by Rhythm shall be for the benefit of Camurus.

(c) Any payments that are not paid within the date such payments are due under this Agreement shall bear interest at an annual rate of interest equal to the London Interbank Offered Rate (**"LIBOR"**), plus five (5) percentage points, calculated on the number of days such payment is delinquent.

5.9 Books and Records; Audit Rights. Rhythm shall keep full and true books of accounts and other records in sufficient detail so that the Royalties payable hereunder can be properly ascertained. Rhythm shall, at the request of Camurus, permit a nationally recognized independent certified public accountant selected by Camurus and reasonably acceptable to Rhythm to have access during ordinary business hours, to such books and records as may be necessary to determine the correctness of any Payment Report or payment made under this Agreement or to obtain information as to Royalties and milestones payable in case of failure to report or pay pursuant to the terms of this Agreement. The auditor shall execute a written confidentiality agreement with Rhythm and shall disclose to Camurus only the amount and accuracy of payments reported and actually paid or otherwise payable under this Agreement. The auditor shall send a copy of the report to Rhythm at the same time it is sent to Camurus. Such examination shall be conducted (a) after at least thirty (30) days prior written notice from Camurus, (b) at the facility(ies) where such books and records are maintained, and (c) no more frequently than once in any calendar year or more than once with respect to a particular year. Camurus shall be responsible for expenses for the independent certified public accountant, except that Rhythm shall reimburse Camurus in full thereof if the independent accountant determines the Royalties and milestones paid by Rhythm to Camurus are less than ninety-five percent (95%) of the amount actually owed for the period of the audit. As a condition to any sublicense granted by Rhythm hereunder, Rhythm shall ensure that Camurus has the same audit rights as those described in this Section 5.9 with respect to any such Rhythm Affiliate or Sublicensee.

6 MANUFACTURE

6.1 Identification of CMO. Rhythm shall have responsibility for, and final decision-making authority with respect to, the manufacture of Product for non-clinical, clinical and commercial use and sale in the Territory. Rhythm, or its designated CMO as applicable, shall be EU and US GMP approved and able to manufacture according to the Regulatory Approvals in the applicable countries in the Territory. Until the tech transfer process to Rhythm or its CMO has been successfully completed as set forth in Section 6.2, Camurus may procure such supply of Rhythm's non-commercial requirements of Product from Camurus' existing CMO at Camurus' Manufacturing Cost. In such case, the Parties shall enter into separate supply agreements governing the terms and conditions of such non-commercial supply from Camurus' CMO to Rhythm and shall use good faith efforts to negotiate and enter into the foregoing within one hundred and twenty (120) days from the Effective Date.

6.2 Technology Transfer. Camurus shall use Commercially Reasonable Efforts to provide such of its manufacturing technology as may be reasonably necessary to enable Rhythm or its designated CMO to manufacture the Product for non-clinical, clinical and commercial use, and shall use Commercially Reasonable Efforts to

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provide technical assistance to enable the use of such manufacturing technology to manufacture the Product. Prior to such technology transfer, the Parties will agree upon a technology transfer plan and corresponding budget. Rhythm shall reimburse Camurus it's out of pocket costs and expenses as well as Camurus' FTE Costs incurred in providing such technology transfer and technical assistance. Camurus shall be reimbursed by Rhythm on a monthly basis, within thirty (30) days of receipt of an invoice setting forth such costs and expenses.

6.3 Rhythm Supply Agreement. If Rhythm uses a CMO, as soon as commercially possible Rhythm shall enter into one or more Rhythm Supply Agreements with the CMO covering the tech transfer, process development, scale-up and manufacture of Product.

7 INTELLECTUAL PROPERTY

7.1 Trademarks.

(a) Rhythm shall have the right to select, and shall register and maintain, at its expense, such Product Trademarks as shall be used for the promotion, marketing and sale of the Product in the Territory. Rhythm shall own such Product Trademarks and all goodwill associated therewith.

(b) Rhythm may use the Camurus Trademark for commercialization of Product in the Territory. If Rhythm opts to use the Camurus Trademark, save to the extent Rhythm may be required to do so by a Regulatory Authority or pursuant to the requirements of a Regulatory Approval, Rhythm shall not conceal or otherwise obscure, remove or otherwise interfere with the Camurus Trademark. Rhythm shall not register or use any Trademark confusingly similar to any Camurus Trademark or any other Trademarks used by Camurus with the FC Technology. Rhythm shall ensure that each reference to and use of the Camurus Trademark in any marketing material related to Product is accompanied by an acknowledgement that the Camurus Trademark is owned by Camurus and used by Rhythm under license. Rhythm shall adhere to any reasonable requests from Camurus relating to Rhythm's use of the Camurus Trademark.

7.2 Ownership of Collaboration Inventions. Subject to the terms hereof, including the licenses and other rights granted hereunder, all Collaboration Inventions shall be owned as follows:

(a) All Collaboration Inventions, including Joint Inventions, relating specifically to [ ]*, shall be exclusively owned by Camurus.

(b) All Collaboration Inventions, including Joint Inventions, relating specifically to [ ]*, shall be exclusively owned by Rhythm.

(c) The ownership of Collaboration Inventions not owned by Camurus or Rhythm in accordance with Section 7.2(a) or Section 7.2(b) shall be determined with reference to inventorship under U.S. patent law. If the Parties fail to agree with respect to inventorship, the dispute will be referred to a Third Party U.S. patent attorney acceptable to each of the Parties for Expert Determination as provided in Exhibit 7.2(c). The Parties shall jointly own all Collaboration Inventions that are

Joint Inventions, other than those covered in Section 7.2(a) or Section 7.2(b), and, subject to the rights granted each Party under this Agreement, each Party may use, sell, keep, license or assign its interest in Joint Inventions and otherwise undertake all activities a sole owner might undertake with respect to such Joint Inventions, without the consent of and without accounting to the other Party. "**Joint Inventions"** means Collaboration Inventions for which it is determined, in accordance with the patent law of the United States, that both: (i) one or more employees, consultants or agents of Camurus or any other persons obligated to assign such Collaboration Invention to Camurus; and (ii) one or more employees, consultants or agents of Rhythm or any other persons obligated to assign such Collaboration Invention to Rhythm, are inventors of such Collaboration Invention. For any Joint IP that could be the subject of an application for a Patent Right, each Party, in conjunction with such Party's patent counsel will make an initial determination of inventorship prior to filing the application therefor to confirm that it is Joint IP. Each Party will provide information and records relevant to such determination to the other Party and such patent counsel

(d) Subject to appropriate confidentiality undertakings, each Party shall promptly notify the other Party when it learns a Collaboration Invention has been made and promptly after the completion of invention disclosure statements for such Collaboration Invention (or, if any provisional or other patent applications are filed claiming such invention, promptly after such filing), and, to the extent a Party is granted rights hereunder in such Collaboration Invention, shall provide a copy of the same to the other Party.

(e) For the avoidance of doubt, neither Party is granted any license rights to any intellectual property rights of the other Party, which may be required for such Party to use a Collaboration Invention, unless otherwise expressly granted herein.

(f) Each of the Parties shall do all such acts and things and execute all such deeds and documents as may be necessary or desirable for them to perfect their rights of ownership as specified in this Section 7.2 and otherwise implement the provisions of this Section 7. Each Party shall, and shall cause its applicable Affiliates, Third Party subcontractors, and their respective employees and agents to, perform at the requesting Party's cost all reasonable acts reasonably requested, including the execution of confirmatory deeds and assignment documents of Patent Rights as may be necessary or desirable for them to perfect their title therein in accordance with the forgoing provisions of this Section.

7.3 Prosecution of Patents.

(a) Patent Prosecution of Camurus IP. Camurus shall control the Prosecution of the Patent Rights within Camurus Platform IP ("**Camurus Platform Patents**") at its own cost and expense using Commercially Reasonable Efforts to Prosecute all patent applications forming part of Camurus Platform Patents to grant with Valid Claims, including conducting any necessary or desirable oral or written proceedings. Camurus shall provide Rhythm with a copy of each new draft application and replies to substantive office actions within the Camurus Platform Patents (including, for clarity, divisional and continuation applications), and shall keep Rhythm informed of all material developments in relation to Camurus

CONFIDENTIAL

* CONFIDENTIAL TREATMENT REQUESTED. OMITTED PORTIONS FILED WITH THE SECURITIES AND EXCHANGE COMMISSION PURSUANT TO RULE 406 PROMULGATED UNDER THE SECURITIES ACT OF 1933, AS AMENDED

Platform Patents and shall provide Rhythm with copies of relevant documents related to the Prosecution of Camurus Platform Patents in the United States and EU and any PCT application. Camurus shall provide relevant documents related to the Prosecution of the Camurus Platform Patents in all other countries in the Territory upon request from Rhythm. In the event that, having filed, Camurus declines to further Prosecute any Camurus Platform Patents in any country of the Territory, Camurus shall provide Rhythm with written notice thereof. Such notice shall be given at least sixty (60) days prior to the expiration of any official substantive deadline relating to such activities. In any such circumstances and provided that no earlier licensee of Camurus has assumed the right to Prosecute such Camurus Platform Patents Rhythm shall have the right to decide that Rhythm should continue to Prosecute such Camurus Platform Patents owned by Camurus at Rhythm's expense and in such case Rhythm shall give written notice to Camurus; provided that if Camurus' decision to decline to further Prosecute any pending Camurus Platform Patents is as a result of the withdrawal of an unpublished patent application and the reason for such withdrawal was to enable the filing of another patent application claiming the same inventions, Rhythm shall not have the right to decide that Rhythm should continue to Prosecute the withdrawn unpublished patent application. Camurus shall upon receipt of any such notice from Rhythm transfer to Rhythm copies of all of its files relating to the relevant Camurus Platform Patents and at Rhythm's reasonable cost and expense execute any documents to otherwise transfer control of such Prosecution to Rhythm. Camurus shall remain the owner of such Camurus Platform Patents and Rhythm shall provide Camurus the same information and rights required under this Section 7.3(a) to be provided Rhythm concerning the Prosecution of such Camurus Platform Patents. Rhythm may deduct the prosecution costs with respect to such Camurus Platform Patents from the royalties payable to Camurus under this Agreement. This Section 7.3 (a) shall apply mutatis mutandis to Patent Rights within Collaboration Inventions solely owned by Camurus pursuant to Section 7.4.

(b) Patent Prosecution of Collaboration Product Patents and Rhythm Product Patents in the Territory. Rhythm shall control the Prosecution of (i) the Patent Rights to any and all Collaboration Inventions owned by Rhythm pursuant to Section 7.2(b), Section 7.2(c) if solely owned by Rhythm or Section 7.4 (jointly **"Collaboration Product Patents"**), and (ii) the Rhythm Product Patents, in the Territory at Rhythm's expense using Commercially Reasonable Efforts to Prosecute all patent applications forming part of the Collaboration Product Patents to grant with Valid Claims, including conducting any necessary or desirable claims or oral or written proceedings. With respect to the Collaboration Product Patents, Rhythm shall provide Camurus the same information and rights required under Section 7.3(a) to be provided Rhythm concerning the Prosecution of the Camurus Platform Patents. In the event that, having filed, Rhythm declines to further Prosecute any Collaboration Product Patents in any country in the Territory, Rhythm shall provide Camurus with written notice thereof. Such notice shall be given at least sixty (60)

days prior to the expiration of any official substantive deadline relating to such activities. In any such circumstances Camurus shall have the right to decide that Camurus should continue to Prosecute such Collaboration Product Patents at Camurus' expense and in such case Camurus shall give written notice to Rhythm. Rhythm shall upon receipt of any

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such notice from Camurus transfer to Camurus all of its files relating to the relevant Collaboration Product Patents and at Camurus' reasonable cost and expense execute any documents to otherwise transfer control of such Prosecution to Camurus. Rhythm shall remain the owner of such Collaboration Product Patents and Camurus shall provide Rhythm the same information and rights required to be provided Camurus under this Section 7.3(b) concerning the Prosecution of such Collaboration Product Patents.

(c) Joint Patents. With respect to the Prosecution of patent applications claiming Joint Inventions subject to Section 7.2(c) (**"Joint Patents"**), Rhythm shall have the right to take such actions as are necessary or appropriate to Prosecute Joint Patents at its sole expense; *provided*, that all such patent applications and patents shall be owned jointly. Rhythm shall furnish Camurus with copies of such Joint Patents and other related correspondence relating to such Joint Inventions to and from patent offices throughout the Territory and permit Camurus to offer its comments thereon before Rhythm makes a submission to a patent office. Rhythm shall inform Camurus of the countries in which it intends to file patent applications. Camurus shall offer its comments promptly, including any request that the patents be filed in additional countries; *provided*, that Rhythm shall determine the appropriate action after considering in good faith any comments or requests from Camurus, and *further provided* that in the event that delay would jeopardize any potential patent right, Rhythm shall have the right to proceed without awaiting Camurus' comments. If Rhythm determines in its sole discretion not to Prosecute any patent or patent application within the Joint Patents in any country, and provided that no other patent applications or patents claiming the same or similar subject matter are then pending or issued in that same country, then Rhythm shall provide Camurus with sixty (60) days prior written notice (or such shorter time period that would permit Camurus a reasonable opportunity to respond in a timely manner) of such determination and Camurus shall have the right and opportunity to Prosecute such patent application or patent on behalf of the Parties at Camurus' sole cost and expense. Camurus shall provide Rhythm the same information and rights required under this Section 7.3(c) to be provided Camurus concerning the Prosecution of such Joint Patents.

(d) As promptly as practicable after the Effective Date (but in no event later than one hundred and twenty (120) days after the Effective Date), Rhythm shall file a patent application with the United States Patent and Trademark Office [ ]*. Camurus shall provide Rhythm with such information and/or invention disclosures reasonably requested by Rhythm, and shall otherwise cooperate with all reasonable requests made by Rhythm, in connection with the preparation, filing and prosecution of such patent application. Notwithstanding anything express or implied anywhere else in this Agreement, all of the inventions claimed in such patent application (other than those of such inventions that are already owned solely by Rhythm as of the Effective Date) shall be deemed and treated, for all purposes of this Agreement, as Collaboration Inventions that are owned solely by Rhythm pursuant to Section 7.2(b) hereof. For clarity, such patent application and all other Patent Rights related to those inventions that are deemed and treated, for all purposes of this Agreement, as Collaboration Inventions shall be deemed and treated as Collaboration Product Patents for all purposes of this Agreement and be subject inter alia to Section 7.3 (b).

(e) Each Party shall at the expense of the requesting Party execute such documents and take such other actions as may be reasonably requested by the other Party in conjunction with prosecution of patents pursuant to this Section 7.3.

7.4 Camurus Platform Patents and Collaboration Product Patents. If, after the Effective Date, any Collaboration Invention relates both to [ ]*, on the one hand, and [ ]*, on the other hand, and patent claims can be made based on the same data, Patent Right or study result, where appropriate Camurus shall, in consultation with Rhythm, file separate patent applications on the same day to any aspect relating to [ ]*, on the one hand, and [ ]*, on the other hand, separately. Any such applications relating specifically to [ ]* shall become part of the Rhythm Collaboration IP and, therefore, shall be exclusively owned by Rhythm, and any such applications relating to [ ]* shall become part of Camurus Platform IP hereunder and, therefore, shall be exclusively owned by Camurus. In the event that the provisions of this Section 7.4 are applicable to any Collaboration Invention, the provisions of this Section 7.4 shall be applied to such Collaboration Invention before the provisions of any of Section 7.2(a) or Section 7.2(b) are given effect with respect to such Collaboration Invention.

7.5 Employee Assignment. Each Party shall ensure that any employee of that Party involved in the performance of this Agreement shall be employed on legally binding written terms which require the assignment of all Patent Rights and Know-How resulting from work carried out by that employee to the employing Party. Each Party shall be responsible for all payments to its employees or others in respect of obtaining rights to any such Patent Rights and Know-How.

7.6 Patent Term Extensions. For all patents within any Patent Rights relating to or claiming a Product for which NDA Approval has been obtained, the Parties shall use reasonable efforts, in each country where NDA Approval for a Product has been obtained and the law of such country permits application for a patent term extension (or any supplementary certificate), to apply for a patent term extension (or any supplementary certificate) for one or more selected patent within such Patent Rights chosen at Rhythm's reasonable discretion with respect to the Territory. Each Party agrees to cooperate with the other Party in the exercise of the authorizations granted under this Section, and to execute such documents and take such additional action as the other Party may reasonably request in connection therewith.

7.7 Third Party Intellectual Property. Each Party shall bring to the attention of the other Party all information regarding potential infringement or misappropriation of Third Party Patent Rights as a result of the manufacture, use, importation, offer for sale, or sale of Product in the Territory.

The Parties shall discuss such information and decide how to handle the matter. This Section 7.7 shall not be interpreted as placing on either Party a duty of inquiry regarding Third Party Intellectual Property rights beyond what is customary for the industry.

7.8 Third Party Infringement. In the case where either Party believes that the development, manufacture, use or sale of the Product or a Competing Product by a Third Party in the Licensed Field infringes any Camurus Platform Patents, any other Patent Rights licensed by Camurus to Rhythm pursuant to this Agreement,

any other Collaboration Product Patents covering the Product (including any method of making or using the same) or the Joint Patents (each, an **"Infringing Activity"**), such Party shall disclose full details of the potential infringement to the other Party. In addition, if either Party believes that development, manufacture, use or sale of the Product or a Competing Product by a Third Party in the Licensed Field infringes any other Patent Rights covering the Product, such Party shall disclose full details of the potential infringement to the other Party. The right to prosecute Infringing Activity pursuant to this Agreement is set out in either Section 7.9 or Section 7.10, as applicable. If the Parties fail to agree with respect to whether an Infringing Activity is subject to Section 7.9 or Section 7.10, the dispute will be referred to a Third Party U.S. patent attorney acceptable to each of the Parties for Expert Determination as provided in Exhibit 7.2(c). For the avoidance of doubt, it is understood and agreed that in this section 7.8 and in Section 7.9, Patent Rights claiming the Product do not include Rhythm Product Patents or any other Patent Rights owned or Controlled by Rhythm (other than Collaboration Product Patents).

7.9 Enforcement with respect to Collaboration Product Patents and Joint Patents. Where an infringement of (x) any Patent Rights specifically claiming the Product (including any method of making or using the same) or (y) any Joint Patents by an Infringing Activity occurs in one or more countries of the Territory, Rhythm shall have the first right to, but shall not be obliged to, at its own cost and expense enforce the same in accordance with the below subparagraphs (i) to (iii).

(i) Rhythm shall have sole conduct of the claim and any proceedings including any counterclaim for invalidity or unenforceability or any declaratory judgment action and including the right to settle. Where Rhythm decides to commence proceedings in relation to any such Patent Rights claiming specifically the Product (including any method of making or using the same) or any Joint Patents it shall be entitled to require Camurus to join Rhythm as co-plaintiff and Camurus shall have the right to join as co-plaintiff. In such case Camurus shall provide all necessary assistance to Rhythm in relation to any such proceeding and Rhythm shall on demand by Camurus pay or promptly reimburse Camurus for the costs of such activity unless Camurus elects to be separately represented (which shall be at Camurus' discretion), in which case such separate representation shall be at Camurus' cost and expense;

(ii) if Rhythm succeeds in any such infringement proceedings whether at trial or by way of settlement, the proceeds of any award or damages or settlement in respect of such infringement proceedings shall first be applied to reimburse (a) an amount equal to Rhythm' costs of taking the proceedings and (b) an amount equal Camurus' costs, with the remainder being retained by Rhythm less [ ]* per cent [ ]* thereof, which amount shall be paid to Camurus;

(iii) if Rhythm fails to take any such proceedings in respect of any such Patent Rights claiming specifically the Product (including any method of making or using the same) or any Joint Patents in the Territory, Camurus may give Rhythm written notice requesting Rhythm to take such proceedings within thirty (30) days of the date of notice and if Rhythm fails to take such action within said period, Camurus shall, subject to the prior written consent of Rhythm, be entitled to do so at its own cost and expense. If Rhythm gives such consent then Camurus shall be entitled to

require Rhythm to join Camurus as co-plaintiff and Rhythm shall have the right to join as co-plaintiff. In such case, Rhythm shall provide all necessary assistance to Camurus in relation to such proceedings and Camurus shall on demand by Rhythm pay or promptly reimburse Rhythm for the costs of such activity, unless Rhythm elects to be separately represented (which shall be at Rhythm' discretion), in which case such separate representation shall be at Rhythm's cost and expense. If Camurus succeeds in any such proceedings, the proceeds of any award or damages or settlement in respect of such proceedings shall first be applied to reimburse (a) an amount equal to Camurus' costs of taking the proceedings and (b) an amount equal Rhythm' costs referred to in this Section 7.9(iii), with the remainder being retained by Camurus, less [ ]* per cent [ ]* thereof, which amount shall be paid to Rhythm. Camurus shall not enter into a settlement, consent judgment or other voluntary final disposition of an action or claim or counterclaim under this Section 7.9 without the prior written approval of Rhythm, such consent not to be unreasonably withheld. For the avoidance of doubt, it is understood and agreed that in this Section 7.9, Patent Rights specifically claiming the Product (including any method of making or using the same) do not include Rhythm Product Patents or any other Patent Rights owned or Controlled by Rhythm (other than Collaboration Product Patents).

7.10 Enforcement with respect to Camurus Platform Patents. Where an infringement of Camurus Platform Patents not specifically claiming the Product (including any method of making or using the same) by an Infringing Activity is occurring in one or more countries of the Territory, Camurus shall have the right, but shall not be obliged, at its own cost and expense to enforce the same. Camurus shall be entitled to require Rhythm to join Camurus as co-plaintiff. In such case Rhythm shall provide all necessary assistance to Camurus in relation to any such proceeding and Camurus shall on demand by Rhythm pay or promptly reimburse Rhythm for the costs of such activity. If Camurus succeeds in any such infringement proceedings whether at trial or by way of settlement, the proceeds of any award or damages or settlement in respect of such infringement proceedings shall first be applied to reimburse (a) an amount equal to Camurus' costs of taking the proceedings and (b) an amount equal Rhythm's costs, if any, with the remainder being retained by Camurus less [ ]* per cent [ ]* thereof, which amount shall be paid to Rhythm.

Camurus shall have the sole right to settle such proceedings, provided that such settlement does not include a license or covenant not to sue under the Camurus Platform IP or causes Rhythm to incur any losses in which case Rhythm's consent to the terms of such license shall be required, such consent not to be unreasonably withheld, conditioned or delayed. If Camurus elects not to enforce any such Camurus Platform Patents, then Rhythm shall have the right, but shall not be obliged, at its own cost and expense to do so in accordance with the following, subject to the prior written consent of Camurus. If Camurus gives such consent, then the following procedures shall apply in these circumstances:

(i) Where Rhythm has requested and been granted approval by Camurus to commence proceedings in relation to any such Camurus Platform Patents not specifically claiming the Product (including any method of making or using the same), Rhythm shall be entitled to require Camurus to join Rhythm as co-plaintiff and Camurus shall have the right to join as co-plaintiff. In such case Camurus shall provide all necessary assistance to Rhythm in relation to any such proceeding and

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Rhythm shall on demand by Camurus pay or promptly reimburse Camurus for the costs of such activity unless Camurus elects to be separately represented (which shall be at Camurus' discretion), in which case such separate representation shall be at Camurus' cost and expense;

(ii) if Rhythm succeeds in any such infringement proceedings whether at trial or by way of settlement, the proceeds of any award or damages or settlement in respect of such infringement proceedings shall first be applied to reimburse (a) an amount equal to Rhythm' costs of taking the proceedings and (b) an amount equal to Camurus' costs referred in this Section 7.10, with the remainder being retained by Rhythm less [ ]* per cent [ ]* thereof, which amount shall be paid to Camurus;

(iii) Rhythm shall not enter into a settlement, consent judgment or other voluntary final disposition of an action or claim or counterclaim under this Section 7.10 without the prior written approval of Camurus, such consent not to be unreasonably withheld.

7.11 Hatch-Waxman Certifications. If either Party (i) reasonably believes that a Third Party may be filing or preparing or seeking to file a generic or abridged NDA that refers to or relies on regulatory documentation for a Product that was submitted by Rhythm to any Regulatory Authority, (ii) receives any notice of certification regarding any Patent Rights included in Camurus Patent Rights (i.e., Patent Rights Controlled by Camurus) or Rhythm Patent Rights (i.e., Patent Rights Controlled by Rhythm) pursuant to the Hatch-Waxman Act claiming that any such Patent Rights are invalid or unenforceable or claiming that the any such Patent Rights will not be infringed by the manufacture, use, marketing or sale of a product for which an ANDA is filed, or (iii) receives any equivalent or similar certification or notice in any other jurisdiction, it shall notify the other Party in writing, identifying the alleged applicant or potential applicant and furnishing the information upon which such determination is based, and provide the other Party a copy of any such notice of certification within five (5) days of receipt and the Parties' rights and obligations with respect to any legal action as a result of such certification shall be as set forth above in Sections 7.9 or 7.10.

8 CONFIDENTIALITY

8.1 Except to the extent expressly authorized by this Agreement including in Sections 8.3 and 8.4 or otherwise agreed in writing, each Recipient and its Affiliates and its Sublicensees and licensees in possession of Confidential Information of the Disclosing Party shall maintain such Confidential Information as confidential and use it only for the purposes of this Agreement in accordance with this Section 8. This obligation shall continue during the term of this Agreement and for a period equal to ten (10) years after the date of expiration or termination of this Agreement; provided, however, that this obligation shall continue to apply after such ten (10) year period to any Know-How, development data, other data, regulatory filings and other information disclosed, provided, licensed, transferred or otherwise made available by either Party to the other Party under this Agreement, until such time as such Know-How, development data, other data, regulatory filings and other information becomes exempt pursuant to subparagraphs (i) through (v) below. Each

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Party shall guard such Confidential Information using the same degree of care as it normally uses to guard its own confidential, proprietary information of like importance, but in any event no less than reasonable care. Notwithstanding the foregoing, the Recipient of the categories of Confidential Information identified in Sections 1.16 (i)-(iv) inclusive shall be relieved of the confidentiality and limited use obligations of this Agreement to the extent that the Recipient establishes by written evidence that:

(i) the Confidential Information was previously known to the Recipient from sources other than the Disclosing Party at the time of disclosure and other than under an obligation of confidentiality and non-use;

(ii) the Confidential Information was generally available to the public or otherwise part of the public domain at the time of its disclosure; or

(iii) the Confidential Information became generally available to the public or otherwise part of the public domain after its disclosure to the Recipient Party other than through any act or omission of the Recipient Party in breach of this Agreement; or

(iv) the Confidential Information is acquired in good faith in the future by the Recipient Party from a Third Party who has a lawful right to disclose such information and who is not under an obligation of confidence to the Disclosing Party with respect to such information; or

(v) the Confidential Information is subsequently developed by or on behalf of the Recipient Party without use of the Disclosing Party's Confidential Information.

8.2 For clarity, specific aspects or details of Confidential Information shall not be deemed to be within the public domain or in the possession of the Recipient Party merely because the Confidential Information is embraced by more general information in the public domain or in the possession of the Recipient Party. Further, any combination of Confidential Information shall not be considered in the public domain or in the possession of the Recipient Party merely because individual elements of such Confidential Information are in the public domain or in the possession of the Recipient Party unless the combination is in the public domain or in the possession of the Recipient Party.

8.3 Notwithstanding the above obligations of confidentiality and non-use a Recipient may disclose Confidential Information:

(i) to a Regulatory Authority as reasonably necessary to obtain and maintain Regulatory Approval in a particular jurisdiction to the extent consistent with the licenses granted under terms of this Agreement, provided that reasonable effort will be taken to ensure confidential treatment of such information.

(ii) disclose Confidential Information: (a) to the extent such disclosure is reasonably necessary to comply with the order of a court; or (b) to the extent such disclosure is required to comply with a legal requirement, including to the extent such disclosure is required in publicly filed financial statements or other public statements or filings under rules governing a stock exchange or pursuant to

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applicable securities laws or regulations (e.g., the rules of the United States Securities and Exchange Commission, NASDAQ, NYSE, or any other stock exchange on which securities issued by either Party may be listed); provided, to the extent possible bearing in mind such legal requirements and subject to the next subsequent sentence of this Section 8.3.(ii), such Party shall provide the other Party with a copy of the proposed text of such statements or disclosure five (5) business days in advance of the date on which the disclosure is to be made to enable the other Party to review and provide comments, unless a shorter review time is agreed. If compliance with a legal requirement requires filing of this Agreement, the filing Party shall to the extent possible seek confidential treatment of portions of this Agreement from the relevant competent authority to the extent that such confidential treatment is available pursuant to applicable law and shall provide the other Party with a copy of the proposed filings at least five (5) business days prior to filing for the other Party to review any such proposed filing and provide comments. Each Party agrees that it will obtain its own legal advice with regard to its compliance with legal requirements and will not rely on any statements made by the other Party relating to such legal requirements; and

(iii) by filing or prosecuting Patent Rights, the filing or prosecution of which is contemplated by this Agreement, without violating Section 8.1; it being understood that publication of such filings occurs in some jurisdictions within eighteen (18) months of filing, and that such publication shall not violate the above secrecy provision.

(iv) to such Recipient's employees, Affiliates, contractors (including clinical researchers and CMO's), licensees, sublicensees, agents, consultants and potential business partners, as such Recipient reasonably determines is necessary to receive the benefit of the licenses and rights granted or available to it under this Agreement or to fulfill its obligations pursuant to this Agreement; provided, however, any such persons must be obligated to substantially the same extent as set forth in Section 8.1 to hold in confidence and not make use of such Confidential Information for any purpose other than those permitted by this Agreement and breach by such persons of their confidentiality obligations shall be deemed a breach by the Recipient of its confidentiality obligations hereunder. For the avoidance of doubt, it is understood and agreed that Camurus may not disclose any Confidential Information relating to the Product to any licensee of the FC Technology without the prior written consent of Rhythm except when exercising its rights under Sections 2.4 and 3.7.

(v) (a) to its actual or potential investment bankers; (b) to existing and potential investors in connection with an offering or placement of securities for purposes of obtaining financing for its business and to actual and prospective lenders for the purpose of obtaining financing for its business and to potential licensees or sublicensees of the FC Technology or any other rights licensed to the Recipient pursuant to this Agreement; and (c) to a bona fide potential acquirer or merger partner for the purposes of evaluating entering into a merger or acquisition, provided, however, any such persons must be obligated to substantially the same extent as set forth in Section 8.1 to hold in confidence and not make use of such Confidential Information for any purpose other than those permitted by this Agreement; and

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(vi) disclose Confidential Information to its legal advisers for the purpose of seeking advice.

8.4 Nothing in this Section 8 restricts either Party from using or disclosing any of its own Confidential Information for any purpose whatsoever; provided that, to the extent Know-How is exclusively licensed by one Party to the other, the licensor may not continue to use and disclose such Know-How in a manner not consistent with the exclusivity of the license granted.

8.5 Other than the press release pertaining to this transaction that the Parties have agreed upon and attached as Exhibit 8.5 to this Agreement and save as permitted in Section 8.3:

(i) neither Party, as a Recipient, shall make any public announcement or statement to the public containing Confidential Information of the Disclosing Party without the prior written consent of the Disclosing Party. No such public announcements or statements shall be made without the prior review and consent of the appropriate individual designated for the purpose by the other Party; and

(ii) save as may otherwise be provided herein neither Party shall mention or otherwise use the name or Trademark of the other Party or its Affiliates in any publication, press release, promotional material or other form of publicity without the prior written consent of the appropriate individual designated for the purpose by the other Party.

8.6 With respect to public disclosure required to be made pursuant to regulatory requirements or stock exchange rules applicable to a Party, each such Party will use reasonable efforts to submit to the other Party a draft of any public announcement ("Proposed Disclosure") directly related to the Product at least three (3) business days prior to the date on which such Party plans to make such announcement, and in any event will submit such draft to the other Party at least twenty-four (24) hours prior to the release of such Proposed Disclosure. If a Party is unable to comply with the foregoing twenty-four (24)-hour notice requirement because of a legal obligation or stock or securities exchange requirement to make more rapid disclosure, such Party will not be in breach of this Agreement but will in that case give telephone and email notice to a senior executive of the other Party and provide a draft of the Proposed Disclosure with as much notice as possible prior to the release of such announcement. A Party that receives a draft of any Proposed Disclosure that the other Party is planning to make may not make any disclosure or public announcement of the substance or content of such Proposed Disclosure until such time as such other Party has released such Proposed Disclosure to the public. Any draft of any Proposed Disclosure provided by one Party to the other pursuant to this Section 8.6 shall be deemed and treated as Confidential Information of the Party that is proposing to make such Proposed Disclosure.

8.7 Notwithstanding the foregoing Camurus shall be entitled to include the name of Rhythm within a list of collaborators.

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9 REPRESENTATIONS AND WARRANTIES

9.1 Mutual Representations and Warranties of Camurus and Rhythm.

Each of Camurus and Rhythm hereby represents and warrants to the other Party as of the Effective Date as follows

(a) It is duly organized, validly existing and in good standing under the laws of the jurisdiction of incorporation. It has the requisite legal and company power and authority to conduct its business as presently being conducted and as proposed to be conducted by it and is duly qualified to do business in those jurisdictions where its ownership of property or the conduct of its business requires

(b) It has all requisite legal and company power and authority to enter into this Agreement and to grant the rights described herein. All company actions on its part, its boards of directors or managers, or similar governing body and its equity holders necessary for (i) the authorization, execution, delivery and performance by it of this Agreement, and (ii) the consummation of the transactions contemplated hereby, have been duly taken.

(c) This Agreement is a legally valid and binding obligation of it, enforceable against it in accordance with its terms (except in all cases as such enforceability may be limited by applicable bankruptcy, insolvency, reorganization, moratorium, or similar laws affecting the enforcement of creditors' rights generally and except that the availability of the equitable remedy of specific performance or injunctive relief is subject to the discretion of the court or other tribunal before which any proceeding may be brought).

(d) Each Party has and shall continue to have written contracts with all Third Parties (including employees and subcontractors) performing services on its behalf under this Agreement where such services are intended to create inventions that may be Collaboration Inventions that assign to such Party all Collaboration Inventions and rights therein.

9.2 Additional Representations and Warranties of Camurus.

Camurus hereby further represents and warrants to Rhythm as of the Effective Date that:

(a) Save with respect to [ ]* that have been disclosed in writing by Camurus to Rhythm prior to the Effective Date, Camurus is not aware of any pending actions, suits or other proceedings against it or any of its Affiliates that questions the validity of any issued Camurus Platform Patents, or that otherwise relate or pertain to, any Camurus Platform IP;

(b) Camurus is not aware that any of the Camurus Platform Patents are invalid, and Camurus is not aware of any defect in Camurus' right, title and interest in and to the Camurus Platform Patents;

(c) To the extent necessary to grant Rhythm the rights provided for in this Agreement, Camurus owns or Controls sufficient rights in the Camurus Platform IP.

(d) Camurus, to its knowledge and belief, has supplied Rhythm with all material documentation and information, possessed by Camurus or any of its Affiliates which have been requested by Rhythm [ ]*, during the course of due diligence prior to execution of this Agreement.

(e) Camurus is not aware of any use, infringement or misappropriation of the Camurus Platform IP in derogation of the rights granted to Rhythm in this Agreement. To the knowledge of Camurus, the practice and use of the Camurus Platform IP by Rhythm, its Affiliates or Sublicensees in the manner permitted or contemplated in this Agreement will not infringe upon, or constitute misappropriation or unauthorized use of, the Intellectual Property of any Third Party.

(f) To the knowledge of Camurus, Camurus and its Affiliates have complied with all the requirements of all United States and foreign patent offices with respect to the filing of applications for Patent Rights in respect of the Camurus Platform Patents, including the duty of disclosure under 37 C.F.R. 1.56 and comparable provisions of foreign patent offices.

(g) (i) To the knowledge of Camurus, Camurus and its Affiliates have complied with all the requirements of all United States and foreign patent offices to maintain the Camurus Platform Patents in full force and effect and (ii) to Camurus' knowledge, all necessary registration, maintenance and renewal fees have been paid and all necessary documents and certificates required to be filed in connection with the issued Camurus Platform Patents and pending applications for Patent Rights in respect of Camurus Platform Patents have been duly filed and the duty of disclosure under applicable patent laws have been fulfilled.

(h) In each case in which Camurus or any of its Affiliates has acquired title to any inventions forming part of Camurus Platform Patents from any person, Camurus or any such Affiliate, as applicable, has obtained an assignment in form sufficient to transfer all rights in such inventions.

(i) Exhibit 1.5 hereto lists all Patent Rights owned or Controlled by Camurus or any of its Affiliates on the Effective Date that cover the FC Technology. Except for the Patent Rights listed on Exhibit 1.5 hereto, neither Camurus nor any of its Affiliates owns or Controls any Patent Rights on the Effective Date pertaining to the FC Technology.

(j) [ ]*.

Notwithstanding anything to the contrary in this Agreement, a Party shall not be entitled to make any claims or bring any action against the other Party based on warranties or representations extended under this Agreement to the extent that the circumstances giving rise to such claim or action were known by or disclosed to the

claiming Party prior to the Effective Date or could reasonably have been inferred from information disclosed by the other Party.

9.3 Disclaimer of Warranties.

EXCEPT AS OTHERWISE EXPRESSLY PROVIDED IN SECTION 9.1 AND SECTION 9.2 OF THIS AGREEMENT OR MANDATED BY APPLICABLE LAW (WITHOUT THE RIGHT TO WAIVE OR DISCLAIM), NEITHER PARTY MAKES ANY REPRESENTATION OR WARRANTY WITH RESPECT TO THE LICENSED COMPOUNDS, PRODUCTS, ANY TECHNOLOGY, GOODS, SERVICES, RIGHTS, OR OTHER SUBJECT MATTER OF THIS AGREEMENT AND HEREBY DISCLAIMS ALL WARRANTIES, CONDITIONS OR REPRESENTATIONS OF ANY KIND, EXPRESS OR IMPLIED, INCLUDING IMPLIED WARRANTIES OF PERFORMANCE, MERCHANTABILITY, SATISFACTORY QUALITY, FITNESS FOR A PARTICULAR PURPOSE OR NON-INFRINGEMENT OF THIRD PARTY INTELLECTUAL PROPERTY RIGHTS

10 INDEMNIFICATION

10.1 Indemnification by Rhythm. Subject to Sections 10. 3, 10.4 and 10.5, Rhythm shall indemnify, defend and hold harmless Camurus, its Affiliates, and its and their respective, directors, officers, employees and agents (collectively, the **"Camurus Indemnified Party"**) against any and all claims, liabilities, losses, damages, costs or expenses, including reasonable attorneys' fees, arising out of any claim or action brought by a Third Party (collectively, **"Losses"**) incurred or suffered by the Camurus Indemnified Party to the extent arising out of or caused by:

(i) the development, use, manufacture distribution, marketing, promotion or sale of Product by or on behalf of Rhythm or its Affiliates or Sublicensees in the Territory (including without limitation any claims based upon product liability and any claims arising from Camurus or its Affiliates provision of services under the Agreement); or

(ii) the breach by Rhythm of one or more of its representations, warranties or other obligations under this Agreement;

provided, however, that Rhythm shall not be required to indemnify, hold harmless or defend any Camurus Indemnified Party against any claim brought pursuant to Section 10.2(i) or (ii) to the extent that Camurus has an obligation to indemnify the Rhythm Indemnified Parties under Section 10.2 (i) or (ii).

10.2 Indemnification by Camurus. Subject to Sections 10.3, 10.4 and 10.5, Camurus shall indemnify, defend and hold harmless Rhythm, its Affiliates, and its and their respective, directors, officers, employees and agents (collectively, the **"Rhythm Indemnified Party"**) against any and all Losses (as defined above) incurred or suffered by the Rhythm Indemnified Party to the extent arising out of or caused by

(i) the practice or use by Camurus or its Affiliates, licensees or sublicensees of the Rhythm Collaboration IP or the Joint IP; or

(ii) the breach by Camurus of one or more of its representations, warranties or other obligations under this Agreement;

provided, however, that Camurus shall not be required to indemnify, hold harmless or defend any Rhythm Indemnified Party against any claim brought pursuant to Section 10.1(i) or (ii) to the extent that Rhythm has an obligation to indemnify the Camurus Indemnified Parties under Sections 10.1(i) or (ii).

10.3 Notification of Liabilities/Losses. In the event that either Party intends to seek indemnification for any claim under any of Sections 10.1 or 10.2, it shall inform the other Party of the claim promptly after receiving notice of the claim.

(i) In the case of a claim for which Camurus seeks indemnification under Section 10.1, Camurus shall permit Rhythm to direct and control the defence of the claim and shall provide such reasonable assistance as is reasonably requested by Rhythm (at Rhythm's cost) in the defence of the claim; provided that nothing in this Section 10.3 shall permit Rhythm to make any admission on behalf of Camurus, or to settle any claim or litigation which would impose any financial obligations on Camurus without the prior written consent of Camurus, such consent not to be unreasonably withheld or delayed.

(ii) In the case of a claim for which Rhythm seeks indemnification under Section 10.2, Rhythm shall permit Camurus to direct and control the defence of the claim and shall provide such reasonable assistance as is reasonably requested by Camurus (at Camurus' cost) in the defence of the claim, provided always that nothing in this Clause 10.3 shall permit Camurus to make any admission on behalf of Rhythm, or to settle any claim or litigation which would impose any financial obligations on Rhythm without the prior written consent of Rhythm, such consent not to be unreasonably withheld or delayed.

10.4 Right to Participate in Defense. Without limiting Section 10.3, any indemnitee will be entitled to participate in, but not control, the defense of a Third Party claim for which it has sought indemnification hereunder and to employ counsel of its choice for such purpose; provided, however, that such employment will be at the indemnitee's own expense unless (a) the employment and reimbursement thereof has been specifically authorized by the indemnifying Party in writing, or (b) the indemnifying Party has failed to assume the defense and employ counsel in accordance with section 10.3 (in which case the indemnified Party will control the defense).

10.5 Cooperation. If the indemnifying Party chooses to defend or prosecute any Third Party claim, the indemnified Party will, and will cause each other indemnitee to, cooperate in the defense or prosecution thereof and will furnish such records, information and testimony, provide such witnesses and attend such conferences, discovery proceedings, hearings, trials and appeals as may be reasonably requested in connection with such Third Party claim. Such cooperation will include access during normal business hours afforded to the indemnifying Party to, and reasonable retention by the indemnified Party of, records and information that are reasonably relevant to such Third Party claim, and making indemnities and other employees and agents available on a mutually convenient basis to provide additional

information and explanation of any material provided hereunder, and the indemnifying Party will reimburse the indemnified Party for all of its reasonable out-of-pocket expenses incurred in connection with such cooperation.

10.6 **Reserved**.

10.7 Exclusive Remedy. Each Party agrees that its sole and exclusive remedy with respect to Losses shall be pursuant to the indemnification provisions of this Section 10.

10.8 Insurance. Immediately upon the first administration of a Product to a human in the Territory by Rhythm, its Affiliates or its permitted Sublicensees, and for a period of [ ]* years after the expiration of this Agreement or the earlier termination thereof, Rhythm shall maintain Commercial General Liability Insurance and Product Liability Insurance, including contractual liability coverage, in an amount not less than [ ]* per occurrence bodily injury/property damage combined and [ ]* aggregate annually. Upon written request, the insuring Party shall provide the other Party with a certificate of insurance attesting to such coverage. It is understood and agreed that this insurance shall not be construed to limit either Party's liability with respect to its indemnification obligations hereunder.

11 TERM AND TERMINATION

11.1 Term of Agreement.

This Agreement shall become effective as of the Effective Date and, unless earlier terminated pursuant to other provisions of this Section 11, shall continue in full force and effect until the expiration of all Royalty Terms (the "**Term**"). On a country-by-country and Product-by-Product basis, after expiration of the Royalty Term for the Product in each country in the Territory, Rhythm shall have a royalty-free, non-exclusive license to develop, make, have made, use, import, market, promote, distribute, sell, and offer for sale and otherwise exploit such Product in such country.

11.2 Rhythm may terminate this Agreement without cause on a Product-by-Product basis or in its entirety at any time by giving not less than three (3) months prior written notice. Rhythm may terminate this Agreement on a Product-by-Product basis or in its entirety immediately following the withdrawal of Product from any market as a result of bona fide concerns based on specific and verifiable information that the applicable Product is unsafe for administration to humans (a **"Valid Safety Issue"**). For the avoidance of doubt, the ninety (90) day notice period applicable to termination under the first sentence of this Section 11.2 shall not apply in the case of termination for a Valid Safety Issue.

11.3 Termination for Material Breach or Bankruptcy.

(a) Upon the material breach by one Party under this Agreement, the other Party shall notify the breaching Party of such breach, and require that the breaching Party cure such breach within sixty (60) days (or, in the case of payment defaults, within thirty (30) days).

(b) In the event that a material breach by Rhythm is not cured within the applicable cure period and without limiting other available remedies, Camurus shall have the right to terminate this Agreement upon written notice within thirty (30) days thereafter and all licenses granted by Camurus to Rhythm hereunder shall terminate, subject to the terms of Section 11.4.

(c) In the event that a material breach by Camurus is not cured within the applicable cure period and without limiting other available remedies, Rhythm shall have the right to terminate this Agreement upon written notice within thirty (30) days thereafter, and, at Rhythm' option, all licenses granted by Camurus to Rhythm hereunder shall continue in full force and effect, subject to the continuing obligation to pay milestone payments, license fees, Royalties and sales milestones. Upon such termination by Rhythm for such Camurus material breach, (i) Camurus' obligations hereunder to provide Know-How and other materials and information to enable the use of such licenses shall continue; (ii) Camurus' right to use any Rhythm Development Data and Regulatory Approvals shall terminate, except in respect of rights which were previously granted by Camurus to a licensee in the Territory prior to date of such termination, and (iii) the following provisions shall also continue: Sections 2.1, 2.2, 2.3, 3.1, 3.5, 3.6, 3.8, 4, 5 and 7. Termination of this Agreement pursuant to this Section 11.3(c) will be without prejudice to any rights that will have accrued to the benefit of a Party prior to the effective date of such termination. Such termination will not relieve a Party from obligations that are expressly indicated to survive the termination of this Agreement.

(d) Either Party may, without limiting other available remedies, terminate this Agreement, in whole by notice to the other Party in the event (i) the other Party shall have become bankrupt or shall have made an assignment for the benefit of its creditors; (ii) there shall have been appointed a trustee or receiver for the other Party or for all or a substantial part of its property; or (iii) any case or proceeding shall have been commenced or other action taken by or against the other Party in bankruptcy or seeking reorganization, liquidation, dissolution, winding-up, arrangement, composition or readjustment of its debts or any other relief under any bankruptcy, insolvency, reorganization or other similar act or law of any jurisdiction now or hereafter in effect, and any such event shall have continued for ninety (90) days undisputed, undismissed, unbonded and/or undischarged.

(e) Rhythm may also terminate this Agreement in accordance with the provisions of Sections 3.6 and 5.2, and if Rhythm fails to deliver notice of termination or continuation to Camurus in accordance with the time periods specified in Sections 3.6 and 5.2 then Camurus may terminate this Agreement with immediate effect by giving written notice to Rhythm.

(f) The Parties may terminate this Agreement, at any time upon mutual written agreement of the Parties.

11.4 Effect of Termination. Upon termination of this Agreement by either Party for any reason (other than termination by Rhythm pursuant to Section 11.3(c) or termination pursuant to Section 11.3(d)):

(a) Subject to Section 11.4(e) below, all licenses granted by Camurus to Rhythm shall terminate (including all rights to use any Camurus Platform IP);

(b) all licenses and other rights granted Camurus to use any of the Rhythm Collaboration IP, Rhythm Development Data, Regulatory Approvals in the Territory shall continue, subject to all indemnity and other obligations of Camurus hereunder in respect thereof;

(c) Rhythm shall discontinue Prosecution and abandon any Patent Rights claiming the Product.

(d) Termination of this Agreement for any reason will be without prejudice to any rights that will have accrued to the benefit of a Party prior to the effective date of such termination. Such termination will not relieve a Party from obligations that are expressly indicated to survive the termination of this Agreement.

(e) In the event this Agreement terminates for Rhythm's breach or bankruptcy, the license granted in Section 2.1 shall remain in force only to the extent required for each of Rhythm's Sublicensees at such time to continue to exercise its sublicensed rights provided, that, upon Camurus' written request, such Sublicensee agrees in writing with Camurus (within 30 days after such written request by Camurus) that Camurus is entitled to enforce all relevant obligations under the provisions of this Agreement directly against such Sublicensee and provided further, that Rhythm shall be jointly liable with such Sublicensee to Camurus for any action or inaction of the Sublicensees under this Agreement.

(f) In case of termination without cause, neither party shall be liable to the other party for any compensation or damages by reason of such termination of this Agreement.

11.5 Termination for Patent Challenge. In the event that Rhythm or any of its Affiliates or Sublicensees commences or otherwise pursues, directly or indirectly (or voluntarily assists Third Parties to do so, other than as required by law or legal process), any proceeding seeking to have any of the Patent Rights forming part of Camurus Platform IP revoked or declared invalid, unpatentable, or unenforceable, Camurus may declare a material

breach hereunder that, if not cured within the thirty (30) days after Camurus gives written notice of such material breach to Rhythm and the applicable Affiliate or Sublicensee, shall give Camurus the right to terminate this Agreement with immediate effect .

11.6 Surviving Provisions. Except as otherwise provided in Section 11.3(c) and Section 11.4 above, in addition to the Sections that are expressly stated to survive termination, the following Sections of this Agreement shall survive any expiration or termination of this Agreement for any reason: Sections 1, 7.3(c), 7.3(e), 8, 9.3, 10, 11.4, 11.6 and 12.

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12 MISCELLANEOUS PROVISIONS

12.1 Consequential Damages. IN NO EVENT SHALL EITHER PARTY OR THEIR AFFILIATES BE LIABLE FOR SPECIAL, PUNITIVE, INDIRECT, INCIDENTAL OR CONSEQUENTIAL DAMAGES AS WELL AS LOST PROFITS, WHETHER BASED ON CONTRACT, TORT OR ANY OTHER LEGAL THEORY AND IRRESPECTIVE OF WHETHER SUCH PARTY HAS BEEN ADVISED OF THE POSSIBILITY OF ANY SUCH LOSS OR DAMAGE; *PROVIDED*, THAT THIS LIMITATION SHALL NOT LIMIT THE INDEMNIFICATION OBLIGATION OF SUCH PARTY UNDER THE PROVISIONS OF SECTION 10 FOR SUCH DAMAGES CLAIMED BY A THIRD PARTY AND NOTHING IN THIS SECTION 12.1 IS INTENDED TO LIMIT RHYTHM'S PAYMENT OBLIGATIONS UNDER SECTION 5 OR EITHER PARTY'S OBLIGATIONS UNDER SECTION 7 OR SECTION 8.

12.2 Assignment. Neither Party shall have the right to assign this Agreement, nor any of its rights hereunder, nor delegate any of its obligations hereunder, without the prior written consent of the other Party, which shall not be unreasonably withheld or delayed. Notwithstanding the foregoing, (i) Camurus and Rhythm may assign this Agreement to any purchaser of all or substantially all of its assets or to any successor entity resulting from any merger or consolidation of Camurus or Rhythm with or into such entity, or (ii) Camurus and Rhythm may assign this Agreement to any of its Affiliates but only for as long as such Affiliate remains an Affiliate of the assigning Party provided that such Affiliate agrees to be bound hereunder. Any attempt to assign this Agreement in breach of the foregoing shall be void. This Agreement shall be binding upon and inure to the benefit of the Parties hereto and each of their successors and permitted assigns.

12.3 Further Actions. Each Party agrees to execute, acknowledge and deliver such further instruments, and to do all such other acts, as may be necessary or appropriate in order to carry out the purposes and intent of this Agreement.

12.4 Compliance with Laws. Each Party shall review in good faith and cooperate in taking actions to ensure compliance of this Agreement and the Parties' activities hereunder with all applicable laws, rules, ordinances, regulations and guidelines. Each Party shall provide the other Party such reasonable assistance as may be required for the Party requesting such assistance to comply with all such laws, rules, ordinances, regulations and guidelines of all governmental entities, bureaus, and agencies having jurisdiction pertaining to this Agreement, including obtaining all import, export and other permits, certificates, licenses or the like required by such laws, rules, ordinances, regulations and guidelines necessary to permit the Parties to perform hereunder and to exercise their respective rights hereunder.

12.5 Force Majeure. Neither Party shall be responsible or liable in any way for failure or delay in carrying out the terms of this Agreement (other than any payment or confidentiality obligations) resulting from fire, flood, other natural disasters, war, labor difficulties, interruption of transit, accident, explosion, civil commotion, and acts of any governmental authority; *provided*, that the Party so affected shall give prompt notice thereof to the other. If any such cause prevents either Party from performing any of its material obligations hereunder for more than ninety (90) days,

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the other Party may then terminate this Agreement upon thirty (30) days prior notice. Except as provided in the preceding sentence, no such failure or delay shall terminate this Agreement, and each Party shall complete its obligations hereunder as promptly as reasonably practicable following cessation of the cause or circumstances of such failure or delay

12.6 Notices. All notices and other communications hereunder shall be in writing and shall be deemed given when delivered personally or by facsimile transmission (receipt verified), five (5) days after mailed by registered or certified air mail (return receipt requested), postage prepaid, or two (2) days after sent by express courier service, to the Parties at the following addresses (or at such other address for a Party as shall be specified by like notice; *provided*, that notices of a change of address shall be effective only upon receipt thereof):

If to Camurus, addressed to:

Camurus AB
att: CEO
Ideon Science Park
Sölvegatan 41
SE_223 70 Lund
Sweden
Phone: +46 46286 5730
Fax: +46 46 286 5739

If to Rhythm, addressed to:

Rhythm Pharmaceuticals, Inc.
855 Boylston Street, 11th Floor
Boston, MA 02116 USA
Attn: Chief Executive Officer
Phone: 857 264 4280
Fax: 857 264 4299

12.7 Amendment. No amendment, modification or supplement of any provision of this Agreement shall be valid or effective unless made in a writing that explicitly refers to this Agreement and that is signed by a duly authorized officer of each Party.

12.8 Waiver. Except to the extent otherwise expressly set forth in this Agreement, the rights and remedies of the Parties set forth herein or otherwise available at law or equity are cumulative and not alternative. No provision of this Agreement shall be waived by any act, omission or knowledge of any Party or its agents or employees except by an instrument in writing expressly waiving such provision and signed by a duly authorized officer of the waiving Party.

12.9 Counterparts. This Agreement shall be executed in two or more counterparts, each of which shall contain the signature of the Parties and all such counterparts shall

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constitute one and the same agreement. Counterparts may be delivered via facsimile, electronic mail (including pdf) or other transmission method and any counterpart so delivered shall be deemed to have been duly and validly delivered and be valid and effective for all purposes.

12.10 Descriptive Headings. The descriptive headings of this Agreement are for convenience only, and shall be of no force or effect in construing or interpreting any of the provisions of this Agreement.

12.11 Severability. Whenever possible, each provision of this Agreement shall be interpreted in such manner as to be effective and valid under applicable law, but if any provision of this Agreement is held to be prohibited by or invalid under applicable law, such provision shall be ineffective only to the extent of such prohibition or invalidity, without invalidating the remainder of this Agreement and the Parties shall in good faith seek to agree on an alternative provision reflecting the intent of the Parties that is enforceable.

12.12 Entire Agreement. This Agreement shall constitute and contain the complete, final and exclusive understanding and agreement of the Parties and cancels and supersedes any and all prior negotiations, correspondence, understandings and agreements, whether oral or written, between the Parties with respect to the subject matter hereof. The Confidentiality Agreement previously entered into between the Parties shall terminate as of the Effective Date and the Parties rights and obligations in respect of the Confidential Information disclosed under the Confidentiality Agreement shall thereafter be governed by this Agreement.

12.13 Governing Law. Except to the extent otherwise expressly provided elsewhere in this Agreement, this Agreement and all disputes arising out of it (including non-contractual disputes) shall be governed by and interpreted in accordance with the substantive laws of England, without regard to the choice of law provisions thereof. The United Nations Convention on Contracts for the International Sale of Goods shall not apply to the transactions contemplated by this Agreement.

12.14 Dispute Resolution.

(a) The Parties recognize that a bona fide dispute as to certain matters may from time to time arise during the Term of this Agreement that relate to any Party's rights or obligations hereunder. In the event of the occurrence of any dispute arising out of or relating to this Agreement, including any question regarding its existence, validity or termination, either Party may, by written notice to the other, have such dispute referred to its respective officer designated below or their successors, for attempted resolution by good faith negotiations within sixty (60) days after such notice is received. If either Party desires to pursue arbitration under paragraph (b) below to resolve any such dispute, a referral to such executives under this paragraph (a) shall be a mandatory condition precedent. Said designated officers are as follows.

For Camurus: Chief Executive Officer

For Rhythm: Chief Executive Officer

(b) In the event that they shall be unable to resolve the dispute by executive mediation within such sixty (60) day period and do not mutually agree to extend the time for negotiation, then subject to Section 3.4 and Section 7.2(b), the dispute shall be submitted to and finally settled by binding arbitration in accordance with the procedure set forth in Sections 12.14(c)-(d).

(c) Except with respect to actions by either Party seeking equitable or declaratory relief as described in Section 12.14(e), any claim or controversy arising in whole or in part under or in connection with this Agreement or the subject matter hereof that is not resolved pursuant to Section 12.14(b) or Section 3.4 or Section 7.2, as applicable, will be referred to and finally resolved by arbitration in accordance with the Rules of the International Chamber of Commerce (the "Rules") as such Rules may be modified by this Agreement, by one arbitrator, who will be agreed upon by the Parties. If the Parties are unable to agree upon a single arbitrator within thirty (30) days following the date arbitration is demanded, three arbitrators will be used, one selected by each Party within ten (10) days after the conclusion of the 30-day period and a third selected by the first two within ten (10) days thereafter. The arbitrator(s) will resolve any discovery disputes. Either Party may commence arbitration proceedings by notice to the other Party. The Arbitration Institute of International Chamber of Commerce shall administer any arbitration proceeding. The place of arbitration shall be London, England. The arbitration shall be conducted in English. The award of arbitration shall be final and binding upon both Parties.

(d) Except to the extent otherwise expressly provided in this Agreement, the arbitrator(s) will apply the laws of England. Judgment on the award granted in any arbitration hereunder may be entered in any court having jurisdiction over the award or any of the Parties or any of their respective assets. The Parties knowingly and voluntarily waive their rights to have their dispute tried and adjudicated by a judge and jury except as expressly provided herein.

(e) Nothing in this Section 12.14 will prevent a Party from resorting to judicial proceedings if: (i) interim relief from a court is necessary to prevent serious and irreparable injury to such Party; or (ii) litigation is required to be filed prior to the running of the applicable statute of limitations. The use of any alternative dispute resolution procedure will not be construed under the doctrine of latches, waiver or estoppel to affect adversely the rights of either Party. Despite such action the Parties shall continue to participate in good faith in the procedures specified in this Section 12.14.

12.15 Independent Contractors. Nothing herein shall be construed to create any relationship of employer and employee, agent and principal, partnership or joint venture between the Parties. Each Party is an independent contractor. Neither Party shall have authority to make any statements, representations, or commitments of any kind, or to take any action which shall be binding on the other Party, except as may be explicitly provided for herein or otherwise authorized in writing.

[Remainder of Page Intentionally Left Blank - Signature Pages to Follow]

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This Agreement has been executed in two (2) original copies of which the (Parties) have taken one (1) each. The Agreement shall come into force on the date given at the beginning of this Agreement.

For and on behalf of Camurus AB

Date: January 4, 2016

Signed by: /s/ Fredrik Tiberg

Full name: Fredrik Tiberg

Position: President & CEO

For and on behalf of Rhythm Pharmaceuticals, Inc.

Date: January 4, 2016

Signed by : /s/ Bart Henderson

Full name: Bart Henderson

Position: President

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EXHIBIT 1.5
CAMURUS PLATFORM IP PATENT RIGHTS

Short title (ref no.)	Filed in (main jurisdictions)	Granted in	Patent #
[ ]*			

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EXHIBIT 1.7
CAMURUS TRADEMARKS

Trademarks	Country	Classes	Registration number
[ ]*			

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EXHIBIT 1.19
DEVELOPMENT PLAN

See Attachment

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EXHIBIT 7.2 (c)
EXPERT'S DETERMINATION

1. Any matter or dispute to be determined by an expert under Section 7.2(c) of this Agreement (**"Expert"**) shall be referred to a person suitably qualified to determine that particular matter or dispute who shall be nominated jointly by the Parties or, failing agreement between the Parties within twenty (20) Business Days of a written request by either Party to the other seeking to initiate the Expert's decision procedure, either party may request the President for the time being of the Association of the British Pharmaceutical Industry or any successor body to it to nominate the Expert.

2. The Parties shall, within fourteen (14) days of the appointment of the Expert, meet with him/her in order to agree a program for oral and written submissions.

3. In all cases the terms of appointment of the Expert by whomsoever appointed shall include:

3.1 a commitment by the Parties to share equally the Expert's fee;

3.2 a requirement on the Expert to act fairly as between the Parties and according to the principles of natural justice;

3.3 intentionally omitted;

3.4 a commitment by the Parties to supply to the Expert the submissions the subject of paragraph 2 and all such assistance, documents and information as he/she may require for the purpose of his or her determination.

3.5 a commitment by the Parties that all negotiations connected with the dispute shall be conducted in confidence and without prejudice to the rights of the parties in any future proceedings.

4. The Expert shall, within forty-five (45) days of his/her appointment, give a written decision which shall contain a factual analysis, his/her conclusions and the reasons for his/her conclusions.

5. The Expert's decision shall be final and binding on the Parties (save in the case of manifest error).

6. The Parties expressly acknowledge and agree that they do not intend the reference to the Expert to constitute an arbitration within the scope of any arbitration legislation, the Expert's decision is not a quasi judicial procedure and the Parties shall have no right of appeal against the Expert's decision except as provided in Paragraph 5.

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EXHIBIT 8.5
PRESS RELEASE

13 Rhythm and Camurus Announce License Agreement for Extended Release FluidCrystal Setmelanotide

BOSTON and LUND, Sweden, January 5, 2016— Rhythm and Camurus announced today a license agreement for the use of Camurus' drug delivery technology, FluidCrystal®, to formulate setmelanotide (RM-493), Rhythm's novel melanocortin-4 receptor (MC4R) agonist. Under the terms of the agreement, Camurus has granted Rhythm a worldwide license to the FluidCrystal technology to formulate setmelanotide and to develop, manufacture, and commercialize this new formulation that has the potential for once-weekly dosing, administered as a subcutaneous injection. Rhythm plans to initiate a Phase I clinical trial with the setmelanotide FluidCrystal formulation after completing GMP manufacturing.

"We have developed a setmelanotide formulation with Camurus with an impressive sustained-duration profile," said Bart Henderson, President of Rhythm. "We believe this new formulation will provide a significant benefit to patients, improving compliance and ease of use with once-weekly dosing."

"The partnership with Rhythm follows the formulation development and preclinical assessment of this compelling drug candidate based on our FluidCrystal Injection depot technology," said Fredrik Tiberg, President and CEO of Camurus. "Rhythm's setmelanotide represents a novel approach to treating patients suffering from life-threatening obesity due to these rare and serious genetic disorders."

The license granted to Rhythm is specific to the FluidCrystal technology incorporating setmelanotide. The formulation has been developed in a collaboration between the companies. Under the terms of the license agreement, Rhythm is responsible for manufacturing, development, and commercialization of the setmelanotide FluidCrystal formulation worldwide. Camurus is eligible to receive an upfront payment and progressive payments of approximately $65 million, of which the majority are sales milestones. In addition, Camurus is eligible to receive tiered, mid to mid-high, single digit royalties on future sales of the product.

About Setmelanotide (RM-493)

Setmelanotide is a potent, first-in-class MC4R agonist in development for the treatment of obesity caused by genetic deficiencies in the MC4 pathway, a key pathway in humans that regulates energy expenditure, homeostasis, and appetite. The critical role of the MC4 pathway in weight regulation was validated with the discovery that single genetic defects along this pathway result in early-onset and severe obesity. A Phase 2 setmelanotide trial is ongoing for the treatment of Prader-Willi syndrome (PWS), a rare genetic disorder that causes life-threatening obesity. Recent scientific evidence implicates defects in the MC4 pathway as the likely cause of the weight and appetite abnormalities in PWS. A second Phase 2 trial is ongoing for the treatment of pro-opiomelanocortin (POMC) deficiency obesity, a very rare, life-threatening genetic disorder of the MC4 pathway associated with unrelenting appetite and obesity.

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About FluidCrystal Injection Depot

The FluidCrystal Injection depot delivers therapeutic levels of drug substance over extended periods—tunable from days to months—from a single injection. While traditional depot therapeutics comprise complicated microsphere technology, Camurus' depot offers a liquid solution that transforms into a controlled release liquid crystal gel matrix in situ on contact with minute quantities of aqueous fluid at site of injection. The FluidCrystal delivery system overcomes traditional side effects associated with high initial drug release on injection (drug burst) and poor drug stability by effectively encapsulating the drug compound in the nanopores of the depot matrix throughout the entire process from injection until final degradation. This, together with the ready-to-use product design, makes the system highly suitable for sustained parenteral delivery of peptides and proteins. FluidCrystal is a registered trademark of Camurus AB.

About Rhythm (www.rhythmtx.com)

Rhythm is a biopharmaceutical company focused on developing peptide therapeutics for the treatment of rare genetic deficiencies that result in life-threatening metabolic disorders. Rhythm's lead peptide product candidate is setmelanotide, a first-in-class melanocortin 4 receptor (MC4R) agonist for the treatment of rare genetic disorders of obesity. The company is based in Boston, Massachusetts.

About Camurus

Camurus is a Swedish research-based pharmaceutical company committed to developing and commercializing innovative and differentiated medicines for the treatment of severe and chronic conditions. New drug products with best-in-class potential are conceived based on the proprietary FluidCrystal® drug delivery technologies and an extensive R&D expertise. Camurus' clinical pipeline includes products for treatment of cancer, endocrine diseases, pain, and addiction, developed in-house and in collaboration with international pharmaceutical companies. The company's share is listed on Nasdaq Stockholm under the ticker "CAMX." For more information, visit www.camurus.com.

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Exhibit 10.9

AMENDED AND RESTATED

PAYROLL SERVICES AGREEMENT

This AMENDED AND RESTATED PAYROLL SERVICES AGREEMENT, dated as of March 21, 2013 (the "Agreement"), by and between RHYTHM METABOLIC, INC., a Delaware corporation ("Metabolic") and RHYTHM PHARMACEUTICALS, INC., a Delaware corporation ("Pharmaceuticals").

WHEREAS, Metabolic desires to contract with Pharmaceuticals to share certain employees, Scientific Advisory Board ("SAB") Members, or other consultants of Pharmaceuticals, in whole or in part, and to reimburse Pharmaceuticals in full for Metabolic's portion of such shared employees', SAB Members', or consultants' compensation and benefits, all in accordance with the terms and provisions of this Agreement; and

WHEREAS, Metabolic and Pharmaceuticals desire to amend and restate the Payroll Services Agreement, to be retroactively effective as of March 21, 2103;

NOW, THEREFORE, in consideration of the premises, the foregoing recitals, and the mutual agreements herein contained, the parties hereto agree as follows:

SECTION 1. EMPLOYEES, SAB MEMBERS, AND CONSULTANTS

1.1 (a) Core Employees. Subject to the terms of this Agreement, Pharmaceuticals hereby agrees to provide to Metabolic certain of its employees on a full time or shared basis under Metabolic's direction and control in the functional areas set forth on a list to be maintained by Metabolic and Pharmaceuticals (as the same may be updated from time to time, the "List") (collectively, the "Core Employees").

(b) Additional Employees. In addition to the Core Employees, Pharmaceuticals hereby agrees to provide to Metabolic certain of its employees on a full time or shared basis under Metabolic's direction and control in certain additional functional areas outside of those addressed by the Core Employees upon which the parties acting in good faith may mutually agree in writing (collectively, the "Additional Employees").

(c) SAB Members. Subject to the terms of this Agreement, Pharmaceuticals hereby agrees now and from time to time in the future to provide to Metabolic certain of its SAB members, as set forth the List to be maintained by Metabolic and Pharmaceuticals (as the same may be updated from time to time), on a shared basis under Metabolic's direction and control upon which the parties acting in good faith may mutually agree in writing (collectively, the "SAB Members").

(d) Consultants. Subject to the terms of this Agreement, Pharmaceuticals hereby agrees now and from time to time in the future to provide to Metabolic certain of its consultants, as set forth on the List to be maintained by Metabolic and Pharmaceuticals (as the same may be updated from time to time), on a shared basis under Metabolic's direction and control upon

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which the parties acting in good faith may mutually agree in writing (collectively, the "Consultants").

1.2 Other Outside Employees. Notwithstanding anything to the contrary contained in Section 1.1 of this Agreement, Metabolic from time to time, at its sole discretion, may retain its own employees, SAB Members, or consultants.

1.3 Personnel. Pharmaceuticals shall initially provide those employees, SAB Members, and Consultants of Pharmaceuticals, as set forth on the List maintained by Metabolic and Pharmaceuticals (as the same may be updated from time to time).

1.4 Intellectual Property. For the avoidance of doubt, each of Pharmaceuticals and Metabolic hereby confirm and agree that any intellectual property developed by any shared Core Employee, Additional Employee, SAB Member, or Consultant in the course of performing his or her services for Metabolic shall be the sole and exclusive property of Metabolic, and Metabolic is an express third party beneficiary of the provisions of such Core Employee's, Additional Employee's, SAB Member's, or Consultant's agreement(s) with Pharmaceuticals relating to such intellectual property.

SECTION 2. REIMBURSEMENT

2.1 Payment. Metabolic shall reimburse Pharmaceuticals for the full cost of each Core Employee or Additional Employee provided to Metabolic on a full-time basis, and the applicable pro rata portion of time spent by any shared Core Employee, Additional Employee, SAB Member, or Consultant (such reimbursement shall be for the fully burdened employment cost of the personnel (including but not limited to, compensation, benefits and taxes)).

2.2 Out-of-Pocket Expenses. Pharmaceuticals shall be entitled to reimbursement for all reasonable out-of-pocket business expenses incurred by Pharmaceuticals in the providing the Core Employees, Additional Employees, SAB Members, and Consultants hereunder.

SECTION 3. TERM AND TERMINATION

3.1 Term of Agreement. The term of this Agreement shall commence on March 21, 2013, and shall expire on March 21, 2018, unless earlier terminated pursuant to the terms hereof. Not less than thirty (30) days prior to the expiration of this Agreement, Metabolic may deliver written notice to Pharmaceuticals requesting that this Agreement be renewed, in whole or in part, for an additional one (1) year term. Such notice shall include an amended List, if necessary. Within fifteen (15) days of receipt of such written notice (if any), Pharmaceuticals shall provide written notice to Metabolic stating whether or not it wishes to renew the Agreement.

3.2 Elective Termination. Metabolic or Pharmaceuticals may terminate this Agreement for any reason upon thirty (30) days' notice. In the event that Metabolic elects pursuant to this Section 3.2 to terminate this Agreement, Metabolic shall reimbursed Pharmaceuticals all

amounts then unreimbursed pursuant to Section 2 of this Agreement at the time of termination, which fees shall be due fifteen (15) days after the date of such termination.

3.3 Remedies Upon Termination. Upon termination of this Agreement, neither party shall have any further obligations under this Agreement except as provided in this Section 3 and Section 4.1. Pharmaceuticals shall be entitled to receive payment of all unreimbursed amounts up to the date of termination, which payment shall be due fifteen (15) days after the date of termination or the date on which such payment was due, whichever is earlier.

SECTION 4. MISCELLANEOUS

4.1 Confidentiality.

(a) Neither party hereto shall use for its own benefit or disclose to any other person (other than its employees and agents who need to know such information to perform the obligations set forth herein) any Confidential Information (as defined herein) of the other party without the prior express written consent of such other party. Each party shall at all times take measures to protect such Confidential Information that are at least as protective as the measures used by it to protect its own confidential information.

(b) Both parties agree not to disclose the Confidential Information to any person or entity not a party to this Agreement other than such of recipient's contractors, agents or employees who (i) have a need to know the Confidential Information in connection with this Agreement or the services provided hereunder; (ii) are apprised of the confidential nature of the Confidential Information; and (iii) execute a confidentiality agreement restricting disclosure of the Confidential Information in a manner consistent with the provisions of this Agreement (except that such contractors, agents and employees shall not be permitted to disclose the Confidential Information to their contractors, agents or employees under any circumstances).

(c) For purposes hereof, "Confidential Information" is any information not of a public nature concerning the terms of this Agreement or the business, business plans, historical and current client information, trade secrets or other properties of the other party, or any information designated as confidential in writing by such other party at the time of disclosure. Confidential Information does not include any information (i) to the extent that the same is required to be disclosed by law, (ii) known generally to the trade or public at the time of the disclosure or (iii) which becomes so known without violation of this Agreement.

(d) If any Confidential Information is obtained by or disclosed to an unauthorized party, in addition to any other remedies available hereunder the parties hereto will cooperate in determining the source of such disclosure and in taking reasonable steps to prevent further such disclosures.

4.2 Indemnification. Metabolic shall indemnify, hold harmless and defend Pharmaceuticals, its officers, directors, shareholders, employees, agents and subcontractors from and against any and all liability, loss, damage, claim, causes of action and expenses (including

reasonable attorneys' fees) ("Claims"), whether or not covered by insurance, cause or asserted to have been caused, directly or indirectly, by or as a result of the performance of any intentional acts, negligent acts or omissions by Metabolic and/or its agents, employees (including employees of Pharmaceuticals under the control and direction of Metabolic at the time of the events giving rise to the Claims) and/or subcontractors during the term hereof. Pharmaceuticals shall indemnify, hold harmless and defend Metabolic, its officers, directors, shareholders and employees, from and against any and all Claims, whether or not covered by insurance, caused or asserted to have been caused, directly or indirectly, by or as a result of the performance of any intentional acts, negligent acts or omissions by Pharmaceuticals and/or its shareholders, agents, employees (other than employees of Pharmaceuticals under the control and direction of Metabolic at the time of the events giving rise to the Claims), and/or subcontractors during the term of this Agreement.

4.3 Waiver. No purported waiver by either party of any term or provision contained herein shall be deemed to be a waiver of such term or provision unless the waiver is in writing and signed by the waiving party. No such waiver shall in any event be deemed a waiver of any subsequent default under the same or other term or provision contained herein.

4.4 Severability. If any provision of this Agreement or its application to any person or circumstance shall be invalid or unenforceable to any extent, the remainder of this Agreement and application of its provisions to other persons or circumstances shall not be affected and shall be enforced to the greatest extent permitted by law.

4.5 Successors and Assigns. Neither party shall assign or transfer any rights or obligations hereunder without the prior written consent of the other party. Subject to the foregoing, this Agreement is binding upon the parties and their respective successors and assigns.

4.6 Entire Agreement; Modification. This Agreement (together with any appendices) constitutes the entire agreement of the parties with respect to the subject matter hereof and may not be amended or modified nor any provisions waived except in a writing signed by the parties hereto.

4.7 Relationship of the Parties. Metabolic and Pharmaceuticals acknowledge and agree that Pharmaceuticals intends to act and perform as independent contractor, and the provisions hereof are not intended to create any partnership, joint venture, agency or employment relationship between the parties.

4.8 Notices. Any notice or other communications required or permitted hereunder shall be deemed to be sufficient if contained in a written instrument delivered in person or duly sent by national overnight courier service or first class certified mail, postage prepaid, or by facsimile addressed to such party at the address or facsimile number set forth below:

(a) if to Rhythm Metabolic, Inc. to it at:

855 Boylston Street
11th Floor
Facsimile: (857) 264-4299
Attention: Bart Henderson

(b) if to Rhythm Pharmaceuticals, Inc. to it at:

Rhythm Pharmaceuticals, Inc.
855 Boylston Street
11th Floor
Facsimile: (857) 264-4299
Attention: Bart Henderson

4.9 Counterparts. This Agreement may be executed in two or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument, and the signature of any party to any counterpart shall be deemed a signature to, and may be appended to, any other counterpart.

4.10 Governing Law. This Agreement shall be governed by and construed in accordance with the laws of the Commonwealth of Massachusetts.

[The remainder of this page is intentionally left blank.]

IN WITNESS WHEREOF, the parties hereto have executed this Agreement as of the date first above written.

RHYTHM METABOLIC, INC.

By: /s/ Keith Gottesdiener
Name: Keith Gottesdiener
Title: Chief Executive Officer

RHYTHM PHARMACEUTICALS, INC.

By: /s/ Keith Gottesdiener
Name: Keith Gottesdiener
Title: Chief Executive Officer

[Signature Page to Amended and Restated Payroll Services Agreement]

Exhibit 10.11

LEASE

between

500 BOYLSTON & 222 BERKELEY OWNER (DE) LLC,

as LANDLORD

and

RHYTHM PHARMACEUTICALS, INC.,

as TENANT

Dated as of November 25, 2015

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FIVE HUNDRED BOYLSTON

Basic Lease Information

This "Basic Lease Information Sheet" is made a part of, and incorporated in, that certain leas dated by and between 500 Boylston & 222 Berkeley Owner (DE) LLC (as "Landlord") and Rhythm Pharmaceuticals, Inc. (as "Tenant").

Date:	November 25, 2015
Tenant:	Rhythm Pharmaceuticals, Inc.,

	a Delaware corporation
Tenant's Address (prior to Term Commencement Date):	855 Boylston Street 11th Floor Boston, MA 02116 Attention: Bart Henderson
Tenant's Address (after Term Commencement Date):	500 Boylston Street 11th Floor Boston, Massachusetts 02116 Attention: Bart Henderson *in either case with a copy to:* Morgan, Lewis & Bockius LLP One Federal Street Boston, MA 02110 Attention: Julio E. Vega, Esq.
Landlord:	500 Boylston & 222 Berkeley Owner (DE) LLC, a Delaware limited liability company
Landlord's Address:	500 Boylston & 222 Berkeley Owner (DE) LLC c/o Oxford Properties Group 222 Berkeley Street Boston, MA 02116 Attn: Property Manager and 500 Boylston & 222 Berkeley Owner (DE) LLC c/o Oxford Properties Group 125 Summer Street Boston, Massachusetts 02110 Attn: Director of Leasing

	with a copy of any notices to Landlord sent to: DLA Piper LLP (US) 33 Arch Street, 26th Floor Boston, MA 02110 Attn: John L. Sullivan, Esq.
Leased Premises:	A portion of the eleventh (11th) floor of the Building located at 500 Boylston Street, Boston, Massachusetts, as shown on Exhibit A, subject to Section 10.01 below.
Net Rentable Area:	6,830 square feet, subject to Section 10.01 below.
Scheduled Term Commencement Date	April 1, 2016, subject to Section 10.01.
Term Commencement Date:	See Section 2.01
Rent Commencement Date:	April 1, 2016, subject to Section 10.01.
Term Expiration Date:	The last day of the fifth (5th) Lease Year. The term "Lease Year" shall mean the successive twelve-(12)-month periods beginning on the Rent Commencement Date and each anniversary thereof; provided that, if the Rent Commencement Date does not occur on the first day of a calendar month, the fifth (5th) Lease Year shall include the balance of the calendar month in which the fifth (5th) anniversary of the Rent Commencement Date occurs.
Net Rent:	$42.00 per square foot of Net Rentable Area per annum, provided that the annual Net Rent rate shall increase by $1.00 per square foot of Net Rentable Area per annum on each anniversary of the Rent Commencement Date.
Tenant Work Allowance:	$55.00 per square foot of Net Rentable Area. See Exhibit B and (if applicable) Section 10.01.
Tenant's Proportionate Share:	See Section 11.01
Tenant's Authorized Representative:	Bart Henderson

Letter of Credit:	The amount of $225,000.00, in accordance with and subject to Section 4.17.
Guarantor:	Not applicable
Brokers:	Transwestern/RBJ (Landlord) Transwestern/RBJ (Tenant)
Parking Spaces:	Two (2) monthly parking spaces in the Project garage, as more particularly set forth in the Parking Addendum to the Lease attached hereto. Additional spaces may be available as set forth in the Parking Addendum.

Certain other defined terms are set forth in Article 11 of this Lease.

THIS LEASE is entered into as of the date hereof between Landlord and Tenant.

ARTICLE 1. LEASE

1.01 Lease. Landlord leases to Tenant and Tenant leases from Landlord the Leased Premises (excluding all Common Areas located therein, and all pipes, ducts, conduits, wires, and appurtenant fixtures located therein serving other parts of the Building) upon all of the terms, covenants and conditions set forth herein.

1.02 Appurtenant Rights. Tenant shall have, as appurtenant to the Leased Premises, rights to use in common (subject to the Building Rules and Regulations under Section 4.14): (a) the common lobbies, corridors, stairways, elevators of the Building serving the Leased Premises in common with others; (b) common walkways necessary for access to the Building; (c) if the Leased Premises include less than the entire rentable area of any floor, the common toilets, corridors and elevator lobby on such floor and serving the Leased Premises; and (d) all other Common Areas and General Common Areas from time to time intended for general use by Tenant, other Building tenants, and Landlord, including without limitation the bike rack currently located on garage level P1. Such appurtenant rights shall include, without limitation, the non-exclusive right to install telecommunications wiring (e.g., T1/T3 and fiber optic and cable lines) in the building in accordance with Building standard procedures and the terms of this Lease.

ARTICLE 2. TERM; RENT

2.01 Term. Except as otherwise provided herein, the Term of this Lease shall commence on the Term Commencement Date and continue through the Term Expiration Date set forth in the Basic Lease Information Sheet, unless earlier terminated as provided herein.

The "Term Commencement Date" shall be the earlier of (i) the Scheduled Term Commencement Date or (ii) the date on which Tenant shall have taken occupancy for the regular conduct of its business of all or any portion of the Leased Premises (which occupancy shall not be deemed to have occurred by virtue of Tenant's entry into the Leased Premises for purposes of Tenant's construction under Exhibit B or the installation or testing of Tenant's furniture, fixtures, and equipment in preparation for such occupancy).

The Leased Premises is currently vacant and available for delivery to Tenant for the commencement by Tenant of Tenant's Initial Construction under Exhibit B. Landlord shall deliver the Leased Premises to Tenant, free and clear of all occupants, in its "as is" condition (subject to Section 10.01, if applicable), and with the existing HVAC equipment in good working condition, which delivery shall be deemed to have been made on the date that is the earlier of (i) the date on which Tenant first commences the performance of Tenant's Initial Construction under Exhibit B in all or any portion of the Leased Premises or (ii) the Scheduled Term Commencement Date. Tenant's obligation to pay Rent and its other obligations under this Lease shall commence upon the Term Commencement Date (or, for the obligations set forth in Section 2.03, on the Rent Commencement Date), except as expressly otherwise provided herein with respect to obligations arising earlier.

2.02 Use. Tenant shall use the Leased Premises solely for the Permitted Use and for no other use or purpose, except as permitted by Landlord pursuant to Landlord's written consent.

2.03 Rent. All obligations of Tenant to make payments to Landlord under this Lease shall constitute Rent. Tenant shall pay the Rent at the times and in the manner hereinafter set forth.

Commencing on the Rent Commencement Date and thereafter during the Term, Tenant shall pay the Gross Rent (consisting of Net Rent and Tenant's Proportionate Share of Estimated Operating Cost and Tenant's Proportionate Share of Estimated Impositions), in twelve (12) equal installments on the first day of each calendar month during each year of the Term and any extensions thereof. Such payments shall be made in lawful money of the United States, in advance without demand, and (except as expressly provided herein) without any reduction, abatement, counterclaim or set off, at the address for Landlord specified on the Basic Lease Information Sheet or at such other address as may be designated by Landlord from time to time. If the Rent Commencement Date occurs on other than the first day of a month, then Gross Rent provided for such partial month shall be equitably prorated, and paid, on such date of commencement. If the Term terminates on other than the last day of a calendar month, then Gross Rent provided for such partial month shall be equitably prorated on such date of termination.

2.04 Operating Cost.

(a) Operating Cost shall mean all expenses and costs of every kind and nature which Landlord shall pay or become obligated to pay because of or in connection with the management, maintenance, preservation or operation of the Building (determined in accordance with generally accepted accounting principles, consistently applied) including, but not limited to the following:

(1) Expenses of the operation, maintenance and security of the Building, including compensation in the form of wages, salaries, and other compensation and benefits (including payroll taxes, federal, state and local unemployment taxes and social security taxes, insurance, welfare and retirement benefits, and related expenses and benefits of all on-site and off-site employees [to the extent involved in the management, maintenance and operation of the Building], reasonably pro-rated to reflect services provided for the Building and other building(s));

(2) Cost for Landlord's office and management office operation for the Building, including the actual cost (or, in the absence of a specific rent charge, the fair market rent) of any space occupied by entities providing management or building services for the Building, reasonably prorated between the Building and the building at 222 Berkeley Street;

(3) All tools, supplies, materials and equipment used in the operation and maintenance of the Building (reasonably pro-rated to reflect services provided for the Building and other building(s)), including rental fees for the same, if such items are not purchased and amortized pursuant to (10) below;

(4) Utilities, including electricity, water, sewer, gas, communication, heating, lighting, air conditioning and ventilating, for the entire Building;

(5) All maintenance, janitorial and service agreements and costs for the Building, including, without limitation, alarm service, landscaping, window cleaning, escalator and elevator maintenance, rubbish and snow removal, pest control, equipment maintenance or servicing or maintenance or cleaning for sidewalks, Building exterior, roof and service areas;

(6) A management fee in connection with the operation of the Building; provided, however, that the share of such cost included in Tenant's Operating Cost under this Lease shall be separately calculated and equal three percent (3%) of all Rent under this Lease, excluding such fee, and that such share shall be in lieu of Tenant's Proportionate Share of the management fee for the entire Building;

(7) Legal and accounting services for the Building, including the costs of audits by certified public accountants, but excluding legal costs (and related costs and expenses) incurred in disputes with or proceedings against any specific tenant or in connection with the development, financing, sale and/or leasing of the Building or any part thereof;

(8) All insurance premiums and costs applicable to the Building and Landlord's personal property used in connection therewith, including but not limited to, the premiums and cost of fire, casualty and liability coverage and rental abatement and business interruption insurance and unreimbursed costs incurred by Landlord that are subject to an insurance deductible;

(9) Repairs, replacements and general maintenance (except for repairs paid by proceeds of insurance or by Tenant or other third parties, and alterations attributable solely to tenants of the Building other than Tenant);

(10) Amortization (together with reasonable actual or imputed financing charges) over its useful life as reasonably determined by Landlord (or such shorter pay-back period as may be reasonably estimated by Landlord for cost-savings items) of capital improvements made to the Building that (i) are reasonably designed to maintain the first-class quality of the Building's operations consistent with Comparable Buildings in Downtown Boston (excluding major lobby reconstruction or other major improvement work in the Building) or to reduce energy consumption or improve the operating efficiency of the Building, (ii) may be required by governmental authorities (other than a failure of the Building to comply with any law, ordinance, order, or other governmental rule or regulation in effect and interpreted to apply to the Property as of the date hereof) or any insurer of the Building consistent with Comparable Buildings in Downtown Boston, or (iii) constitute equipment of a capital nature contemplated in (3) above (such as, for example, snow blowers, vacuums and sweepers), which in Landlord's reasonable judgment, is ultimately less costly to purchase than to rent.

(b) Notwithstanding any other provision herein to the contrary, in the event that the Building is not fully occupied during any year of the Term, an adjustment shall be made in computing Operating Cost for such year so that Operating Cost shall be computed as though the Building had been fully occupied during such year; provided, however, that in no event shall Landlord collect in total, from Tenant and all other tenants of the Building, an amount greater than one hundred percent (100%) of the actual Operating Cost during any

year of the Term, To the extent items of Operating Cost are incurred for the Building and other buildings (including the other building in the Project), the costs of such items shall be reasonably allocated by Landlord between the Building and such other building(s).

(c) Operating Cost shall not include (i) costs associated with the operation of the parking garage forming part of the Building (including the elevators serving the garage) or any validated parking, or with the development, construction, financing, sale or leasing of the Building, (ii) specific costs for tenant electricity (of the type specified in Section 3.01(b)) or for extra services (of the type specified in Section 3.02) that are separately billed to and paid by specific tenants leasing space in the Office Section of the Building, or those costs and expenses which are specifically attributable to and separately paid by the tenants in the Commercial Section of the Building and not provided to Tenant hereunder, (iii) that portion of the costs and expenses relating to the loading dock facilities and the General Common Areas which exclusively serves the Commercial Section of the Building or is paid by the tenants in the Commercial Section of the Building, (iv) compensation (including salaries, wages, fringe benefits, profit-sharing, bonuses and other employee benefit plans) paid to any executives or principals of Landlord above the grade of senior property manager (other than costs of such personnel who actually perform services that would have been included in Operating Cost hereunder if performed by a third party),

(v) franchise, corporate excise or income taxes imposed on Landlord, (vi) capital expenses (whether for repairs, replacements or improvements), depreciation, amortization, or other non-cash items of the Building (except as provided in clause (a)(10) above), (vii) debt service or ground lease payments, other costs of financing or refinancing of any Mortgage, or costs incurred in connection with any other financing, sale, or syndication of the Building or any interest therein, or in the defense of Landlord's title thereto, (viii) advertising costs, promotional expenses, signs, brokerage commissions, tenant improvement allowances, costs of design or construction of tenant improvements, moving expenses, attorneys' fees and other expenses incurred in marketing tenant spaces, negotiating leases with current or prospective tenants of the Building or preparing such tenants' spaces for occupancy, (ix) costs of capital items, except as expressly included above in clause (10) in Operating Cost, (x) costs for which Landlord is reimbursed under insurance policies, warranties, or otherwise by building service contractors or other third parties (including other tenants for separately reimbursable charges, such as overtime HVAC or special services), but not for Operating Cost charges, (xi) penalties, fines, or interest that Landlord is obligated to pay by reason of a failure by Landlord to comply with applicable legal requirements or to timely pay Impositions, utility bills or similar third party payments of Operating Cost; (xii) the cost of services provided to Landlord by any affiliate or subsidiary of Landlord, to the extent such costs exceed the costs that would have been paid by Landlord in an arm's length transaction, provided that this clause shall not be construed to affect the management fee charged under Section 2.04(a)(6) above; (xiii) charitable contributions or similar donations, (xiv) costs of purchasing works of art, (xv) bad debt or rental loss or any reserves, (xvi) costs of organizing or maintaining Landlord as an entity, such as trustees' fees, annual fees, partnership expenses, and legal and accounting fees in organizing or maintaining Landlord as an entity, (xvii) costs of services provided to other tenants and not to Tenant, (xviii) costs of assessment or remediation of specific releases or spills of hazardous materials in the Building, other than

those caused by Tenant or any Tenant Party (which may be separately chargeable to Tenant) or incurred in the ordinary course of owning, operating, and maintaining a first-class mixed-use high-rise building in downtown Boston (e.g., periodic air quality testing or the handling or disposal of cleaning materials or other materials used in mechanical equipment or in providing building services, all of which are includable in Operating Cost); or (xix) costs directly resulting from the ascertained negligence or willful misconduct of Landlord or its employees, agents, or contractors or other tenants, (xx) costs directly resulting from the ascertained negligence or willful misconduct of Landlord or its employees, agents, or contractors or other tenants, or (xxi) costs directly resulting from the violation by any tenant of the Building of its lease obligations, to the extent not reimbursed by such party and not otherwise excluded hereunder, (xxii) damages, penalties, fines, or interest that Landlord is obligated to pay by reason of failure by Landlord to comply with applicable law or its lease obligations; (xxiii) taxes (other than sales or use taxes in connection with Building services, operations or repairs) imposed on Landlord, or (xxiv) costs of repairs or restoration due to casualty or condemnation affecting all or part of the Building, except as expressly included above in clause (8) in Operating Costs.

2.05 Impositions. Impositions shall mean all real estate or personal property taxes, or similar governmental charges, business or license taxes or fees, service payments in lieu of such taxes or fees, annual or periodic governmental license or use fees, excises, assessments, levies, fees or charges, general and special, ordinary and extraordinary, unforeseen as well as foreseen, of any kind (including fees "in-lieu" of any such tax or assessment) which are assessed, levied, charged, confirmed, or imposed by any public authority upon the Land, the Building, its operations or the Rent (or any portion or component thereof) including, in the year paid, all fees and costs incurred by Landlord in seeking to obtain an abatement or reduction of, or a limit on any increase, in any taxes, regardless of whether any abatement, reduction or limitation is obtained, but excluding (i) inheritance, gift, estate, franchise, documentary or transfer taxes imposed upon or assessed against the Building, or any part thereof or interest therein, (ii) taxes computed upon the basis of the net income derived from the Building by Landlord or the owner of any interest therein, and (iii) that portion of the items enumerated in this Section which is allocated by Landlord to the Commercial Section or the garage serving the Building. Landlord shall credit, to the Impositions allocable to Tenant under this Lease, the Tenant's Proportionate Share of any abatement actually received by Landlord (net of fees and costs not previously included in Tenant's share of Impositions) for Impositions for any year included in the Term for which Tenant previously paid such Impositions, provided that Tenant is not in default under the Lease continuing beyond any applicable notice and cure period.

2.06 Computation of Operating Cost and Impositions Adjustment. Landlord shall from time to time give Tenant written notice of the applicable Estimated Operating Cost and Estimated Impositions and any adjustments thereto. Landlord shall, after the end of each calendar year of the Term, give written notice to Tenant containing or accompanied by a statement of the Operating Cost and Impositions during such calendar year, and also accompanied by a computation of the Operating Cost Adjustment and the Impositions Adjustment, if any. Landlord shall use reasonable efforts to provide such statement within one hundred twenty (120) days after the end of each calendar year for which an adjustment is due, but Landlord's failure to give such statement within such period shall not release either party from the obligation to make the adjustment provided for in Section

2.07. Such statement shall be deemed accepted if not disputed, within eight (8) months after Tenant's receipt thereof, by written notice to Landlord stating the specific grounds for dispute. The provisions of this paragraph shall survive the expiration or earlier termination of the Term.

2.07 Adjustment for Variation Between Estimated and Actual. If the Operating Cost and/or the Impositions for any calendar year exceed the Estimated Operating Cost and/or the Estimated Impositions, Tenant shall pay to Landlord Tenant's Proportionate Share of such excess within thirty (30) days after presentation of Landlord's statement pursuant to Section 2.06. If the Operating Cost and/or Impositions for any calendar year is less than the Estimated Operating Cost and/or the Estimated Impositions, then Landlord shall pay to Tenant Tenant's Proportionate Share of such difference within thirty (30) days after the Operating Cost Adjustment and/or the Impositions Adjustment is finally determined. Should the Term commence or terminate at any time other than the first day of a calendar year, Tenant's Proportionate Share of the Operating Cost Adjustment and/or Impositions Adjustment shall be prorated for the exact number of calendar days for which Tenant is obligated to pay Gross Rent, and in the case of the expiration of this Lease or any early termination, the provisions of this Section 2.07 shall survive such expiration or termination.

ARTICLE 3. LANDLORD'S COVENANTS

3.01 Basic Services.

(a) Landlord or its affiliates shall furnish the following Basic Services to Tenant during Business Hours (unless otherwise stated herein) during Tenant's occupancy of the Leased Premises:

(i) Water (hot and cold) used by the building standard cooling, drinking, lavatory, and sanitation systems, and for maintenance and janitorial services. (Equipment and piping for hot and cold water for Tenant's kitchenettes or private restrooms, if any, are Tenant's responsibility under Section 4.07 and other applicable provisions of this Lease.)

(ii) Central heat and air conditioning in season, at such temperatures and in such amounts as are from time to time furnished to tenants in Comparable Buildings in Downtown Boston, or as may be permitted or controlled by applicable laws, ordinances, rules and regulations.

(iii) Maintenance, repairs, structural and exterior maintenance (including exterior glass and glazing), painting and electric lighting service for all Common Areas, Building Common Areas and General Common Areas in the manner and to the extent customarily provided by landlords in Comparable Buildings in Downtown Boston.

(iv) Janitorial service after Business Hours on Business Days in accordance with the cleaning specifications attached as Exhibit E (or such other specifications as Landlord may from time to time

adopt that are consistent with prevailing standards for Comparable Buildings in Downtown Boston).

(v) Electricity for (1) tenant light fixtures and plugs for standard office equipment, not to exceed four (4) watts of demand per square foot of Net Rentable Area (the cost of which is a separate charge to Tenant under Section 3.01(b) below), and (2) building standard air handling units and related HVAC equipment for the floor on which the Leased Premises are located, not to exceed two (2) watts per square foot of Net Rentable Area (the cost of which is included in Operating Cost), by means of base building facilities operated in a manner consistent with Comparable Buildings in Downtown Boston.

(vi) Initial lamps, bulbs, starters and ballasts for building standard fixtures used within the Leased Premises.

(vii) A system of access control for the Building during hours when the Building is not generally open to the public and during such other hours as Landlord may from time to time designate. During such hours, Landlord may employ a system of monitoring and limiting access to the office floors in the Building based on reasonable systems of identification. Landlord reserves the right from time to time to modify components of such system, to change the number of lobby attendants, or to institute, modify, supplement, or discontinue any access control procedures or equipment for the Building or the Project, whether during or after business hours. Landlord does not warrant or guarantee the effectiveness of any such system or procedures. Tenant expressly disclaims any such warranty, guarantee, or undertaking by Landlord with respect thereto and acknowledges that access control procedures from time to time in effect are solely for the convenience of tenants generally and are not intended to secure the Leased Premises or guarantee the physical safety of tenants' employees or invitees in or about the Leased Premises or the Project. Tenant shall be responsible for securing the Leased Premises, subject to Landlord's approval under Section 4.07 of Tenant's installation of access card readers or other security equipment for the Leased Premises.

(viii) Public elevator service serving the floors on which the Leased Premises are situated, including a freight elevator. Access to the Leased Premises shall be available on a 24-hours-a-day, 7-days-a-week basis, subject to temporary interruptions for annual power testing and emergencies and the terms and conditions of this Lease.

(b) Tenant shall pay to Landlord, as Additional Rent, the cost of electricity provided under Section 3.01 (a)(v). Such charges shall be based on the usage shown on the check meter installed for the floor on which the Leased Premises are located, with the cost equitably apportioned among tenants on the floor. If Tenant's electricity usage exceeds the standard level set forth in Section 3.01(a)(v), charges for such additional usage shall be payable under Section 3.02.

(c) To the maximum extent permitted by law, Landlord shall not be liable for injuries to persons or damage to property, nor shall Landlord be deemed to have evicted Tenant, nor shall there be any abatement of Rent, nor shall Tenant be relieved from performance of any covenant on its part to be performed hereunder or have any right to terminate the Lease by reason of any (i) deficiency in the provision of Landlord services under this Article 3, (ii) breakdown of equipment or machinery utilized in supplying services, or (iii) curtailment or cessation of services or any other failure by Landlord to perform any obligation under the Lease, except as expressly provided in this Lease. Landlord shall use reasonable diligence to make such repairs as may be required to machinery or equipment within the Building to provide restoration of services and, where the cessation or interruption of service has occurred due to circumstances or conditions beyond Building boundaries, to cause the same to be restored, by diligent application or request to the provider thereof. In no event shall any mortgagee referred to in Section 4.11 be or become liable for any default of Landlord under this Section 3.01(c), subject to the provisions of Section 4.11. The preceding sentence shall not be construed to relieve the then existing Landlord from its obligations to perform the Landlord's routine maintenance and repair obligations under this Lease during the period of its ownership.

Notwithstanding the foregoing, in the case of fire or other casualty, Tenant shall have the abatement and termination rights set forth in Section 5.07. With respect to matters not covered by Section 5.07, if Tenant is prevented, on account of Landlord's failure to perform any of its service obligations under this Lease where the failure is caused by matters within Landlord's reasonable control, from using all or a substantial portion (meaning at least twenty five percent) of the Leased Premises for more than five (5) Business Days following notice to Landlord, then from and after the end of such five-(5)-Business-Day period until the Leased Premises (or such portion) is rendered usable, Gross Rent and other charges allocable to the Leased Premises, or a just and proportionate part thereof, shall be abated until such time as the service is restored.

3.02 Extra Services. Landlord shall provide to Tenant at Tenant's sole cost and expense at standard Building charges in effect from time to time (and subject to the limitations hereinafter set forth) the following:

(a) Heating, ventilation, air conditioning or extra service provided by Landlord to Tenant (i) during hours other than Business Hours, or (ii) on days other than Business Days, said heating, ventilation and air conditioning or extra service to be furnished solely upon the prior request of Tenant given with such advance notice as Landlord may from time to time reasonably require in accordance with its standard operating procedures for the Building;

(b) Additional air conditioning and ventilating capacity or chilled and/or condenser water required for supplemental HVAC equipment installed by Tenant under Exhibit B or Section 4.07 or by reason of any electrical, data processing or other equipment or facilities or services required to support the same, in excess of that which would be required for Building Standard Improvements;

(c) Repair and maintenance which is the obligation of Tenant hereunder but which Tenant fails to perform under Section 3.06;

(d) Customary tenant pantry cleaning, together with additional cleaning and janitorial services requested by Tenant in accordance with Building standard practices or provided by Landlord if the quality, quantity or use of Tenant improvements are not consistent with Building Standard Improvements and reasonably require more service in order to maintain the Leased Premises in accordance with the terms of this Lease;

(e) Additional electricity above the standards specified in Section 3.01 (a)(v), in which case Tenant shall pay to Landlord, as Additional Rent, the costs of such additional electricity usage (which shall be charged at the same rate as described in Sections 3.01(a)(v) and 3.01(b)) based either on a separate check-meter or meters (which shall be installed by Tenant under Section 4.07 or Exhibit B, as the case may be) measuring such electrical consumption or (during any period in which such check-meters have not been installed or are inoperable) on a reasonable determination by Landlord's engineer as to the level of electrical consumption in the Leased Premises, which reasonable determination (absent manifest error) shall be conclusive and binding on the parties. Tenant shall be responsible for the costs of installing such meters and all electrical equipment reasonably required for such additional electricity usage. All work necessary for such installation shall be done in accordance with the requirements of Section 4.02 (regarding Tenant Improvements).

(f) Maintenance and replacement of initial lamps, bulbs, starters and ballasts;

(g) Any Basic Service in amounts reasonably determined by Landlord to exceed the amounts required to be provided under Section 3.01(a), but only if Landlord elects to provide such additional or excess service.

The cost chargeable to Tenant for all extra services shall constitute Additional Rent. If the same extra service is provided to Tenant and other tenants (such as regularly scheduled, above-standard cleaning services), Tenant's share shall equal the total cost thereof multiplied by the quotient of the Net Rentable Area of the Leased Premises over the total Net Rentable Areas of all areas to which such extra service is provided. Landlord may include the estimated monthly amount of any regularly provided extra service in the Estimated Operating Cost for the Leased Premises, subject to adjustment under Section 2.06 and 2.07. Unless otherwise provided herein, all payments of Additional Rent shall be due within thirty (30) days after billing.

3.03 Window Covering. All window covering shall be provided by Landlord as Building Standard Improvements. Tenant shall not place or maintain any window covering, blinds or drapes (other than those supplied by Landlord) on any exterior window without Landlord's prior written approval which Landlord shall have the right to grant or withhold in its reasonable discretion. Tenant shall comply with Landlord's Building-standard requirements (which Landlord shall provide upon request) for lighting all portions of the Leased Premises that are visible from the exterior. Tenant acknowledges that breach of this Section 3.03 will directly and adversely affect the exterior appearance of the Building.

3.04 Graphics and Signage. Landlord shall install, at Landlord's expense, the initial listing for Tenant in the Building directory in the ground floor lobby and the initial

Building standard directional signage for Tenant in the elevator lobby on any multi-tenant floor on which the Leased Premises are located; thereafter, any changes to such signage shall be at Tenant's expense. Tenant shall install, at Tenant's expense, identification of Tenant's name (and, if desired, its suite numerals) at the main entrance door to the Leased Premises (or, at Tenant's election, on an adjacent window panel next to such door and/or on an interior wall within the Leased Premises visible from such entrance), with the size, materials, colors, and graphics reasonably approved by Landlord. Any other signs, notices and graphics of every kind or character, located on such entrance door (or adjacent window panel) shall be subject to Landlord's prior written approval, which Landlord shall not unreasonably withhold, condition, or delay, provided the same comply with the provisions of this Lease and are suitable for a multi-tenant common area. Except as set forth above, Tenant shall not be permitted to maintain any signage in the public corridors, the Common Areas, the Building Common Areas, or the General Common Areas, on the exterior of the Leased Premises, or in a location otherwise visible from the exterior of the Leased Premises.

3.05 Initial Tenant Improvements. Except as set forth in Section 2.01 and except for Landlord's ongoing repair obligations provided for elsewhere in this Lease, Landlord shall not be required to perform any work in the Leased Premises, and Tenant shall accept the Leased Premises in their "as is" condition on the date on which the Leased Premises are delivered to Tenant under Section 2.01. Except for the Tenant Work Allowance set forth in the Basic Lease Information sheet, Landlord shall not be required to furnish any allowance for the costs incurred by Tenant in preparing the Leased Premises for occupancy by Tenant. Tenant shall perform such work in accordance with the terms of the Lease, including without limitation Exhibits B, B-l and B-2 attached hereto.

3.06 Repair Obligation. Subject to the terms and conditions of this Lease, Landlord shall maintain in good operating repair (which may be effected by Landlord's replacement of worn-out items) and condition, reasonable wear and tear and damage by fire or casualty excepted, (i) the structural portions of the Building, (ii) the exterior wall of the Building, including glass and glazing, (iii) the roof, (iv) mechanical, electrical, plumbing and life safety systems, serving to the perimeter of the Leased Premises (together with any base building equipment, if any, located within the Leased Premises that does not exclusively serve the Leased Premises), and (v) Common Areas, Building Common Areas and General Common Areas. Upon reasonable prior notice to Tenant (which may be given orally or in writing, except in the case of an emergency when no such notice shall be required, it being acknowledged that the reasonableness of such prior notice may take into account, among other things, the risk to persons or property, the potential adverse effect on other tenants, building systems, or common areas, and/or the visibility of the affected areas outside of the Leased Premises), Landlord shall have the right, but not the obligation, to undertake maintenance or repair work which Tenant is required to perform pursuant to Section 4.04 and which Tenant fails or refuses to perform in a timely and efficient manner; and all costs reasonably incurred by Landlord in performing any such repair for the account of Tenant that Tenant has so failed to perform shall be repaid by Tenant to Landlord upon demand, together with an amount equal to ten percent (10%) of such costs, to reimburse Landlord for its administration and managerial effort arising from Tenant's failure to perform its repair obligations hereunder.

3.07 Quiet Enjoyment. So long as Tenant pays the Rent and performs all of Tenant's covenants and agreements contained in this Lease within applicable notice and cure periods, Tenant shall peacefully have, hold and enjoy the Leased Premises during the Term of this Lease, free from claims of any party claiming under Landlord, subject to the terms and provisions of this Lease and other matters to which this Lease is or may (in accordance with this Section 3.07) become subject and subordinate, including without limitation that certain Amended and Restated Sale and Construction Agreement by and among the City of Boston, the Boston Redevelopment Authority, New England Mutual Life Insurance Company and Gerald D. Hines Interests, Inc., dated April 15, 1986, recorded with the Suffolk Registry of Deeds in Book 12515, Page 78, the covenants therein relating to the land being incorporated by reference herein, as required pursuant to the terms of Section 1304 thereof, as hereafter amended from time to time provided, however, that no such instrument to which the Lease is or may become subordinate shall unreasonably interfere with Tenant's use of the Leased Premises for the Permitted Uses or prevent access to the Leased Premises, so long as Tenant pays the Rent and performs all of Tenant's covenants and agreements contained in this Lease within applicable notice and cure periods. This covenant is in lieu of any other so-called covenant of quiet enjoyment, either express or implied. This covenant and the other covenants of Landlord contained in this Lease shall be binding upon Landlord and its successors only with respect to breaches occurring during its and their respective ownerships of Landlord's interest hereunder.

ARTICLE 4. TENANT'S COVENANTS

4.01 Obligations of Tenant To Furnish Floor Plans. Tenant shall deliver to Landlord plans and specifications for Tenant's initial tenant improvement work and obtain Landlord's approval of such plans and specifications pursuant to Exhibit B.

4.02 Construction of Tenant Improvements. Tenant shall comply with the obligations set forth in Exhibit B with respect to all Tenant Improvements to be installed and constructed by Tenant.

4.03 Taxes on Personal Property. In addition to, and wholly apart from its obligation to pay Tenant's Proportionate Share of Operating Costs and Impositions, Tenant shall be responsible for and shall pay, prior to delinquency, taxes or governmental service fees, possessory interest taxes, fees or charges in lieu of any such taxes, capital levies, or other charges imposed upon, levied with respect to or assessed against its personal property, or the value of its Tenant Improvements (if applicable and, if so, only to the extent such Tenant Improvements exceed the level of finishes represented by Building Standard Improvements or the Initial Improvement Work), or its interests pursuant to this Lease. To the extent that any such taxes are not separately assessed and billed to Tenant, Tenant shall pay the amount thereof as invoiced to Tenant by Landlord. Tenant shall have the right, at Tenant's sole cost and expense, by appropriate proceedings authorized by any law, to contest or review the amount or validity of all such amounts, to the extent the same do not give rise to a lien on the Building or the Leased Premises or any improvements therein or fixtures thereto.

4.04 Repairs by Tenant. Tenant shall maintain and repair the Leased Premises, keep the same in such good order, repair and condition as the same are in on the Term Commencement Date or thereafter may be put in compliance with the Lease and, upon expiration of the Term, surrender the same to Landlord in the condition

required under Section 4.07, reasonable wear and tear, damage by fire or other casualty, and maintenance and repairs that are Landlord's obligation excepted. Tenant's obligation shall include, without limitation, the obligation to maintain and repair all walls (except the exterior surface or structural portion of the Building or any building systems, unless the damage thereto is caused by the negligence of Tenant or any of its Invitees, in which event, subject to Section 5.05, the maintenance or repair of the exterior surface or structural portion of the Building or building systems shall be performed by Landlord and Tenant shall pay to Landlord the costs of such maintenance or repair), floors, ceilings, windows (except for windows located on the exterior of the Building), doors and fixtures and to repair all damage caused by Tenant or its Invitees to the Leased Premises or anywhere in the Building. At the request of Tenant, Landlord shall perform the maintenance and repair work required under this Section 4.04 at Tenant's sole cost and expense and as an extra service to be rendered pursuant to Section 3.02. Any work of repair and maintenance performed by or for the account of Tenant by persons other than Landlord shall be

performed by contractors reasonably approved by Landlord in accordance with Section 4.07 and in accordance with procedures that Landlord shall from time to time establish. Nothing herein contained, however, shall be deemed to impose upon Tenant the obligation to perform maintenance and repair work required by reason of the negligence or wrongful acts of Landlord or its agents, contractors, or employees.

4.05 Waste. Tenant shall not commit or allow any waste or damage (except as set forth in Section 5.07) to be committed in any portion of the Leased Premises.

4.06 Assignment or Sublease.

(a) In the event Tenant intends to assign this Lease or sublet the Leased Premises or any part thereof to a person or entity which controls, is controlled by or is under common control with Tenant (hereinafter, "Affiliate"), or an entity into or with which Tenant is merged or consolidated or to which all or substantially all of Tenant's assets are transferred (hereinafter, "Successor"), then Tenant shall give Landlord written notice of such intent. As used herein, "control" shall mean ownership of more than 50% of the shares or beneficial interests of the entity in question, together with the power to control and manage the affairs thereof either directly or by election of directors and/or officers, and an "assignment" shall be deemed to further include any transfer of Tenant's interest in this Lease by operation of law, merger or consolidation of Tenant into any other firm or corporation, and the transfer or sale of a controlling interest in Tenant, whether by sale of its capital stock or otherwise. Landlord's consent to such a sublease to an Affiliate or an assignment to a Successor (collectively, a "Permitted Transfer") shall not be required, provided that, on reasonable prior notice before the consummation of such Permitted Transfer (except where such prior notice is prohibited by applicable law, in which event such notice shall be provided promptly after such notice is permitted by applicable law, and except where such prior notice is prohibited by a confidentiality agreement, in which event such notice shall be given as early as permitted thereunder and in all events not later than thirty (30) days after the closing of such transaction, provided that Landlord reserves all of its rights hereunder in the event that such transaction does not satisfy the requirements for a Permitted Transfer hereunder), (i) Tenant shall furnish Landlord with reasonable evidence of such transaction, (ii) the transaction otherwise complies with the terms of this Lease, including without limitation this Section 4.06, and (iii) in the case of an assignment to a

Successor, Tenant provides Landlord with reasonable evidence that the financial condition of the Successor is equivalent to or better than that of the original Tenant hereunder or such financial condition is otherwise reasonably satisfactory to Landlord, taking into account the then remaining obligations under this Lease.

(b) Tenant shall have the right to seek an assignment or subletting of the Leased Premises, or a reasonable portion thereof, to a person or entity other than pursuant to a Permitted Transfer, in accordance with the following conditions. In the event Tenant intends to assign this Lease or sublet the Leased Premises, or any portion thereof, to a person or entity other than pursuant to a Permitted Transfer, Tenant shall give Landlord written notice of such intent. Tenant shall provide Landlord with (i) the name of the proposed assignee or subtenant, (ii) such information as to the financial responsibility and standing of such assignee or subtenant as Landlord shall reasonably require, (iii) the proposed form of sublease or assignment or (if such form is not then available and Tenant desires to obtain Landlord's response under clause (b) prior to Tenant's negotiation of such form) a letter of intent or term sheet containing all of the relevant terms and provisions upon which the proposed assignment or subletting is to be made as Landlord shall reasonably require, and (iv) any additional information or documents reasonably requested by Landlord after receipt of Tenant's initial submission (in which event Tenant shall provide such additional information or documents to Landlord). If Tenant proposes to sublet a portion of the Leased Premises, Landlord reserves the right to reasonably approve the size and configuration of such separately demised portion of the Leased Premises and to require Tenant at the end of the Term to remove such internal demising walls and restore the affected areas to single tenant occupancy. Tenant shall not assign this Lease, nor sublet the Leased Premises or any portion thereof to any person or entity who is then a tenant in the Project (unless Landlord, after Tenant's request, notifies Tenant that no suitable space is available therein to lease to such party on a direct basis); any party with whom Landlord or any affiliate of Landlord is then negotiating with respect to space in the Project; or any entity owned by, owning, or affiliated with, directly or indirectly, any tenant or other party as set forth in this sentence.

(c) Landlord shall have a period of thirty (30) days after receipt of (x) Tenant's notice under clause (b) containing the items under clauses (b)(i) through (b)(iii) above and (y) any additional information requested by Landlord under clause (b)(iv), within which to notify Tenant in writing whether or not Landlord elects to terminate this Lease as to the space in the Leased Premises so affected as of the date specified by Tenant for the proposed term thereof (if the sublease or assignment is for substantially all of the remaining Term), in which event Tenant will be relieved of all further obligations hereunder as to such space from and after such date for such term. If Landlord should fail to notify Tenant in writing of such election within said thirty-(30)-day period, Landlord shall be deemed to have elected not to terminate the Lease as provided above. If Landlord does make the election to terminate the Lease as provided above, then Tenant may, by notice given to Landlord within ten (10) days after Landlord makes such election, rescind Tenant's notice under clause (b), in which event Landlord's election to terminate shall not be effective, and Tenant shall recommence the process under this Section 4.06 with respect to any further sublease or assignment. If Landlord shall not elect to terminate the Lease as provided above, then Landlord shall then approve or disapprove

the proposed assignee or sublessee within the aforesaid thirty-(30)-day period, which approval shall not be unreasonably withheld or delayed so long as (x) the use of the Leased Premises by such proposed assignee or sublessee would be a Permitted Use, (y) the character and business reputation of the proposed assignee or sublessee is consistent with the character of the Building as a first-class office building, and (z) the proposed assignee or sublessee is of sound financial condition as reasonably determined by Landlord. In no event shall a failure by Landlord to approve a proposed subtenant or assignee cause a termination of this Lease. If Landlord terminates this Lease as to a portion of the Leased Premises as provided above, Landlord and Tenant shall enter into a modification of this Lease so as to equitably reflect the effect of such termination of such space.

(d) In the event, if any, that (i) all rent and other consideration which Tenant receives as a result of a Transfer (as defined below) exceeds (ii) the Rent payable to Landlord for the portion of the Leased Premises and Term covered by the Transfer, then Tenant shall, at Landlord's election, pay to Landlord an amount equal to fifty percent (50%) of such excess, from time to time on a monthly basis upon Tenant's receipt of such excess; provided that in determining any such excess, Tenant may deduct from the excess all reasonable and customary expenses directly incurred by Tenant in connection with such Transfer (including, without limitation, reasonable legal fees, commissions, advertising and marketing costs, and other reasonable costs and concessions relating to such sublease or assignment), except that any construction costs incurred by Tenant in connection with such Transfer shall be deducted on a straight-line basis over the term of the applicable Transfer. If Tenant is in Default, Landlord may require that all sublease payments be made directly to Landlord, in which case Tenant shall receive a credit against Rent in the amount of Tenant's share of payments received by Landlord. This clause (d) shall not apply to any sublease or assignment pursuant to a Permitted Transfer under Section 4.06(a) above.

(e) In any subletting or assignment proposed to be undertaken by Tenant, Tenant shall in good faith seek to obtain, and shall not advertise or publicly offer the space for a rate less than, the Fair Market Net Rent for the space in question. The foregoing shall not restrict Tenant from listing the space with a broker (so long as the rate, if less than the Fair Market Rent Rate, is not advertised or publicized by Tenant's broker, including without limitation on any website, flyer, or other listing or marketing materials), from responding to inquiries from particular prospective tenants as to the proposed rent rate, or from negotiating with a particular prospective tenant for a proposed subletting or assignment in accordance with this Section 4.06 at a rate less than the Fair Market Rent Rate.

(f) Except as expressly provided in this Section 4.06 above, Tenant shall not assign the Lease or sublease the Leased Premises or any portion thereof. In the case of each assignment or sublease hereunder (each, a "Transfer"): (i) Tenant and the assignee or subtenant, as the case may be, shall execute an assignment or sublease which shall include terms that do not materially differ from those theretofore disclosed to Landlord and shall otherwise be in a form reasonably approved by Landlord (provided that, in the case of a Permitted Transfer, the form of such instrument shall not require Landlord's approval so long as the same contains terms that are not inconsistent with the provisions of this Lease, including without limitation the terms of this Section 4.06

applicable to such Permitted Transfer as set forth above); (ii) within five (5) Business Days after the execution thereof, an executed copy of the assignment or sublease shall be delivered to Landlord; (iii) except in the case of a Permitted Transfer, the terms and provisions of any such assignment or sublease shall specifically prohibit the assignment of the interest of the sublessee or assignee, or the sub-subletting of all or any portion of the Leased Premises covered by the sublease without the prior written consent of the Landlord, which consent may be withheld in Landlord's absolute discretion, unless otherwise expressly agreed by Landlord at the time of such consent; (iv) no assignment or subletting shall affect the continuing primary liability of Tenant (which, following assignment or sublease, shall be joint and several with the assignee or subtenant, as the case may be; however, Landlord shall have no obligation to name any such assignee or sublessee, in connection with enforcing any of Landlord's right against Tenant hereunder); (v) no consent by Landlord to any of the foregoing in the specific instance shall operate as a waiver in any subsequent instance; (vi) no assignment or subletting requiring Landlord's consent hereunder shall be permitted to the extent the same causes Landlord to be in default under any Mortgage or Tenant to be in default under any Subordination, Non-Disturbance and Attornment Agreement to which it is a party; (vii) no assignment or subletting shall permit the assignee, sublessee or any other person or entity having an interest in the possession, use, occupancy or utilization of the Leased Premises, to receive or to pay rental or payment on account of the use, occupancy or utilization of the Leased Premises based in whole or in part on the net income or profits derived by any person or entity from any property leased, used, occupied or utilized (other than an amount based on a fixed percentage or percentages of receipts of sales); and (viii) no assignment shall be binding upon Landlord, unless Tenant shall deliver to Landlord an instrument in recordable form which contains a covenant of assumption by the assignee and in form and in substance reasonably satisfactory to Landlord) running to Landlord and all persons claiming by, through and under Landlord, but the failure or refusal of the assignee to execute such instrument of assumption shall not release or discharge the assignee from its primary liability as Tenant hereunder. If Tenant enters into any sublease or assignment, Landlord may from time to time require that such subtenant or assignee agree directly with Landlord to be liable, jointly and severally with Tenant, to the extent of the obligation undertaken by or attributable to such subtenant or assignee, for the performance of Tenant's agreements under this Lease (including payment of rent and other charges under the sublease or assignment), and every sublease or assignment shall so provide. In the event of an Event of Default by Tenant under the Lease, Landlord may collect rent and other charges from the subtenant or assignee and apply the net amount collected to the rent and other charges due under the Lease, but no such collection shall be deemed a waiver of the provisions of Section 4.06, or the acceptance of the subtenant or assignee, as a tenant, or a release of Tenant from its direct and primary liability for the performance of all of Tenant's obligations under the Lease.

(g) No assignment or subletting by Tenant shall relieve Tenant of any obligation under this Lease. Any assignment or subletting which conflicts with the provisions hereof shall be void.

(h) If Tenant has failed to execute an assignment or sublease within six (6) months following the giving by Tenant of written notice of its intent to effect

an assignment or subletting under Section 4.06(b) above, Tenant shall again be obligated to notify Landlord of any intent to assign this Lease or sublet all or any portion of the Leased Premises, and Landlord shall again have the right to approve any proposed assignment or sublease or to recapture under Section 4.06(c).

4.07 Alterations and Surrender. Tenant shall not make or allow to be made any alterations or physical additions in or to the Leased Premises without obtaining the prior written consent of Landlord, which consent shall not be unreasonably withheld, conditioned or delayed with respect to proposed alterations and additions which (i) comply with all applicable laws, ordinances, rules and regulations, (ii) are compatible with the Building and its mechanical, electrical, HVAC and life safety systems, and do not excessively burden the capacity of

such systems; (iii) will not interfere with the use and occupancy of any other portion of the Building; (iv) will not affect the structural integrity of the Building; (v) will not require any unusual expense to re-adapt the Leased Premises, or otherwise diminish the value of the Leased Premises, for any general purpose office use; and (vi) satisfy the standards and comply with the procedures and requirements required for Tenant Improvements, as set forth in Exhibit B. (Notwithstanding the foregoing, Tenant shall not be required to obtain Landlord's prior approval of plans for cosmetic alterations in the Leased Premises (such as painting, carpeting, or installations of built-in workstations, furniture, cabinets, or decorations), provided that such alterations (i) comply with the preceding sentence and do not include or affect any mechanical, electrical, or plumbing work or life safety or other Building systems or any structural elements of the Building, (ii) the cost of such alterations does not exceed $10 per square foot of Net Rentable Area in the aggregate per project (or related series of projects) and (iii) such alterations shall otherwise be performed by Tenant, with reasonable prior notice to Landlord, in accordance with the terms and provisions of this Lease including, without limitation, this Section 4.07.) Specifically, but without limiting the generality of the foregoing, Landlord's right of consent shall encompass plans and specifications for proposed alterations or additions, construction means and methods, the identity of any contractor or subcontractor to be employed on the work of alterations or additions, and the time for performance of such work. Tenant shall supply to Landlord any documents and information reasonably requested by Landlord in connection with its consent hereunder. Landlord's approval of the plans, specifications and working drawings for Tenant's alterations shall create no responsibility or liability on the part of Landlord for their completeness, design sufficiency, or compliance with all laws, rules and regulations of governmental agencies or authorities. All alterations and additions permitted hereunder shall be made and performed by Tenant without cost or expense to Landlord. Tenant shall take such steps as Landlord or its mortgagee may deem reasonably necessary to avoid the filing, perfection or enforcement of any lien for labor or materials against the Land or the Building by reason of work performed by or on behalf of Tenant, including without limitation the furnishing of such payment and performance bonds as Landlord may reasonably require (based on the scope of the work) for the particular work in question. All Tenant Improvements under Section 3.05, and all alterations, physical additions or improvements made to the Leased Premises by Tenant under this Section 4.07, shall become the property of Landlord upon the termination of this Lease and shall be surrendered to Landlord upon the termination of this Lease by lapse of time or otherwise; provided, however, that (a) this clause shall not apply to business equipment, exercise equipment, trade fixtures, or related installations or any other moveable equipment, furniture or personal property, all of which shall

be removed by Tenant, at Tenant's expense, prior to the expiration of the Term, and (b) Tenant shall further remove (i) any private bathrooms, shower facilities, raised flooring, internal stairs, and telecommunications/data cabling (subject to the next sentence) at the expiration or earlier termination of this Lease and (ii) any other special installations, plumbing, fixtures or other additions or improvements that would require unusual expense to re-adapt the Leased Premises for general office purposes and are so specified by Landlord for removal (which items Landlord, if so requested by Tenant, shall specify at the time of Landlord's approval of the construction documents for such work), all of which shall be removed by Tenant, at Tenant's expense, prior to the expiration of the Term. Tenant shall be responsible for leaving the Leased Premises clean, tenantable, and otherwise in good condition, reasonable wear and tear and damage by fire or other casualty excepted. Title to all alterations, physical additions or improvements and Tenant Improvements not removed by Tenant pursuant to this paragraph on or prior to the termination of the Term shall automatically be conveyed and transferred by Tenant to Landlord upon such expiration or termination, and shall be deemed abandoned by Tenant and shall thereupon become the property of Landlord. Tenant shall execute such documentation confirming and ratifying such conveyance and transfer as Landlord shall reasonably require. Tenant shall repair at its sole cost and expense all damage caused to the Leased Premises or the Building by removal of Tenant's moveable equipment, or graphics, or furniture and such other alterations and additions as Tenant shall be allowed or required to remove from the Leased Premises by Landlord. If Tenant fails to perform any of its obligations under this paragraph prior to the expiration or earlier termination of the Term, then (without limiting any other remedies for such default) at Landlord's election at any time thereafter Landlord may perform such work for Tenant's account and at Tenant's expense, and upon demand Tenant shall reimburse Landlord for all reasonable costs thereof (including the administrative fee set forth in Section 3.06) as an extra service hereunder. The obligations of Tenant under this paragraph shall survive any expiration or termination of this Lease.

4.08 Compliance with Laws and Insurance Standards. Tenant shall not occupy for use, or permit any portion of the Leased Premises to be occupied or used, for any business or purpose which is disreputable or creates a fire hazard, or permit anything to be done which would in any way increase the rate of insurance coverage on the Building and/or its contents (it being acknowledged that general office uses consistent with the Permitted Uses do not result in such an increase). If Tenant does or permits anything to be done which shall increase the cost of any insurance policy required to be carried hereunder, then Tenant shall reimburse Landlord, within thirty (30) days after demand, for any such additional premiums. Landlord shall deliver to Tenant a written statement setting forth the amount of any such insurance cost increase and showing in reasonable detail the manner in which it has been computed. Tenant shall comply with all laws, ordinances, orders, rules and regulations (state, federal, municipal or promulgated by other agencies or bodies having or claiming jurisdiction) now in force or which may hereafter be in force related to the use, condition or occupancy of the Leased Premises (excluding any matters that are part of Landlord's maintenance or repair obligations for structural portions of the Building, base building systems, and other matters as set forth in Section 3.06) or the conduct of Tenant's business therein, including but not limited to, any requirements concerning hiring of employees and provisions for the disabled, and Tenant shall keep the Leased Premises equipped with all safety appliances required by any law or ordinance or other regulation of any public authority because of any use made by Tenant of the

Leased Premises, and shall procure all licenses and permits so required because of such use, and, if required by Landlord, do any work so required because of such use, it being understood that the foregoing provisions shall not be construed to broaden in any way the Permitted Use. Tenant's Alterations in and use of the Leased Premises shall comply with applicable base building structural load requirements, and nothing done by Tenant in its use or occupancy of the Leased Premises shall create, require or cause imposition of any requirement by any public authority for structural or other upgrading of or improvement to the Building. Tenant shall not allow to be brought into the Leased Premises or the Building any biologically or chemically active or other hazardous substances or materials, except for ordinary office and cleaning supplies used in the ordinary course of Tenant's business in compliance with applicable law. If a lender or governmental agency shall require monitoring or testing to ascertain whether there has been a release of such materials or substances, then the reasonable costs thereof shall be reimbursed by Tenant to Landlord if the requirement is based upon a release caused by Tenant or any person acting under or through Tenant.

4.09 Entry for Repairs and Leasing. Upon reasonable prior notice to Tenant (which may be given orally or in writing at least two (2) days in advance, except in the case of an emergency when no such notice shall be required), Landlord, its agents and representatives, shall have the right to enter the Leased Premises to inspect the same, to exercise such rights as may be permitted hereunder, to make repairs or alterations to the Building or other tenant spaces therein, to deal with emergencies, to post such notices as may be permitted or required by law to prevent the perfection of liens against Landlord's interest in the Building or to exhibit the Leased Premises to prospective tenants, purchasers, encumbrancers or others, or for any other purpose as Landlord may deem reasonably necessary or desirable; provided, however, that Landlord shall exercise all such entry rights into the Leased Premises in a manner consistent with Comparable Buildings in Downtown Boston and use reasonable efforts not to unreasonably interfere with Tenant's business operations. Except as set forth in Section 3.01(c), Tenant shall not be entitled to any abatement of Rent by reason of the exercise of any such right of entry.

4.10 No Nuisance. Tenant shall conduct its business and control its agents, employees, invitees and visitors in such manner as not to create any nuisance, or interfere with, annoy or disturb any other tenant or Landlord in its operation of the Building. Without limiting the generality of the foregoing, in the event Tenant desires to use a portion of the Leased Premises for a private exercise area (including related private shower and bathroom facilities), such facilities shall be solely for use by Tenant and its employees and any other permitted occupants of the Leased Premises under the terms of this Lease; provided that (a) any such exercise equipment shall be installed (e.g., with sufficient sound or vibration insulators) and operated only at times or in a manner that does not disturb any other tenant or occupant of the Building, (b) in the event that Landlord receives a complaint of any objectionable noise or vibration arising from Tenant's use of any such exercise equipment in the Leased Premises, Tenant will immediately, upon receipt of such notice and without any cure period, cease the use of the equipment creating such objectionable noise or vibration and shall not resume such use until the source or cause of the objectionable noise or vibration has been remedied, and (c) Landlord reserves the right to require Tenant to suspend the use of the exercise equipment that creates objectionable notice or vibration until such time as Landlord reasonably determines that the equipment will be used only at times or in a manner that does not disturb other tenants or occupants of the Building.

4.11 Subordination. This Lease and the rights of Tenant hereunder shall be subject and subordinate to the lien of any Mortgage, and to any and all advances made thereunder, interest thereon or costs incurred in connection therewith. Without the consent of Tenant, the holder of any such Mortgage shall have the right to elect to be subject and subordinate to this Lease, such subordination to be effective upon such terms and conditions as such holder may direct which are not inconsistent with the provisions hereof. Notwithstanding any foreclosure or sale under any such Mortgage (or deed in lieu thereof), but subject to the applicable terms of a subordination, nondisturbance and attornment agreement as provided below, this Lease (at the option of the holder of the Mortgage, the purchaser at a foreclosure sale or grantee of deed in lieu of foreclosure) shall remain in full force and effect, but Tenant shall attorn to the holder or the purchaser at any such sale or foreclosure or the grantee of any such deed. Upon such attornment, this Lease shall continue in full force and effect as a direct lease between such mortgagee, purchaser or grantee, as a successor landlord, and Tenant, upon all the terms, conditions and covenants set forth herein, except that such mortgagee, purchaser or grantee (unless formerly the Landlord under this Lease) shall not be (a) bound by any payment of Rent for more than one month in advance; (b) bound by any amendment or modification of this Lease made without the consent of the holder of the Mortgage; (c) liable in any way to Tenant for any act or omission, neglect or default on the part of Landlord under this Lease, (d) obligated to perform any work or improvements to be done by Landlord in the Leased Premises; or (e) subject to any counterclaim or set off which theretofore accrued to Tenant against Landlord. (The preceding sentence shall not be construed to relieve the then existing Landlord from its obligations to perform the Landlord's routine maintenance and repair obligations under this Lease during the period of its ownership.) Tenant further agrees that this Lease shall be subject and subordinate to any amendment hereafter made to the recorded instruments referenced in Section 3.07, and to any other instrument by which Landlord may subject the Building and the Land to easements in connection with the development, redevelopment, alteration, improvement, operation, maintenance or repair thereof, provided the same do not prevent access to the Leased Premises or unreasonably interfere with Tenant's use of the Leased Premises. The provisions of this Section 4.11 shall be self-operative, with no further instrument of subordination being required. Within ten (10) days after request, Tenant shall execute, acknowledge and deliver any documents reasonably appropriate to confirm such provisions. No owner of the Leased Premises shall be liable under this Lease except for breaches of Landlord's obligations occurring while such person is the owner of the Leased Premises.

Notwithstanding the foregoing paragraph, so long as Tenant is not in default under the Lease (beyond any applicable notice and cure period), Tenant's obligation to subordinate the Lease to a future mortgage as set forth above shall be conditioned on such mortgagee executing and delivering a subordination, non-disturbance and attornment agreement in such mortgagee's customary form for comparable transactions (which, among other things, will provide for a customary non-disturbance of Tenant's occupancy of the Leased Premises in the event of a foreclosure or deed in lieu of foreclosure, subject to customary qualifications regarding Tenant's compliance with its obligations under the Lease), provided that Tenant shall be responsible for any costs or fees in connection therewith. If so requested by Tenant, Landlord shall request that such mortgagee make commercially reasonable changes to the mortgagee's form for comparable

transactions, provided that Tenant shall be responsible for all costs or fees imposed by such mortgagee in connection with any requests for such changes.

4.12 Estoppel Certificate. At Landlord's request, Tenant shall execute (within fifteen (15) days after Tenant receives any such request) estoppel certificates on a form reasonably requested by Landlord, addressed to (i) any mortgagee or prospective mortgagee of Landlord or (ii) any purchaser or prospective purchaser of all or any portion of, or interest in, the Building, certifying as to such facts (if true) and agreeing to such notice provisions and other matters as such mortgagee(s) or purchaser(s) may reasonably require; provided, however, that in no event shall any such estoppel certificate require an amendment of the provisions hereof or otherwise affect or abridge Tenant's rights hereunder. At Tenant's request, Landlord shall execute (within fifteen (15) days after Landlord receives any such request) an estoppel certificate to a proposed subtenant, assignee, or lender of Tenant on a form reasonably requested by Tenant, certifying as to such facts (if true) regarding the Lease as are customarily addressed in such estoppel certificates; provided, however, that in no event shall any such estoppel certificate require an amendment of the provisions hereof or otherwise affect or abridge Landlord's rights hereunder.

4.13 Tenant's Remedies. Tenant shall look solely to Landlord's interest in the Building for recovery of any judgment from Landlord. Landlord, its agents, its employees, and (if Landlord is a partnership or joint venture) its partners, whether general or limited, or (if Landlord is a corporation), its directors, officers, and shareholders, or (if Landlord is a limited liability company), its members, manager, and officers, or (if Landlord is a trust) its trustees and beneficiaries, shall never be personally liable for any such judgment. Any lien obtained to enforce any such judgment and levy of execution thereon shall be subject and subordinate to any Mortgage. Landlord shall not be deemed to be in default of any obligation hereunder unless Tenant has given Landlord written notice of the alleged default specifying the applicable provision of this Lease and the same remains uncured after thirty (30) days (or, except in cases of imminent risk to person or property, such longer period as may be reasonably necessary to cure the same). In no event shall Landlord be liable for consequential or indirect damages. In addition to the other remedies provided in this Lease, Tenant shall be entitled to the restraint by injunction of the violation or attempted or threatened violation of any of the covenants, conditions or provisions of this Lease by Landlord or to a decree compelling specific performance of any such covenants, conditions or provisions. No termination remedy that is not expressly set forth in this Lease for any breach or failure by Landlord to perform any obligation under this Lease shall be implied or applicable as a matter of law. This Lease shall be construed as though Landlord's and Tenant's covenants contained herein are independent and not dependent, and Tenant hereby waives the benefit of any statute or judicial law to the contrary.

4.14 Rules and Regulations. Tenant shall comply with the rules and regulations for the Building attached as Exhibit C and such amendments thereto as Landlord may adopt from time to time with prior notice to Tenant (the "Building Rules and Regulations"). The Building Rules and Regulations shall not be enforced or enacted against Tenant in a discriminatory manner. In the event of a conflict between the Building Rules and Regulations and the specific terms of this Lease, the terms of the Lease shall govern.

4.15 Personal Property at Tenant's Risk. All of the furnishings, fixtures, equipment, effects and property of every kind, nature, and description of Tenant and of all persons claiming by, through and under Tenant which, during the continuance of this Lease or any occupancy of the Leased Premises by Tenant or anyone claiming under Tenant, may be on the Leased Premises or elsewhere in the Building, shall be at the sole risk and hazard of Tenant to the maximum extent permitted by law, and if the whole or any part thereof shall be destroyed or damaged by fire, water or otherwise, by the leakage or bursting of water pipes, steam pipes, or other pipes, or by theft or from any other cause, no part of said loss or damage is to be charged to or be borne by Landlord, except Landlord shall in no event be held harmless or exonerated for any liability to Tenant or to any other person, for any injury, loss, damage or liability to the extent such indemnity, hold harmless or exoneration is prohibited by law.

4.16 Payment of Landlord's Expenses. Tenant shall pay, as Additional Rent, all reasonable out of pocket costs, counsel and other fees incurred by Landlord in connection with all requests by Tenant for consent or approval under this Lease, and the enforcement by Landlord of any obligation of Tenant under this Lease with which Tenant failed to comply.

4.17 Letter of Credit. On the execution of this Lease, Tenant shall deliver to Landlord a letter of credit securing the performance of the obligations of Tenant hereunder, in the amount specified therefor in the Basic Lease Information Sheet. Such letter of credit shall comply with the requirements of Exhibit D attached hereto (as more particularly defined therein, the "Letter of Credit"), which is incorporated herein by reference. Any cash security deposit from time to time held hereunder may be mingled with other funds of Landlord and no fiduciary relationship shall be created with respect to such deposit, nor shall Landlord be liable to pay Tenant interest thereon. If Tenant shall fail to perform any of its obligations under this Lease after the expiration of any applicable notice and cure period (or fail to perform any of its obligations under the Lease and transmittal of a default notice or running of a cure period is barred or tolled by applicable law), Landlord may, but shall not be obliged to, draw on the Letter of Credit and/or apply any cash security deposit to the extent necessary to cure such failure to pay, and Tenant shall reinstate such cash security deposit or Letter of Credit to the original amount thereof upon demand. Within thirty (30) days after the expiration or sooner termination of the Term the cash security deposit or Letter of Credit, to the extent not applied, shall be returned to the Tenant, without interest.

As used herein, the "Initial Amount" shall mean the amount of the Letter of Credit set forth in the Basic Lease Information Sheet. In the event that, as of the applicable Reduction Date set forth below, Tenant shall then have at least Fifteen Million Dollars ($ 15,000,000.00) in available cash as evidenced by documentation provided by Tenant and reasonably satisfactory to Landlord, the Initial Amount of the Letter of Credit required to be maintained hereunder may be decreased upon Tenant's request to an amount equal to the Reduced LC Amount set forth below for the applicable Reduction Date; provided that no draw on the Letter of Credit has been made and no default by Tenant (after the expiration of any applicable notice and cure periods) has occurred within the preceding twelve-(12)-month period and no event has occurred or condition then exists which with notice and the passage of time would constitute such a default.

Reduction Date	Reduced LC Amount
18 months after Rent Commencement Date	$ 150,000.00
36 months after Rent Commencement Date	$ 75,000.00

Upon the satisfaction of the conditions set forth in the preceding sentence for the reduction of the amount of the Letter of Credit, Landlord shall provide such confirmation or acknowledgement as Tenant may reasonably request to effect the reduction of the Letter of Credit in accordance with the preceding sentence.

4.18 Tenant's Financial Condition. Within ten (10) Business Days after request from Landlord in connection with a sale, financing or other investment in the Project (but not more often than once in any twelve-(12)-month period), Tenant shall deliver to Landlord a copy of Tenant's financial statements (audited, if available) for the most recent fiscal year for which such statements are available and (if not audited) certified by Tenant's chief financial officer. Such financial statements shall be requested only as reasonably necessary to satisfy the needs of Landlord's current and prospective mortgagees, lenders, purchasers, and investors. All financial statements shall be confidential

and shall be used only for the purposes set forth in this Lease. If requested by Tenant, any such non-public financial information shall be provided pursuant to a confidentiality agreement in such form as may be mutually and reasonably acceptable to the parties.

4.19 Energy Conservation. Tenant agrees to reasonably cooperate with Landlord and to abide by all Building regulations which Landlord may, from time to time, reasonably prescribe, consistent with a first-class high-rise office complex in downtown Boston, for the proper functioning and protection of the heating, air-conditioning, lighting, and electrical systems and in order to maximize the effect thereof and to conserve heat, air-conditioning, and electricity. Notwithstanding anything to the contrary in this Lease, Landlord may institute such policies, programs and measures as may be in Landlord's reasonable judgment necessary, required or expedient for the conservation or preservation of energy or energy services, or as may be necessary to comply with applicable codes, rules, regulations or standards, so long as such policies, programs or measures do not adversely affect Tenant's operations in a manner inconsistent with the operation of first-class commercial office space in Comparable Buildings in Downtown Boston.

4.20 Discharge of Mechanic's and Materialman's Liens. Tenant agrees within ten (10) Business Days after notice of filing to discharge of record by payment, filing of the necessary bond, order of a court of competent jurisdiction, or other means acceptable to Landlord, any mechanic's, materialman's or other lien against the Leased Premises and/or Landlord's or Tenant's interest therein (or any portion of the Building when such lien arises out of work performed or claimed to have been performed in or on the Leased Premises by Tenant or any party acting under or through Tenant), which liens may arise out of any payment due for, or purported to be due for, any labor, services, materials, supplies or equipment alleged to have been furnished to or for the Tenant in, upon or about the Leased Premises. In the event Tenant contests any such mechanic's or materialman's liens, Tenant shall either (i) deposit with Landlord an amount equal to the claims made by such lien, together with interest thereon as it may from time to time become due, as security for the payment and discharge thereof prior to execution or (ii) deliver to Landlord a bond of a recognized surety authorized to write surety bonds in Massachusetts

assuring the payment and removal of such lien, together with any interest or penalty thereon, and naming Landlord as a co-obligee. Any judgment or other process issued in such a contest shall be paid and discharged before execution thereof. If Tenant fails to keep this covenant, in addition to all other remedies available to Landlord under this Lease, Landlord may, at its option, purchase a surety bond at twice the amount of the lien, securing such lien, and Tenant agrees to pay to Landlord, as Additional Rent, the cost thereof, plus (i) an administrative charge often percent (10%) of such cost to compensate Landlord for its expenses and overhead incurred as a result of Tenant's failure to perform its obligations hereunder, and (ii) Landlord's reasonable attorneys' fees.

ARTICLE 5. CASUALTY, EMINENT DOMAIN

5.01 Landlord's Casualty Insurance. Landlord shall maintain, or cause to be maintained, a policy or policies of all risk or special form insurance insuring the Building against loss or damage by fire or other insurable hazards and contingencies, with coverages and amounts required from time to time by Landlord's first mortgagee or, if there is no such requirement, in then commercially reasonable types of coverage and amounts as determined from time to time by Landlord to be necessary or appropriate for the Building as a first-class mixed-use project in the Back Bay district of Boston; provided, that Landlord shall not be obligated to insure any furniture, equipment, machinery, goods or supplies not covered by this Lease which Tenant may keep or maintain in the Leased Premises, or any alteration, addition or improvement that exceeds the level of finishes represented by Building Standard Improvements. If the annual premiums charged Landlord for such casualty insurance exceed the standard premium rates because the nature of Tenant's operations in the Leased Premises results in extra-hazardous exposure, then Tenant shall, upon receipt of appropriate premium invoices, reimburse Landlord for such increases in premium as Additional Rent.

5.02 Landlord's Liability Insurance. Landlord shall maintain, or cause to be maintained, a policy or policies of commercial general liability insurance, with coverages and amounts required from time to time by Landlord's first mortgagee or, if there is no such requirement, in then commercially reasonable types of coverage and amounts as determined from time to time by Landlord to be necessary or appropriate for the Building as a first-class mixed-use project in the Back Bay district of Boston.

5.03 Tenant's Insurance. Tenant shall maintain the following coverages in the following amounts:

(a) Commercial General Liability insurance covering claims of bodily injury, personal injury, and property damage arising out of Tenant's operations and contractual liabilities, including coverage formerly known as broad form, on an occurrence basis, with minimum primary limits of $1,000,000 each occurrence and $2,000,000 annual aggregate (and not more than $25,000 self-insured retention) and a minimum excess/umbrella limit of $2,000,000.

(b) Property insurance covering (i) all office furniture, business and trade fixtures, office equipment, free-standing cabinet work, movable partitions, merchandise and all other items of Tenant's property in the Leased Premises installed by, for, or at the expense of Tenant ("Tenant's Property"), and (ii) any Tenant Improvements and insurance on all plate glass in, or enclosing,

the Leased Premises for the replacement value of such plate glass ("Tenant-Insured Improvements"), and business interruption insurance covering periods of not less than one (1) year in the following amounts: (i) for the first twelve (12) months of the Term an amount equal to 1½ times the Gross Rent; and (ii) for each succeeding twelve-(12)-month period, in amounts not less than the Gross Rent and Tenant's other operating expenses for the preceding twelve-(12)-month period, provided that Tenant may, at its option, elect not to maintain business interruption coverage, provided, however, that if Tenant elects not to maintain such business interruption coverage, any loss or damage to Tenant which would have been covered by such business interruption coverage shall be deemed, for the purposes of this Lease, to be covered by insurance. Such insurance shall be written on a special cause of loss form for physical loss or damage, for the full replacement cost value (subject to reasonable deductible amounts) without deduction for depreciation of the covered items and in amounts that meet any co-insurance clauses of the policies of insurance, and shall include coverage for damage or other loss caused by fire or other peril, including vandalism and malicious mischief, theft, water damage of

any type, including sprinkler leakage, bursting or stoppage of pipes, and explosion, and providing business interruption coverage for a period of one year (subject to the proviso above).

(c) Worker's Compensation and Employer's Liability or other similar insurance to the extent required by Law. If alcoholic beverages are sold, used, delivered or stored on, in or from the Leased Premises, and such alcoholic beverages shall only be sold, used, delivered or stored if Tenant's Permitted Use expressly so allows, Tenant shall maintain throughout the Term at its expense, liquor liability insurance or dram shop liability insurance (as applicable) ("Dram Shop Insurance") with combined single limits of not less than $2,000,000 per occurrence covering any claims relating to the manufacture, storage, sale, use or giving away of any alcoholic or other intoxicating liquor or beverage, which claims could be asserted against Landlord, Tenant or the Leased Premises.

(d) The minimum limits of insurance required to be carried by Tenant shall not limit Tenant's liability. Such insurance shall (i) be issued by an insurance company that has an A.M. Best rating of not less than A-VIII; (ii) be in form and content reasonably acceptable to Landlord; and (iii) provide that it shall not be canceled or materially changed without thirty (30) days' prior notice to Landlord, except that ten (10) days' prior notice may be given in the case of nonpayment of premiums. Tenant's Commercial General Liability Insurance shall (a) name Landlord, Landlord's managing agent, and any other party designated by Landlord ("Additional Insured Parties") as additional insureds; and (b) be primary insurance as to all claims thereunder and provide that any insurance carried by Landlord is excess and non-contributing with Tenant's insurance. Landlord shall be designated as a loss payee with respect to Tenant's Property insurance on any Tenant-Insured Improvements. Tenant shall deliver to Landlord, on or before the Term Commencement Date and at least fifteen (15) days before the expiration dates thereof, certificates from Tenant's insurance company on the forms currently designated "ACORD 28" (Evidence of Commercial Property Insurance) and "ACORD 25-S" (Certificate of Liability Insurance) or the equivalent. Attached to the ACORD 25-S (or equivalent) there shall be an endorsement naming the Additional Insured Parties as additional insureds which shall be binding on Tenant's insurance company and shall expressly require the insurance

company to notify each Additional Insured Party in writing at least thirty (30) days before any termination or material change to the policies, except that ten (10) days' prior notice may be given in the case of nonpayment of premiums. Upon Landlord's request, in connection with a claim by Landlord as an additional insured or loss payee under any such policy, Tenant shall deliver to Landlord, in addition to such certificates, copies of the policies of insurance required to be carried under Section 5.03(a) showing that the Additional Insured Parties are named as additional insureds.

(e) Tenant shall maintain such increased amounts of the insurance required to be carried by Tenant under this Section 5.03, and such other types and amounts of insurance covering the Leased Premises and Tenant's operations therein, as may be reasonably requested by Landlord, but not in excess of the amounts and types of insurance then being required by landlords of Comparable Buildings in Downtown Boston. In the event that Tenant fails to provide evidence of insurance required to be provided by Tenant hereunder, Landlord shall be authorized (but not required) to procure such coverage in the amounts stated with all costs thereof to be chargeable to Tenant as Additional Rent, and payable by Tenant upon receipt of written invoice thereof.

5.04 Indemnity and Exoneration. Except to the extent such indemnity or exoneration is prohibited by law,

(a) Landlord shall not be liable to Tenant for injury to any person or any loss or damage to any property or any inconvenience caused by (i) theft, burglary or acts of unauthorized persons in on about the Building, (ii) any act of Force Majeure or (iii) except as expressly provided in this Lease, any repair or alteration of any part of the Building or failure to make any such repair;

(b) Except to the extent of Landlord's negligence or willful misconduct, Tenant shall indemnify Landlord and hold Landlord harmless of and from any and all loss, cost, damage, injury or expense arising out of or related to claims of injury to or death of persons or damage to property occurring or resulting directly or indirectly from the use or occupancy of the Leased Premises or the activities of Tenant in or about the Leased Premises or from the negligence or misconduct of Tenant elsewhere in the Building, such indemnity to include, without limitation, the obligation to provide all costs of defense against any such claims; and

(c) Tenant shall hold and save Landlord harmless and indemnify Landlord of and from any and all loss, cost, damage, injury or expense arising out of or in any way related to any breach by Tenant of its obligations under this Lease (subject to the limitations set forth in Section 6.03 below) or any claims for work or labor performed, materials or supplies furnished to or at the request of Tenant or in connection with performance of any work done for the account of Tenant in the Leased Premises or the Building, such indemnity to include, without limitation, the obligation to provide all costs of defense against any such claim.

(d) Subject to the provisions of this Lease (including without limitation Section 5.05 below), Landlord shall indemnify and hold Tenant harmless of and from any claims against Tenant arising from the negligence or willful misconduct of Landlord in the Project Common Areas to the extent not arising from the negligent or wrongful act or omission by Tenant or any party acting under or

through Tenant, such indemnity to include, without limitation, the obligation to provide all costs of defense against any such claims.

5.05 Waiver of Subrogation Rights. Anything in this Lease to the contrary notwithstanding, Landlord and Tenant each waive all rights of recovery, claim, action or cause of action against the other, its agents (including partners, both general and limited), officers, directors, shareholders, members trustees, beneficiaries, or employees, for any loss or damage that may occur to the Leased Premises, or any improvements thereto, to the Building or to any personal property of such party therein, by reason of fire, the elements, or any other cause which is required to be insured against under the terms of the insurance policies obtained pursuant to this Lease, regardless of cause or origin, including negligence of the other party hereto, its agents, officers or employees; and each party covenants that no insurer shall hold any right of subrogation against such other party. Each party shall advise its insurers of the foregoing waiver of subrogation and such waiver shall be a part of each policy maintained by Tenant which applies to the Leased Premises, any part of the Building or Tenant's use and

occupancy of any part thereof; provided that this waiver shall be null and void if such waiver is not generally obtainable from insurance companies in the Commonwealth of Massachusetts, and provided further that all costs associated with obtaining insurer consent shall be borne by the party benefited by such waiver.

5.06 Condemnation and Loss or Damage.

(a) If the Leased Premises or any substantial portion thereof or any portion of the Building shall be taken or condemned for any public purpose to such an extent as to render the Leased Premises or such portion untenantable, this Lease shall, at the option of either party (provided such option shall be exercised by the giving of notice by the exercising party to the other party within sixty (60) days from the date the exercising party has been notified in writing of such taking or condemnation) forthwith cease and terminate as of the date of the taking. All proceeds from any taking or condemnation of the Leased Premises shall belong to and be paid to Landlord and Tenant hereby assigns to Landlord its interest in said proceeds subject to the rights of any holder of any Mortgage; provided, however, that Landlord shall cooperate with Tenant if Tenant seeks, in a separate proceeding, to recover, at its cost and expense, compensation for its moving expenses and personal property. In no event shall any such recovery by Tenant have the effect of diminishing or delaying the award payable to Landlord on account of any taking or condemnation.

(b) In the event of a temporary taking of a portion of the Leased Premises not exceeding thirty (30) days, there shall be an equitable abatement of Rent with respect to the untenantable portion of the Leased Premises, and Tenant shall otherwise remain fully obligated for performance of all of the covenants and obligations on its part to be performed pursuant to the terms of this Lease and shall be entitled to any award for the use of such space during such temporary taking. For any temporary taking exceeding thirty (30) days, Gross Rent shall be equitably abated in proportion to the nature and extent of the taking, and for any temporary taking exceeding six (6) months the termination rights under (a) above shall apply. All proceeds awarded or paid with respect thereto shall belong to Landlord.

5.07 Damage Due to Fire and Casualty. In the event of a fire or other casualty in the Leased Premises, Tenant shall immediately give notice thereof to Landlord. In the event of a fire or other casualty in the Leased Premises, the following provisions shall then apply whether or not Tenant has given notice to Landlord:

(a) If the damage is limited solely to the Leased Premises and Landlord determines that the Leased Premises can be made tenantable with substantially all damage repaired within six (6) months from the date such work begins, then, subject to any limitation contained in any Mortgage, Landlord shall be obligated to rebuild the same and shall proceed diligently to do so; provided, however, that Landlord shall have no obligation to repair or restore the Leased Premises or Tenant Improvements except to the extent that Landlord realizes insurance proceeds, if any, sufficient for such purposes and for all other restoration and repair purposes and to the extent such proceeds are not applied on account of the indebtedness secured by any Mortgage.

(b) If portions of the Building outside the boundaries of the Leased Premises are damaged or destroyed (whether or not the Leased Premises are also damaged or destroyed) and Landlord determines that the Leased Premises and the Building can both be made tenantable with substantially all damage repaired within six (6) months from the date work begins, and provided that Landlord determines that such repair and restoration is economically feasible, then subject to any limitation contained in any Mortgage, Landlord shall be obligated to do so; provided, however, that Landlord shall have no obligation to repair or restore the Leased Premises or Tenant Improvements except to the extent that Landlord realizes insurance proceeds, if any, allocable thereto and sufficient for such purpose and for all other restoration and repair purposes.

(c) If neither subsection 5.07(a) nor 5.07(b) above applies, because Landlord has determined that either the Leased Premises or the Building, or both, as applicable, cannot be made tenantable within six (6) months from the date work begins, Landlord shall notify Tenant within sixty (60) days after the date of damage or destruction, and either Tenant or Landlord may terminate this Lease within thirty (30) days after the date of such notice; provided, however, that if the Leased Premises are not damaged Landlord shall not terminate the Lease unless it terminates all similarly situated leases in the Building; and provided further that Landlord or its mortgagee shall have the right to elect to reconstruct the Building and the Leased Premises, in which event Landlord or its mortgagee shall so notify Tenant within said sixty (60) day period and Tenant shall thereupon have no right to terminate this Lease, unless the restoration is not substantially completed within nine (9) months from the date of casualty (as reasonably extended for any delay by Tenant, or as reasonably extended for other Force Majeure event(s), but not in excess of three (3) months in the aggregate for such other Force Majeure event(s)), in which event Tenant may terminate the Lease within thirty (30) days thereafter if the restoration is not then substantially completed.

(d) During any period when the Leased Premises or any portion thereof are rendered untenantable by damage or destruction, Gross Rent shall abate proportionately until such time as the Leased Premises are made tenantable and no portion of the Rent so abated shall be subject to subsequent recapture.

(e) The proceeds from any insurance paid by reason of damage to or destruction of the Building or any part thereof, the Building Standard Improvements or any other element, component or property insured by Landlord shall belong to and be paid

to Landlord, subject to the rights of the holder of any Mortgage, and Tenant hereby assigns to Landlord any interest in said proceeds.

(f) Notwithstanding any provisions contained in this Section 5.07 to the contrary in no event shall any fire or other casualty give Tenant the right to require or demand that Landlord repair or restore any part of the Building (other than the Leased Premises or access thereto, and then only to the extent required elsewhere in this Section 5.07).

ARTICLE 6. DEFAULT

6.01 Events of Default. The occurrence of any of the following shall constitute an "Event of Default" on the part of the Tenant:

(a) Nonpayment of Rent. Failure to pay any payment of Rent (or any installment or portion thereof) upon the date when payment is due, such failure continuing for a period of five (5) Business Days after written notice of such failure; provided, however, that Landlord shall not be required to provide such notice for any monthly installment of Gross Rent more than twice during any twelve-month period of the Term, the third such non-payment constituting default without requirement of notice;

(b) Other Obligations. Failure to perform any obligation, agreement or covenant under this Lease other than those matters specified in Section 6.01(a), such failure continuing for thirty (30) days after written notice of such failure (or, except in cases of imminent risk to person or property, such longer period as is reasonably necessary to remedy such default, provided that Tenant shall within such thirty (30) day period have commenced such remedy and thereafter Tenant shall continuously and diligently pursue such remedy until such default is cured), provided, however, that the cure period for any failure to perform any restoration obligations under Section 4.07 shall be five (5) Business Days;

(c) Abandonment. Abandonment of the Leased Premises or any part thereof during the Term. Tenant shall be deemed to have abandoned the Leased Premises if the Leased Premises remain substantially vacant or unoccupied for a period of ninety (90) consecutive days. Notwithstanding the foregoing, for purposes of this clause (c), Tenant shall not be deemed to have abandoned the Leased Premises provided Tenant continues to pay all Rent due and payable under this Lease for the Term of the Lease within applicable notice and cure periods;

(d) General Assignment. A general assignment by Tenant for the benefit of creditors;

(e) Bankruptcy. The filing of any voluntary petition in bankruptcy by Tenant, or the filing of an involuntary petition by Tenant's creditors, which involuntary petition remains undischarged or unstayed for a period of ninety (90) days. In the event that under applicable law the trustee in bankruptcy or Tenant has the right to affirm this Lease and continue to perform the obligations of Tenant hereunder, such trustee or Tenant shall, in such time period as may be permitted by the bankruptcy court having jurisdiction, cure all defaults of Tenant hereunder outstanding as of the date of the affirmance of this Lease and provide to Landlord such adequate assurances as may be necessary to

ensure Landlord of the continued performance of Tenant's obligations under this Lease (including, at a minimum, the maintenance of a security deposit equal to six (6) monthly installments of Gross Rent);

(f) Receivership. The employment of a receiver to take possession of all or substantially all of Tenant's assets or the Leased Premises, if such receivership remains undissolved for a period of sixty (60) days after creation thereof;

(g) Attachment. The attachment, execution or other judicial seizure of all or substantially all of Tenant's assets or the Leased Premises, if such attachment or other seizure remains undismissed or undischarged for a period of thirty (30) days after the levy thereof;

(h) Insolvency. The admission by Tenant in writing of its inability to pay its debts as they become due, the filing by Tenant of a petition seeking any reorganization, arrangement, composition, readjustment, liquidation, dissolution or similar relief under any present or future statute, law or regulation, the filing by Tenant of an answer admitting or failing timely to contest a material allegation of a petition filed against Tenant in any such proceeding, or if within ninety (90) days after the commencement of any proceeding against Tenant seeking any reorganization, or arrangement, composition, readjustment, liquidation, dissolution or similar relief under any present or future statute, law or regulation, such proceeding shall not have been dismissed. As used in subsections (d) through (h) above, the term "Tenant" shall be deemed to include any one or more of Tenant and any person or entity that is liable for Tenant's obligations under this Lease, including without limitation any Guarantor or general partner of Tenant.

6.02 Remedies upon Default.

(a) If an Event of Default occurs, Landlord shall have the right, upon notice but without any further demand or opportunity to cure, immediately to terminate this Lease, and at any time thereafter recover possession of the Leased Premises or any part thereof and expel and remove therefrom Tenant and any other person occupying the same, by notice, by entry or by any other lawful means, and again repossess and enjoy the Leased Premises without prejudice to any of the remedies that Landlord may have under this Lease, or at law or equity by reason of Tenant's default or of such termination.

(b) Even though Tenant has breached this Lease, this Lease and the right to recover Rent as it becomes due shall continue in effect for so long as Landlord does not terminate this Lease under Section 6.02(a) hereof. Acts of maintenance, preservation or efforts to lease the Leased Premises or the appointment of a receiver upon application of Landlord to protect Landlord's interest under this Lease shall not constitute an election to terminate Tenant's right to possession.

6.03 Damages upon Termination. Should Landlord terminate this Lease pursuant to the provisions of Section 6.02(a) hereof, Landlord shall have all the rights and remedies of a landlord in law or in equity. Upon such termination, in addition to any other rights and remedies of a Landlord may be entitled under applicable law, Landlord shall be entitled to recover from Tenant: (i) the worth at the time of award of the unpaid Rent and other amounts which had been earned at the time of

termination; (ii) the worth at the time of award of the amount by which the unpaid Rent which would have been earned after termination until the time of award exceeds the amount of such Rent loss that the Tenant proves could have been reasonably avoided; (iii) the worth at

the time of award of the amount by which the unpaid Rent for the balance of the Term after the time of award exceeds the rental value of the Leased Premises for the balance of the Term, taking into account reasonable projections of vacancy and the time required to re-lease the Leased Premises of at least six months; and (iv) any other amount necessary to compensate Landlord for all damages proximately caused by Tenant's failure to perform its obligations under this Lease; provided that Tenant shall not be liable for consequential damages (which term shall not be construed to apply to damage remedies expressly set forth in this Article 6 or Section 8.02). Tenant further covenants, as an additional cumulative obligation after any such termination, to punctually pay to Landlord all sums and perform all obligations which Tenant covenants in this Lease to pay and to perform, as if this Lease had not been terminated. In calculating the amounts to be paid by Tenant pursuant to this Section 6.03, Tenant shall be credited with any amount paid to Landlord pursuant to this Section 6.03 and also (in respect of the amounts referred to in (i) and (ii)) the net proceeds of rent obtained by Landlord by reletting the Leased Premises through the time of award, after deducting all Landlord's expenses in connection with such reletting, including, without limitation, all repossession costs, brokerage commissions, fees for legal services and expenses of preparing the Leased Premises for reletting as Landlord in its reasonable judgment considers advisable or necessary to relet the same, it being agreed by Tenant that Landlord may (x) relet the Leased Premises or any part thereof for a term or terms which may at Landlord's option be equal or less than or exceed the period which would otherwise have constituted the balance of the Term and may grant such concessions and free rent as Landlord in its reasonable judgment considers advisable or necessary to relet the same and (y) make such alterations, repairs and decorations in the Leased Premises as Landlord in its reasonable judgment considers advisable or necessary to relet the same, and no action of Landlord in accordance with the foregoing or failure to relet or collect rent under Landlord's reletting of the Leased Premises shall operate or be construed to release or reduce Tenant's liability as aforesaid. Any obligation imposed by law upon Landlord to relet the Leased Premises shall be subject to Landlord's right to lease the Leased Premises or any part thereof to high quality tenants, to develop the Building in a harmonious manner with an appropriate mix of uses, tenants, floor areas and terms of tenancies, and the like, and to first lease otherwise available space in the Building to prospective tenants, and Landlord shall not be required to lease any space at a rate or on other terms inconsistent with its marketing or leasing plan for the Building or to any party that Landlord determines is not of sound financial condition or is otherwise not in keeping with the first class image of the Building. The "time of award" shall refer to such time as (I) Tenant shall, as a settlement of the amounts due pursuant to this Section 6.03, pay to Landlord such sums pursuant to a written agreement in form and substance satisfactory to Landlord, or (II) the date on which a judgment shall be entered in a court of competent jurisdiction to the effect that Tenant shall pay Landlord the amounts due and owing pursuant to this Section 6.03. The "worth at the time of award" of the amounts referred to in (i) and (ii) shall mean such amounts together with interest at twelve percent (12%) per annum (or, if greater, the prime rate of interest from time to time published in the Wall Street Journal plus four percent per annum), provided that in no event shall such interest rate exceed the maximum rate allowed by law. The "worth at the time of award" of the amount referred to in (iii) shall mean such amounts as computed by reference to competent appraisal

evidence or the formula prescribed by and using the Federal Reserve Discount Rate.

6.04 Computation of Rent for Purposes of Default. For purposes of computing unpaid Rent which would have accrued and become payable under this Lease pursuant to the provisions of Section 6.03, unpaid Rent shall consist of the sum of:

(1) the total Net Rent for the balance of the Term, plus

(2) a computation of the Operating Cost and Impositions for the balance of the Term, the assumed Operating Cost for the calendar year of the default and each future calendar year in the Term to be equal to the Operating Cost for the calendar year prior to the year in which the default occurs compounded at a per annum rate equal to the mean average rate of inflation for the preceding five (5) calendar years as determined by the United State Department of Labor, Bureau of Labor Statistics Consumer Price Index (All Urban Consumers, All Items, 1967 equals 100) for the Metropolitan Area or Region of which Boston, Massachusetts is a part. If such Index is discontinued or revised, the average rate of inflation shall be determined by reference to the index designated as the successor or substitute index by the government of the United States.

6.05 Liquidated Damages. In lieu of the damages provided for in Section 6.03, Landlord, at its sole option, may by written notice to Tenant, at any time within six (6) months after this Lease is terminated pursuant to Section 6.02(a) or is otherwise terminated for breach of any obligation of Tenant, elect to recover, and Tenant shall thereupon pay, as liquidated damages, an amount equal to the aggregate of Gross Rent for the one-year period ending on the first day of the month immediately prior to any such termination (or, if lesser, the remainder of the Term), plus the amount of Gross Rent accrued and unpaid at the later of (i) the time of any such termination, or (ii) the time when Tenant vacates the Leased Premises, and less the amount of any recovery by Landlord under the provisions of Section 6.03.

6.06 Rights of Landlord in Bankruptcy. Nothing contained in this Lease shall limit or prejudice the right of Landlord to prove for and obtain in proceedings for bankruptcy or insolvency, by reason of the termination of this Lease, an amount equal to the maximum allowed by any statute or rule of law in effect at the time when, and governing the proceeding in which, the damages are to be proved, whether or not the amount be greater, equal to, or less than the amount of the loss or damages referred to in this Article 6.

6.07 Late Charge. In addition to its other remedies, Landlord shall have the right to add to the amount of any payment required to be made by Tenant hereunder, and which is not paid on or before the date the same is due, an amount equal to the greater of (a) Two Hundred Fifty Dollars ($250.00) or (b) one percent (1.0%) of the delinquency for each month or portion thereof that the delinquency remains outstanding, the parties agreeing that Landlord's damage by virtue of such delinquencies would be difficult to compute and the amount stated herein represents a reasonable estimate thereof. (Notwithstanding the foregoing, such late charge shall not apply to the first delinquency during any twelve-(12)-month period during the Term, if Tenant cures the delinquency within five (5) Business Days after written notice from Landlord.) The late charge shall be due upon

demand by Landlord. Tenant shall reimburse Landlord for all costs and expenses (including reasonable attorney's fees) incurred by Landlord to recover the late charges due hereunder.

ARTICLE 7. APPRAISAL

7.01 Appraisal of Fair Market Rent. In the event that Tenant disputes the amount claimed by Landlord as Fair Market Net Rent, and such dispute has not been resolved by mutual agreement within thirty (30) days, the dispute shall be submitted to the appraisal process hereinafter set forth. The amount of Fair Market Net Rent determined pursuant to such appraisal process shall be final and binding between the parties. The appraisal process shall be conducted as follows:

(a) Tenant shall make demand for appraisal in writing within thirty (30) days after service of Landlord's determination of Fair Market Net Rent is given under the terms of this Lease, specifying therein the name and address of the person to act as the appraiser on its behalf. The appraiser shall be a real estate appraiser with at least ten (10) years' experience in the field and a qualified member of the American Institute of Real Estate Appraisers, or any successor of such Institute (or if such organization or successor shall no longer be in existence, a recognized national association or institute of land appraisers) familiar with the fair market rent of first-class commercial office space in Comparable Buildings in Downtown Boston. Failure on the part of Tenant to make a timely and proper demand for such appraisal shall constitute a waiver of the right thereto. Within ten (10) Business Days after the service of the demand for appraisal, Landlord shall give notice to Tenant, specifying the name and address of the person designated by Landlord to act as appraiser on its behalf who shall be similarly qualified. If Landlord fails to notify Tenant of the appointment of its appraiser, within or by the time above specified, then the Tenant may thereafter send a second notice to Landlord indicating such failure and requesting Landlord to appoint such an appraiser. If Landlord fails to notify Tenant of the appointment of its appraiser within ten (10) Business Days after the giving of such second notice by Tenant then the appraiser appointed by Tenant shall be the sole appraiser to determine the issue.

(b) In the event that two (2) appraisers are chosen pursuant to Section 7.01(a) above, the appraisers so chosen shall meet within ten (10) Business Days after the second appraiser is appointed and, if within ten (10) Business Days after such first meeting the two appraisers shall be unable to agree upon a determination of Fair Market Net Rent, they, themselves, shall appoint a third appraiser, who shall be a competent and impartial person with qualifications similar to those required of the first two appraisers. In the event they are unable to agree upon such appointment within five (5) Business Days after expiration of said ten (10) Business Day period, the third appraiser shall be selected by the parties themselves, if they can agree thereon, within a further period often (10) Business Days. If the parties do not so agree, then either party, on behalf of both, may request appointment of such a qualified person by an officer of the Greater Boston Real Estate Board in Boston. The three (3) appraisers shall decide the dispute, if it has not previously been resolved, by following the procedure set forth in Section 7.01 (c) below.

(c) Where the issue cannot be resolved by agreement between the two appraisers selected by Landlord and Tenant or settlement between the parties during the course of the appraisal process, the issue shall be resolved by the three appraisers

in accordance with the following procedure. The appraiser selected by each of the parties shall each state in writing his determination of the Fair Market Net Rent, supported by the reasons therefor, with counterpart copies to each party. The appraisers shall arrange for a simultaneous exchange of such proposed determinations. The role of the third appraiser shall be to select which of the two proposed determinations most closely approximates his own determination of Fair Market Net Rent. The third appraiser shall have no right to propose a middle ground or any modification of either of the two proposed determinations. The determination he chooses as most closely approximating his determination shall constitute the decision of the appraisers and be final and binding upon the parties.

(d) This provision for determination by appraisal shall be specifically enforceable to the extent such remedies are available under applicable law, and any determination hereunder shall be final and binding upon the parties hereto, and either party shall have the right to enter judgment thereon, unless otherwise provided by applicable law. If a determination of Fair Market Net Rent is to be made pursuant to this Section 7.01, Landlord and Tenant shall each pay for the fees and disbursements of any appraiser appointed by it and shall share equally in the fees and expenses of any third appraiser.

(e) In the event of a failure, refusal or inability of any appraiser to act, his successor shall be appointed by him, but in the case of the third appraiser, his successor shall be appointed in the same manner as provided for appointment of the third appraiser.

ARTICLE 8. MISCELLANEOUS

8.01 No Waiver. Failure of Landlord or Tenant to declare any default immediately upon occurrence thereof, or delay in taking any action in connection therewith, shall not waive such default, but Landlord or Tenant, as the case may be, shall have the right to declare any such default at any time thereafter.

8.02 Holding Over. In the event of holding over by Tenant after expiration or termination of this Lease without the written consent of Landlord, Tenant shall pay, for each month or partial month of hold-over tenancy, an amount equal to one hundred twenty five percent (125%) for any hold-over tenancy not exceeding thirty (30) days (and thereafter one hundred fifty percent (150%)) of the greater of the Gross Rent for the month immediately preceding the end of the Term or the then fair market Gross Rent for the Leased Premises, together with such other amounts as may become due hereunder. No holding over by Tenant after the Term shall operate to extend the Term. In the event of any unauthorized holding over that continues for more than thirty (30) days, Tenant shall indemnify Landlord (i) against all claims for damages by any other tenant to whom Landlord may have leased all or any part of the Leased Premises covered hereby effective upon the termination of this Lease, and (ii) for all other losses, costs and expenses, including reasonable attorney's fees, incurred by Landlord by reason of such holding over. Any holding over with the consent of Landlord in writing shall thereafter constitute a lease from month to month.

8.03 Amendments and Modifications. This Lease may not be altered, changed or amended, except by an instrument in writing signed by both parties hereto. If in connection with obtaining financing for the Building, a bank, insurance company, pension trust or other institutional lender shall request reasonable modifications in

this Lease as a condition to such financing, Tenant will not unreasonably withhold or delay its consent thereto, provided that such modifications are at no out-of-pocket cost to Tenant and do not increase the obligations or reduce the rights of Tenant, reduce the obligations or increase the rights of Landlord hereunder, or adversely affect the leasehold interest hereby created.

8.04 Transfers by Landlord. Landlord shall have the right to transfer and assign, in whole or in part, all of its rights and obligations hereunder in the Building. In such event and upon such transfer, no further liability or obligations shall thereafter accrue against the transferring or assigning person as Landlord hereunder with respect to the period after the closing, to the extent such obligations are assumed by such transferee.

8.05 Severability. If any term or provision of this Lease, or the application thereof to any person or circumstances, shall to any extent be invalid or unenforceable, the remainder of this Lease, or the application of such provision to persons or circumstances other than those as to which it is invalid or unenforceable, shall not be affected thereby, and each provision of this Lease shall be valid and shall be enforceable to the fullest extent permitted by law.

8.06 Notices. All notices, demands, consents and approvals which may be or are required to be given by either party to the other hereunder shall be in writing and shall be deemed to have been fully given by personal delivery, or when delivered to a nationally recognized, overnight courier service providing receipts, or when deposited in the United States mail, certified or registered, postage prepaid, and addressed to the party to be notified at the address for such party specified on the Basic Lease Information Sheet, or to such other place as the party to be notified may from time to time designate by at least fifteen (15) days' notice to the notifying party.

8.07 No Joint Venture. This Lease shall not be deemed or construed to create or establish any relationship of partnership or joint venture or similar relationship or arrangement between Landlord and Tenant hereunder.

8.08 Successors and Assigns. This Lease shall be binding upon and inure to the benefit of Landlord, its successors and assigns (subject to the provisions hereof, including, but without limitation, Section 8.04); and shall be binding upon and inure to the benefit of Tenant, its successors, and to the extent assignment may be permitted as of right or approved by Landlord hereunder, Tenant's assigns.

8.09 Applicable Law. All rights and remedies of Landlord and Tenant under this Lease shall be construed and enforced according to the laws of the Commonwealth of Massachusetts.

8.10 Time of the Essence. Time is of the essence for each and every covenant of Tenant herein contained.

8.11 Submission Not an Option. The submission of this Lease for examination does not constitute a reservation of or option for the Leased Premises or an offer to lease, it being understood and agreed that neither Landlord nor Tenant shall be legally bound with respect to the leasing of the Leased Premises unless and until this Lease has been executed and delivered by both Landlord and Tenant.

8.12 Brokerage. Tenant and Landlord each warrant to the other that it has had no dealings with any broker or agent in connection with this Lease other than the Brokers named in Basic Lease Information, and each covenants to defend (with counsel reasonably approved by the other party), hold harmless and indemnify the other party from and against any and all costs, expense or liability for any compensation, commission and charges claimed by any broker or agent except the Brokers named in Basic Lease Information, whose fees and expenses shall be paid in full by Landlord, arising out of the warranting party's dealings in connection with this Lease or the negotiation thereof.

8.13 Waiver of Jury Trial. Landlord and Tenant hereby waive trial by jury in any action, proceeding or counterclaim brought by either of the parties hereto against the other, on or in respect of any matter whatsoever arising out of or in any way connected with this Lease, the relationship of Landlord and Tenant hereunder, Tenant's use or occupancy of the Leased Premises, and/or any claim of injury or damages.

8.14 All Agreements Contained. This Lease contains all of the agreements of the parties with respect to the subject matter hereof and supersedes all prior dealings between them with respect to such subject matter.

8.15 Cumulative Remedies. The specific remedies to which Landlord may resort under the terms of this Lease are cumulative and are not intended to be exclusive of any other remedies or means of redress to which it may be lawfully entitled in case of any breach or threatened breach by Tenant of any provisions of this Lease. In addition to the other remedies provided in this Lease, Landlord shall be entitled to the restraint by injunction of the violation or attempted or threatened violation of any of the covenants, conditions or provisions of this Lease or to a decree compelling specific performance of any such covenants, conditions or provisions.

8.16 Failure To Enforce; Accord and Satisfaction. The failure of Landlord to seek redress for violation of, or to insist upon strict performance of any covenant or condition of this Lease, or with respect to such failure of Landlord to enforce any of the rules and regulations referred to herein, whether heretofore or hereafter adopted by Landlord, shall not be deemed a waiver of such violation nor prevent a subsequent act which would have originally constituted a violation from having all the force and effect of the original violation, nor shall the failure of Landlord to enforce any of said rules and regulations. The receipt by Landlord of Rent with knowledge of the breach of any covenant of this Lease shall not be deemed a waiver of such breach. No provision of this Lease shall be deemed to have been waived by Landlord, unless such waiver shall be in writing and signed by Landlord. No consent or waiver, express or implied, by Landlord to any breach of any agreement or duty shall be construed as a waiver or consent to or of any other breach of the same or any other agreement or duty. Unless Landlord otherwise notifies Tenant in writing, no acceptance by Landlord of a lesser sum than all Gross Rent and other charges then due shall be applied or deemed to be applied except as follows: first, to charges due under Section 6.07; and second, to the installments of Gross Rent and other charges most recently due. No endorsement or statement by Tenant on or accompanying any check or payment shall alter the application of such check or payment as set forth above. No such endorsement or statement shall be deemed an accord and satisfaction, and Landlord may accept such check or payment without prejudice to Landlord's right to recover the balance of all amounts due or pursue any other remedy provided in this Lease.

The delivery of keys to Landlord or to Landlord's managing agent shall not operate as a termination of this Lease or a surrender of the Leased Premises.

8.17 Substitution. Landlord shall have the right to substitute the entire Leased Premises, on one occasion following the expiration of the second Lease Year, upon all of the following terms, covenants and conditions:

(a) The Substituted Leased Premises ("Substituted Leased Premises") must constitute space on the same side of the Building as the Leased Premises on a floor in the Building not lower than the seventh (7th) floor. The right of substitution may only be exercised if the Substituted Leased Premises designated by Landlord are similar in area, fit-out and finishes and in appropriateness for Tenant's purposes and the substitution is made for the purpose of accommodating a tenant who will occupy Net Rentable Area on the floor on which the Leased Premises are located which is at least five thousand (5,000) square feet of Net Rentable Area in excess of the Leased Premises. Landlord shall give Tenant not less than twelve (12) months prior notice of such substitution and shall carry out such substitution in a manner designed not to unreasonably interfere with Tenant's business operations (such as coordinating the move on a weekend).

(b) Landlord shall pay the cost of moving Tenant, its property and equipment to the Substituted Leased Premises (including without limitation reasonable move management fees and reasonable costs of moving all communications cabling, wiring and infrastructure) and shall, without cost or expense to Tenant, improve the new Leased Premises with improvements substantially similar to those located in the Leased Premises to be vacated. Landlord shall also reimburse Tenant for the costs of new business cards, stationary and the like incurred by Tenant on account of the substitution of the Leased Premises.

(c) All of the other terms, covenants and conditions of the Lease shall remain unchanged and in full force and effect with respect to the Substituted Leased Premises, except that the Basic Lease Information sheet shall be revised: (i) to identify the floor of the Substituted Leased Premises; (ii) to state as the Net Rentable Area the square footage of the Substituted Leased Premises as determined by Landlord's architect; and (iii) to revise, as appropriate, Tenant's Proportionate Share; provided, however, in no event shall the Net Rent for the Substituted Leased Premises exceed the Net Rent for the Leased Premises.

8.18 Notice of Lease. Tenant agrees not to record this Lease, but on the request of either party hereto, both parties hereto shall execute and deliver (i) a notice of this Lease in form appropriate for recording or registration, (ii) an agreement setting forth the Term Commencement Date, (iii) a notice in form appropriate for recording or registration of any amendment of this Lease, (iv) an agreement by Tenant to make payments and give notices to whatever individual or entity shall be designated by Landlord for receiving any such notice or payment and to comply with the provisions of any assignment of rents granted to the holder of any Mortgage, and (v) if this Lease is terminated before the expiration of the Term, an instrument in form appropriate for recording or registration pursuant to which Tenant acknowledges the date of termination. If a notice of lease has been recorded and, following the expiration or earlier termination of the Lease, Tenant unreasonably refuses to execute a termination of such notice of lease, in recordable form, within ten (10) Business Days after Landlord gives notice to Tenant requesting execution of the same, Landlord may effect such execution on behalf of Tenant as Tenant's attorney-in-fact and Tenant hereby grants to

Landlord an irrevocable power of attorney solely for the purpose of executing on behalf of Tenant such termination of such notice of lease, which power is coupled with an interest.

8.19 Consents. Tenant hereby waives any claim for damages against Landlord which it may have based upon any assertion that Landlord has unreasonably withheld or unreasonably delayed any such consent or approval, and Tenant agrees that its sole remedy shall be an action or proceeding to enforce any such provision or for specific performance, injunction or declaratory judgment. In the event of a determination favorable to Tenant, the requested consent or approval shall be deemed to have been granted; however, Landlord shall have no liability to Tenant for its refusal or failure to give such consent or approval.

8.20 Vacancy. If Tenant vacates substantially all of the Leased Premises at any time within the last three (3) months of the Term, Landlord may enter the Leased Premises (or such portion) under Section 4.09 for the purpose of making inspections and (without damage to any furniture or equipment that Tenant intends to remove) commencing preparation work for any future tenant; provided, however, that (a) Tenant shall have no obligation or liability to Landlord for such work or any damage caused by any party acting under Landlord in connection therewith and (b) Tenant shall not be responsible for repairs to or restoration of any portion of the Leased Premises affected by such work by Landlord. The exercise of such right of entry by Landlord (which shall not include the right of any future tenant to occupy or conduct business in any portion of the Leased Premises during the Term) will not affect Tenant's obligations to pay Rent with respect to the Leased Premises (or such portion), which obligations shall continue without abatement until the end of the Term.

8.21 Tenant's Authorized Representative. Tenant designates the person named from time to time as Tenant's Authorized Representative to take all acts of Tenant hereunder. Landlord may rely on the acts of such Tenant's Authorized Representative without further inquiry or evidence of authority. Tenant's Authorized Representative shall be the person so designated in the Basic Lease Information Sheet and such successors as may be named from time to time by the then current Tenant's Authorized Representative or by Tenant's president.

8.22 Assignment of Rents. If at any time Landlord assigns this Lease or the rents payable hereunder to the holder of any Mortgage, whether such assignment is conditional in nature or otherwise, (i) such assignment to the Mortgagee shall not be deemed an assumption by the Mortgagee of any obligations of Landlord hereunder unless such Mortgagee shall, by written notice to Tenant, specifically otherwise elect; (ii) except as aforesaid, the Mortgagee shall be treated as having assumed Landlord's obligations hereunder (subject to Section 4.13) only upon foreclosure of its mortgage (or voluntary conveyance by deed in lieu thereof) and the taking of possession of the Leased Premises and, with respect to obligations regarding return of any security deposit, only upon receipt of the funds constituting such security deposit; and (iii) if Tenant alleges that Landlord is in default under this Lease, Tenant shall give the Mortgagee (to which Tenant was given written notice) a copy of any notice of default served upon Landlord and, if Landlord fails to cure such default within the time provided herein or by law or

such additional time as may be provided in such notice to Landlord, the Mortgagee shall have thirty (30) days after the end of Landlord's cure period to cure such default (or such additional time as may be necessary to cure such default, if within such thirty day period the Mortgagee has commenced and is

diligently pursuing the remedies necessary to effect such cure), in which event (except as set forth in Section 3.01(c)) Tenant shall have no right to an abatement of Rent or to terminate this Lease with respect to such default while such remedies are being diligently pursued by the Mortgagee.

8.23 Tenant Confirmations. Tenant represents and warrants to Landlord that (a) the person(s) executing this Lease on behalf of Tenant are duly authorized and have full power to execute and deliver this Lease, (b) Tenant has no claim, offset, or defense against the enforcement of the Lease in accordance with its terms, and (c) Tenant is not acting, directly or indirectly, for or on behalf of any person, group, entity, or nation named by any Executive Order or the United States Treasury Department as a terrorist, "Specially Designated National and Blocked Person", or other banned or blocked person, group, entity, nation, or transaction pursuant to any law, order, rule, or regulation that is enforced or administered by the Office of Foreign Assets Control and that it is not engaged in this transaction, directly or indirectly, on behalf of, or instigating or facilitating this transaction, directly or indirectly, on behalf of any such person, group, entity, or nation.

8.24 Rents from Real Property. Tenant and Landlord intend that all amounts payable by Tenant to Landlord shall qualify as "rents from real property," and will otherwise not constitute "unrelated business taxable income" or "impermissible tenant services income," all within the meaning of both Sections 512(b)(3) and 856(d) of the Internal Revenue Code of 1986, as amended (the "Code") and the U.S. Department of Treasury Regulations promulgated thereunder (the "Regulations"). In the event that Landlord determines that there is any risk that any amount payable under the Lease may not qualify as "rents from real property" or will otherwise constitute unrelated business taxable income or impermissible tenant services income within the meaning of Sections 512(b)(3) or 856(d) of the Code and the Regulations promulgated thereunder, Tenant agrees (a) to cooperate with Landlord by entering into such amendment or amendments as Landlord deems necessary to qualify all amounts payable under the Lease as "rents from real property" and (b) to permit (and, upon request, to acknowledge in writing) an assignment of the obligation to provide certain services under the Lease, and, upon request, to enter into direct agreements with the parties furnishing such services (which shall include but not be limited to a taxable REIT subsidiary of Landlord). Notwithstanding the foregoing, Tenant shall not be required to take any action pursuant to the preceding sentence (including acknowledging in writing an assignment of services pursuant thereto) if such action would result in (A) Tenant's incurring more than de minimis additional liability under the Lease or (B) more than a de minimis negative change in the quality or level of Building operations or services rendered to Tenant under the Lease. For the avoidance of doubt, (i) if Tenant does not acknowledge in writing an assignment as described in clause (b) above (it being agreed that Tenant shall not unreasonably withhold, condition, or delay such acknowledgment so long as the criteria in clauses (A) and (B) are satisfied), then Landlord shall not be released from liability under the Lease with respect to the services so assigned; and (ii) nothing in this Section shall limit or otherwise affect Landlord's ability to assign its entire interest in the Lease to any party as part of a conveyance of Landlord's ownership interest in the Building.

ARTICLE 9. OPTIONS

9.01 Extension Option. Tenant shall have the option to extend the Term of the Lease for one (1) additional period of five (5) years (the "Extension Term"), by written

notice given to Landlord at least twelve (12) months before the scheduled expiration of the initial Term and not earlier than eighteen (18) months before the scheduled expiration of the initial Term, on the terms set forth below (the "Extension Option"). Tenant's notice exercising the Extension Option must be unconditional and irrevocable in order to be effective. Failure to timely deliver Tenant's notice exercising the Extension Option shall constitute Tenant's waiver of the Extension Option. Tenant's lease of the Leased Premises during the Extension Term shall be on all of the terms and conditions of this Lease in effect on the last day of the expiring Term, except that Net Rent during the Extension Term shall be the Fair Market Net Rent as determined hereunder. Tenant shall have no option to extend the Term beyond the end of the Extension Term. Any dispute over Fair Market Net Rent shall be resolved in accordance with Article 7. All references in this Lease to "Term" shall mean the initial Term as extended by any Extension Term.

For any part of the Extension Term during which the Net Rent is in dispute hereunder, Tenant shall make payment on account of Net Rent at the rate estimated by Landlord, and the parties shall adjust for any overpayments or underpayments upon the issuance of the arbitrators' decision. The failure by the parties to complete the process contemplated under this Section 9.01 prior to commencement of the Extension Term shall not affect the continuation of the Term or the parties' obligation to make any adjustments for any overpayments or underpayments for the Net Rent due for the Extension Term promptly after the determination thereof is made.

If Tenant shall exercise the Extension Option in accordance with this Section 9.01, the provisions of this Section shall be self-operative, but upon request by either party after determination of the Net Rent for the Extension Term, the parties shall execute an agreement specifying the Net Rent for the Extension Term and acknowledging the extension of the Term.

Notwithstanding any provision of this Section to the contrary, Tenant's option to extend the Term shall be void, at Landlord's election, if (i) Tenant is in default hereunder, after any applicable notice and cure periods have expired, at the time Tenant elects to extend the Term or at the time the Term would expire but for such extension, or (ii) any Transfer under Section 4.06 has occurred on or before either such time, other than a Permitted Transfer or sublease(s) covering less than half of the Leased Premises in the aggregate.

ARTICLE 10. INITIAL PREMISES

10.01 Initial Premises. Notwithstanding anything to the contrary in the Basic Lease Information Sheet and Exhibit B, Landlord shall have the right (the "Swap Right"), in its sole discretion, to change the location of the Leased Premises from the eleventh (11th) floor of the Building

described in the Basic Lease Information Sheet (the "11th Floor Leased Premises") to be a portion of the thirteenth (13th) floor of the Building containing approximately 8,391 square feet of Net Rentable Area as shown on Exhibit A-2 attached hereto (the "13th Floor Leased Premises"), subject to the following terms and conditions. If Landlord desires to exercise the Swap Right under this Section 10.01, Landlord shall deliver written notice (in the manner set forth in Section 8.06) of such exercise to Tenant on or before January 6, 2016. If Landlord so exercises the Swap Right under this Section 10.01, then:

(a) the Leased Premises originally described in the Basic Lease Information Sheet shall be deemed to have been amended to refer solely to the 13th Floor Leased Premises described in the first sentence of this Section 10.01, and all references therein to the 11th Floor Leased Premises shall be deemed to have been deleted;

(b) solely with respect to the initial Term of this Lease, the Net Rent and Tenant's Proportionate Share for the 13th Floor Leased Premises shall be calculated as if the Net Rentable Area thereof contained the number of square feet originally set forth in the Basic Lease Information Sheet for the 11th Floor Leased Premises;

(c) with respect to any extension (if any) of the Term beyond the end of the initial Term set forth in the Basic Lease Information Sheet, the Net Rent and Tenant's Proportionate Share for the 13th Floor Leased Premises shall be calculated based on the Net Rentable Area of the 13th Floor Leased Premises set forth in the first sentence of this Section 10.01;

(d) with respect to the Tenant's Initial Construction of the 13th Floor Leased Premises under Exhibit B:

(1) Landlord shall, at its sole expense, demolish the existing improvements in the 13th Floor Leased Premises and deliver such space to Tenant in shell condition (equivalent to the currently existing shell condition of the 11th Floor Leased Premises) on or before the date on which Tenant commences the performance of the Tenant's Initial Construction under Paragraph B.5 of Exhibit B attached hereto,

(2) Landlord shall, at its sole expense, provide new Mecho shades (or equivalent) for the 13th Floor Leased Premises prior to Tenant's commencement of occupancy thereof for the regular conduct of its business,

(3) Landlord shall, at its sole expense, renovate the common corridor on the 13th floor of the Building using Building standard finishes prior to the Rent Commencement Date for the 13th Floor Leased Premises, and

(4) the Tenant Work Allowance provided by Landlord under Exhibit B for the 13th Floor Leased Premises shall be increased to equal the sum of (i) the Tenant Work Allowance originally provided for the 11th Floor Leased Premises and (ii) $ 110,000.00;

(e) the Scheduled Term Commencement Date and the Rent Commencement Date set forth in the Basic Lease Information Sheet shall be the earlier of (1) the date that is thirty (30) days after the date on which Tenant first occupies all or part of the Leased Premises for the regular conduct of business (as determined under clause (ii) of Section 2.01) or (2) June 1, 2016; provided that, if Landlord fails to timely deliver the 13th Floor Leased Premises to Tenant as set forth in subparagraph (d)(1) above, the date in the preceding clause (2) of this

Section 10.01(e) shall be delayed by the number of days of such delay in delivery.

(f) If Landlord exercises the Swap Right under this Section 10.01, Landlord's delivery of such exercise notice shall be self-operative on the terms and conditions set forth above, without the necessity of the parties to execute and deliver any further instruments, but at the request of either party the parties shall execute and deliver a confirmatory amendment to this Lease evidencing such exercise of the Swap Right on the terms and conditions set forth above.

ARTICLE 11. DEFINITIONS

11.01 Definitions. Terms used herein shall have the following meanings:

"Additional Rent" shall mean all monetary obligations of Tenant hereunder, other than the obligation for payment of Gross Rent.

"Basic Services" shall mean the services described in Section 3.01 hereof.

"Buildable Area" shall mean the Net Rentable Area of the Leased Premises in question less the portion of such Net Rentable Area attributable to Building Common Areas and Common Areas.

"Building" shall mean the 25-story building (consisting of a 6-story low-rise portion, a 19-story high-rise portion and 3 levels of parking space below grade) located on the Land, and comprising the Office Section, the Commercial Section and common areas such as mechanical rooms, elevator machine rooms, loading dock facilities, janitor and utility rooms, electrical and communication closets and similar facilities.

"Building Common Areas" shall mean all areas of the Building servicing more than one floor of the Building as a whole, including, but not limited to central mechanical rooms, elevator machine rooms, pump rooms, loading dock facilities, electrical and communication rooms, postal, security and janitorial facilities and the public spaces (and if any such area is bordered by any demising wall which abuts any space that is leasable, such area shall be measured from the midpoint of such demising wall), but excluding General Common Areas and the parking garage forming part of the Building.

"Building Standard Improvements" shall mean the level of Tenant Improvements described in Exhibit B-2.

"Business Days" shall mean Monday through Friday, excluding Building holidays.

"Business Hours" shall mean 8 A.M. to 6 P.M. on Business Days.

"Commercial Section" shall mean that portion of the Building dedicated to commercial and retail uses.

"Common Areas" shall mean all areas on the particular floor of the Building devoted to uses such as corridors, lobbies, fire vestibules, elevator foyers, service elevator

receiving areas, mailrooms, electric and communication closets and other similar facilities for the benefit of all tenant(s) or invitees on that particular floor.

"Comparable Buildings in Downtown Boston" shall mean comparable first-class, high-rise office buildings in the Back Bay or financial districts of Boston.

"Estimated Impositions" for any calendar year shall mean Landlord's estimate of Impositions for such calendar year.

"Estimated Operating Cost" for any calendar year shall mean Landlord's estimate of Operating Cost for such calendar year.

"Fair Market Net Rent" shall mean the annual fair market rental value, net of Operating Cost and Impositions, of comparable space in the Building or in Comparable Buildings in Downtown Boston, Massachusetts, in each case taking into consideration the following factors related to the Leased Premises: floor level, tenant improvements, proposed term of lease, extent of services provided or to be provided, the time the particular rate under consideration became or is to become effective and any other relevant terms or conditions.

"Force Majeure" shall mean any circumstance beyond the reasonable control of Landlord, including, without limitation, acts of God, acts of the public enemy, governmental interference, court orders, requisition or orders of governmental bodies or authorities, requirements under any statute, law, rule, regulation or similar requirement of a governmental authority which shall be enacted or shall arise following the date of this Lease, inability to obtain labor, insurrection, riot, civil commotion, lock-out, or any other unforeseeable event (other than the inability to obtain financing), the occurrence of which would prevent or preclude Landlord from fully and completely carrying out and performing its obligations under this Lease.

"General Common Areas" shall mean those areas forming part of the Building and devoted to non-exclusive uses which are not measured, including, but not limited to, walkways, arcades and all landscaped areas (including pools and fountains). General Common Areas shall not include any portion of the parking garage forming part of the Building.

"Gross Rent" shall mean, for each year of the Term, the sum of Net Rent and Tenant's Proportionate Share of Estimated Operating Cost and Tenant's Proportionate Share of Estimated Impositions.

"Impositions" shall have the meaning given in Section 2.05.

"Impositions Adjustment" for any calendar year shall mean the amount of the Impositions in excess of or less than the amount of Estimated Impositions.

"Invitees" shall mean agents, servants, employees, licensees and business invitees.

"Land" shall mean the parcel of real property owned by the Landlord, located in the City of Boston, Suffolk County, Massachusetts, and bounded in part by Clarendon and Boylston Streets and St. James Avenue and more specifically described in Exhibit A-l attached hereto.

"Leased Premises" shall mean the floor area more particularly shown on Exhibit A attached hereto, containing the Net Rentable Area specified on the Basic Lease Information Sheet, but subject to relocation pursuant to Section 8.17.

"Mortgage" shall mean any and all current or future mortgages securing indebtedness for money borrowed by Landlord or indebtedness for the refinancing of any such indebtedness, provided any such mortgage grants a lien on all or any portion of the Building, including all amendments and modifications thereto, from time to time. Any reference to "Mortgage" and "Mortgagee" herein shall include a sale and leaseback and the grantee-lessor of a sale and leaseback used for financing purposes.

"Net Rent" shall mean the annual rate set forth in the Basic Lease Information Sheet.

"Net Rentable Area" shall mean the area or areas of the space within the Building determined as follows:

(a) Net Rentable Area on a single tenancy floor shall consist of:

(i) the area determined by measuring from the inside surface of the outer glass of each exterior wall (and extensions of the plane thereof in non-glass areas) to the inside surface of the outer glass on opposite exterior wall (and extensions of the plane thereof in

non-glass areas) and shall include all areas within the outside walls, but shall exclude vertical penetrations, including without implied limitation fire stairs, elevator shafts, flues, vents, stacks, and Building Common Areas on the floor; plus

(ii) Tenant's Allocation of Building Common Areas;

(b) Net Rentable Area for a multi-tenancy floor shall consist of:

(x) all space within the demising walls (measured from the mid-point of the demising walls; and in the case of exterior walls, measured as defined in (i) above); plus

(y) Tenant's Allocation of Building Common Areas; plus

(z) Tenant's Floor Share of all Common Areas.

No deductions from Net Rentable Area shall be made for columns or projections necessary to the Building, or for vertical penetrations which are for the specific use of Tenant (such as, but not limited to, special elevators or stairs, mechanical and electrical facilities and air conditioning equipment). The Net Rentable Area of the Leased Premises has been calculated on the basis of the foregoing definition and is hereby stipulated for all purposes hereof to be the amount, expressed in terms of square feet, stated on the Basic Lease Information Sheet.

"Office Section" shall mean that portion of the Building dedicated to office uses.

"Operating Cost" shall have the meaning given in Section 2.04.

"Operating Cost Adjustment" for any calendar year shall mean the amount of Operating Cost in excess of or less than the amount of Estimated Operating Cost.

"Permitted Use" shall mean corporate, executive and professional office use in the Leased Premises of a kind appropriate in a building of the type and quality of the Building (together with ancillary uses thereto consistent with Comparable Buildings in Downtown Boston and the provisions of this Lease); provided, however, that Permitted Use shall not include (a) offices of any agency or bureau of the United States or any state or political subdivision thereof; (b) offices or agencies of any foreign government or political subdivision thereof; (c) offices of any health care professionals or service organization; (d) schools or other training facilities which are not ancillary to corporate, executive or professional office use; (e) retail or restaurant uses (except in the Commercial Section); (f) communications firms, such as radio and/or television stations; (g) employment agency or (h) an executive suites business, a virtual office, or a similar provider or user of temporary office space, meeting rooms, and/or professional office services on a contract basis (e.g., Regus, Interactive Offices Worldwide, or similar office space provider); or (i) any use or activity which is disreputable, creates a fire hazard or would cause Landlord's insurance rate to be increased.

"Project" shall mean the Building and, for so long as it is under common ownership or control with the Building, the adjacent building known as 222 Berkeley Street.

"Rent" shall mean Gross Rent plus Additional Rent.

"Sublease" shall include any sublease, underletting at any level, tenancy, concession, license, franchise or other arrangement providing for the use or occupancy of all or any portion of the Leased Premises.

"Tenant Improvements" shall mean all tenant improvements in the Leased Premises including any installed by Tenant pursuant to Exhibit B.

"Tenant's Allocation" shall mean an area determined by multiplying the total square footage of the Building Common Areas by the ratio of the Net Rentable Area of the Leased Premises (excluding any allocation of Building Common Areas) to the Net Rentable Area of the Office Section (excluding only the Building Common Areas).

"Tenant's Floor Share" shall mean the ratio of Tenant's Buildable Area to the aggregate Buildable Area on Tenant's floor.

"Tenant's Proportionate Share" is initially as specified on the Basic Lease Information Sheet and shall be adjusted from time to time to reflect the ratio which the Net Rentable Area of the Leased Premises bears to the greater of (i) ninety-five percent (95%) of the total Net Rentable Area of the Office Section, or (ii) the Total Leased Net Rentable Area.

"Term" shall mean a period of calendar years, or fractions thereof, commencing with the Term Commencement Date and ending on the Term Expiration Date stated on the Basic Lease Information Sheet, as the same may be extended upon the timely exercise of any extension options contained in the Lease.

"Term Commencement Date" shall mean the date when the Term commences as determined pursuant to Section 2.01 hereof.

"Term Expiration Date" shall mean the date specified on the Basic Lease Information Sheet when the Term shall end, unless sooner terminated or extended pursuant to the terms of this Lease.

"Total Leased Net Rentable Area" shall mean the sum of the Net Rentable Area leased to all Office Section tenants over the course of a year, determined on the basis of a weighted averaging of the sum of the Net Rentable Area leased to all Office Section tenants on each day of that year. Landlord reserves the right from time to time to change or recalculate the Total Leased Net Rentable Area of the Office Section.

Other terms used on the Basic Lease Information Sheet which is a part of this Lease, or elsewhere in this Lease shall have the meaning given them thereon and herein.

In WITNESS WHEREOF, the parties hereto have executed this Lease as a sealed instrument as of the day and year first above written.

"Landlord":

500 BOYLSTON & 222 BERKELEY OWNER (DE) LLC, a Delaware limited liability company

By: /s/ Chris Lankin
Name: Chris Lankin
Title: VP Legal

By: /s/ Chad Remis
Name: Chad Remis
Title: City Head Boston

"Tenant":

RHYTHM PHARMACEUTICALS, INC.,
a Delaware corporation

By: /s/ Bart Henderson
Name: Bart Henderson
Title: President

EXHIBIT A

Floor Plan

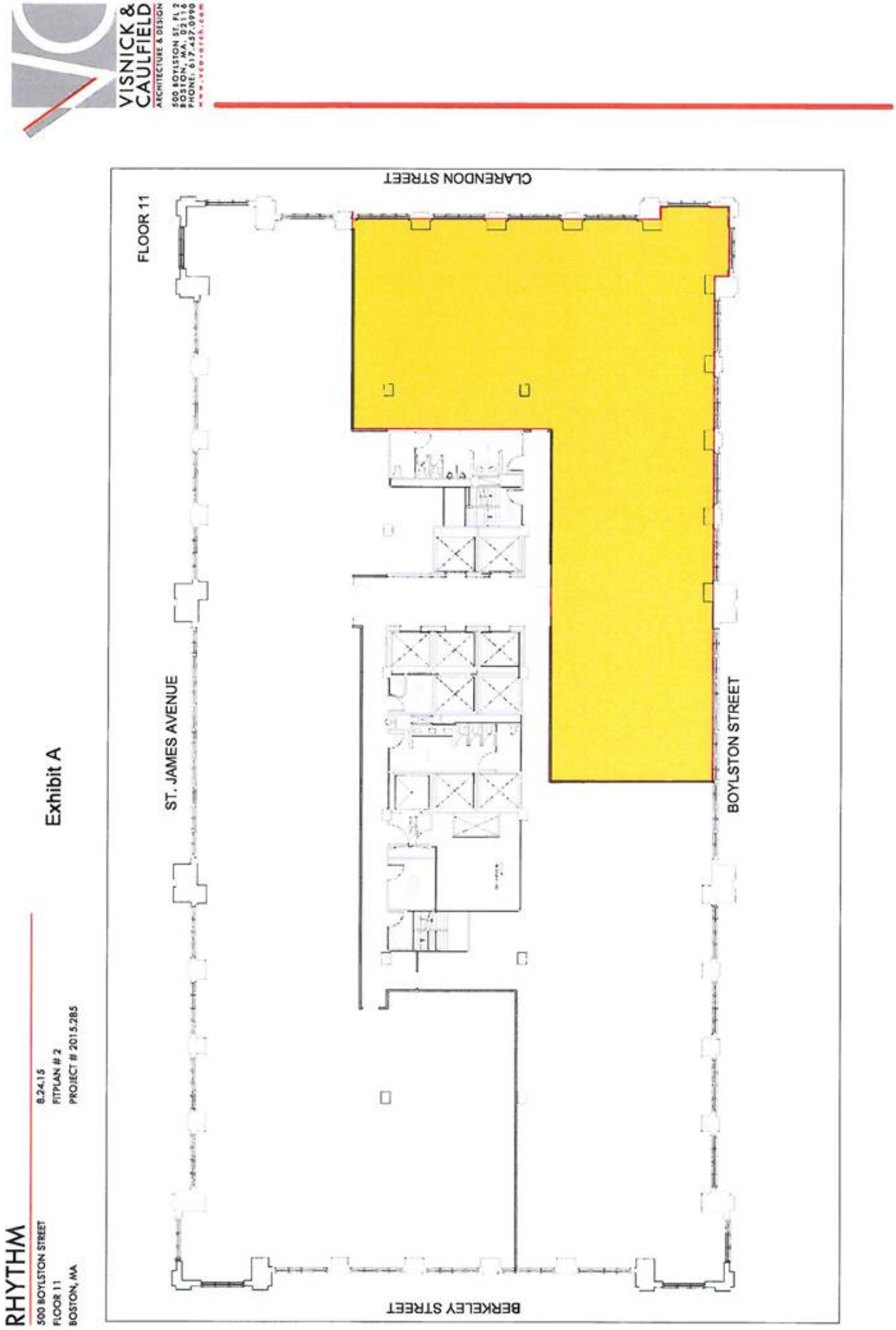

EXHIBIT A-l

Description of Land

Real property in the City of Boston, County of Suffolk, Commonwealth of Massachusetts, described as follows:

That certain parcel of land on the South of Boylston Street, the East side of Clarendon Street and the North side of St. James Avenue in Boston, Suffolk County, Massachusetts, along with all buildings and other improvements thereon, shown as Lot A on a plan of land entitled "500 Boylston Street Subdivision Plan of Land in Boston, MA, Suffolk County" dated 21 January 1986, revised 27 February 1986, by Survey Engineers of Boston and recorded with Suffolk Deeds at the end of Book 12397, which parcel is bounded and described according to the plan as follows:

Beginning at the Northwest corner of the premises at the southeasterly corner of the intersection of Boylston and Clarendon Streets; thence running

North 69°45'00"W East by Boylston Street, 322.37 feet; thence

South 20°15'00" East by land formerly of the Mill Dam Trust and of New England Mutual Life Insurance Company, 249.97 feet to St. James Avenue; thence

South 69°44'51" West by St. James Avenue, 322.34 feet to the Northeast corner of the intersection of St. James Avenue and Clarendon Street thence

North 20°15'31" West by Clarendon Street, 249.98 feet to the point of beginning.

Containing, according to the plan 80,581 square feet of land, more or less.

Included within the above-described parcel are three parcels of registered land bounded and described as follows:

First Registered Parcel

That certain parcel of land situated in said Boston, bounded and described as follows:

Northerly by the southerly line of Boylston Street, 28.30 feet;

Easterly by land formerly of the Mill Dam Trust, 125 feet;

Southerly by land formerly of New England Mutual Life Insurance Company, 28.30 feet and

Westerly by land formerly of New England Mutual Life Insurance Company, 126 feet.

This first registered parcel is shown on a plan drawn by Survey Engineers of Boston and filed with the Engineering Office of the Land Court in Boston, Massachusetts as Plan No. 2025B, being a subdivision of the land described in Suffolk Registry District Certificate of Title No. 94648 in Registration Book 469, Page 48.

Second Registered Parcel

That certain parcel of land situated in said Boston, bounded and described as follows:

Northwesterly by the southeasterly line of Boylston Street, 24 feet;

Northeasterly by land now or formerly of Andrew D. MacLachlan, the line running in part through the middle of a party wall, 125 feet;

Southeasterly by land of New England Mutual Life Insurance Company, 24 feet; and

Southwesterly by land now or formerly of Frederick Ayer, the line running in part through a party wall, 125 feet.

All of said boundaries are determined by the Court to be located as shown on a plan drawn by Aspinwall & Lincoln, Civil Engineers, dated May 13, 1912, as approved by the Court, filed in the Land Registration Office as Plan No. 3811A, a copy of a portion of which is filed with Certificate of Title No. 4596.

Third Registered Parcel

That certain parcel of land situated in said Boston, bounded and described as follows:

Northwesterly by the southeasterly line of Boylston Street, 72.23 feet;

Northeasterly by land now or formerly of Julius P. Passett, the line in part running through the middle of a 12" brick party wall, 125 feet;

Southeasterly by land of New England Mutual Life Insurance Company, 72.23 feet; and

Southwesterly by land now or formerly of Andrew D. MacLachlan, the line in part running through the middle of a 12" brick party wall, 125 feet.

All of said boundaries are determined by the Court to be located as shown upon plan numbered 32268A which is filed with Certificate of Title No. 72280.

EXHIBIT A-2

Floor Plan of Alternative Premises
(see Section 10.01)

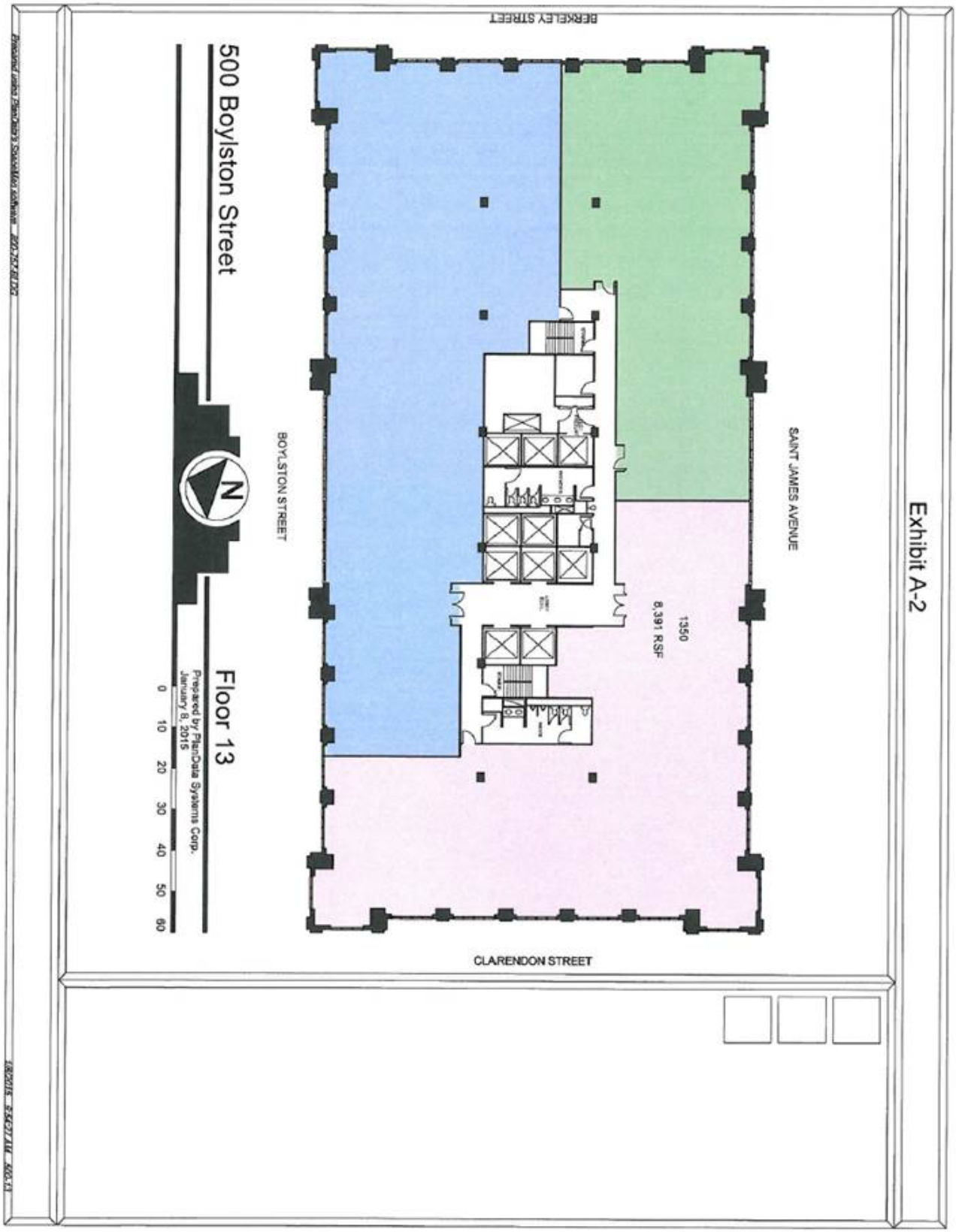

EXHIBIT B

Initial Improvement of the Leased Premises

B.l Condition of Leased Premises. Landlord shall deliver the Leased Premises to Tenant in accordance with Section 2.01 of the Lease for commencement by Tenant of the Tenant's Initial Construction under this Exhibit B. Prior to Tenant's commencement of such work, Landlord shall, at its expense, construct the demising wall (studs and sheetrock, taped and sanded only) separating the Leased Premises from the adjacent vacant space ("Landlord's Demising Work") in accordance with applicable code requirements.

B.2 Construction Documents. Tenant shall prepare, at Tenant's expense (subject to reimbursement from the Tenant Work Allowance), and deliver to Landlord detailed plans and specifications (the "Construction Documents") showing all Tenant Improvement work required to prepare the Leased Premises for Tenant's initial occupancy ("Tenant's Initial Construction") subject to all of the terms and requirements set forth in the Lease. Such Construction

Documents shall meet or exceed the level of Building Standard Improvements and substantially conform to Exhibit B-l hereof. The Construction Documents will be subject to Landlord's review and approval and must incorporate the Project's standard doors and hardware, light fixtures and ceiling system to maintain the continuity of the appearance and the optimal mechanical system performance of the Project in accordance with Section 4.07 of the Lease. Subject to Landlord's prior approval, not to be unreasonably withheld or delayed, Tenant shall have the right to use any qualified general contractor for Tenant's Initial Construction. Landlord shall use reasonable efforts to review and approve (or provide comments on) the Construction Documents no later than ten (10) Business Days after submission (or such longer period as any special features of the proposed improvements may reasonably require).

B.3 Tenant Work Allowance. Landlord shall provide Tenant with an allowance for the costs (the "Allowance Costs") of constructing Tenant's Initial Construction in the Leased Premises for Tenant's initial occupancy (including, without limitation, architectural and engineering fees with respect thereto and costs of cabling, conduits, consulting fees, and Tenant's furniture, fixtures and equipment) in an amount not to exceed the Tenant Work Allowance set forth in the Basic Lease Information sheet; provided that no more than $10.00 per square foot of Net Rentable Area of the Tenant Work Allowance may be used for architectural and engineering fees and other so-called soft costs. All construction and design costs for the Leased Premises in excess of the Tenant Work Allowance shall be paid for entirely by Tenant, and Landlord shall not provide any reimbursement therefor.

The Tenant Work Allowance is sometimes referred to as the "Allowance." The Allowance shall be disbursed as requisitioned by Tenant not more frequently than monthly, within thirty (30) days after requisition in accordance herewith. For each disbursement, Tenant shall submit a requisition package to Landlord, with an itemization of the costs being requisitioned, a certificate by an officer of Tenant that all such costs are Allowance Costs and have been incurred and paid for by Tenant, and appropriate back up documentation including, without limitation, lien releases (in a form reasonably approved by Landlord) and paid invoices

and bills. If the total estimated cost of Tenant's Initial Construction exceeds the Allowance, Landlord reserves the right to disburse each individual disbursement of the Allowance in the proportion that the Allowance bears to the total estimated cost of Tenant's Initial Construction, and further reserves the right to withhold disbursement of the last ten percent (10%) of the Allowance until such time as the Tenant's Initial Construction is completed, and Tenant has provided Landlord with a copy of the final certificate of occupancy for the Leased Premises and completed all construction-related requirements under the Lease. Tenant shall not be entitled to any unused portion of the Tenant Work Allowance that is not requisitioned within one (1) year after the Term Commencement Date. Landlord shall have no obligation to disburse any portion of the Tenant Work Allowance at any time when there exists a default under the Lease (provided that such disbursement shall be made promptly after the event or condition giving rise to such default has been corrected or cured by Tenant).

B.4 Tenant Work. Tenant's Initial Construction and all Tenant Improvements in the Leased Premises shall be constructed by Tenant in accordance with, and subject to, the provisions of the Lease. Any structural work, to the extent (if any) required to reinforce portions of the floor of the Leased Premises for filing rooms or similar uses, shall be done with Landlord's reasonable prior approval under Section 4.07, specifically including any Landlord requirements concerning access to adjacent tenant areas. Landlord shall not be responsible for any aspects of the design or construction of Tenant's Initial Construction or other Tenant Improvements, the correction of any defects therein, or any delays in the completion thereof. Tenant shall pay to Landlord, subject to reimbursement from the Tenant Work Allowance, a construction supervision charge in the amount of two percent of the Tenant Work Allowance in respect of the administrative time and coordination work provided by Landlord's construction management staff in connection with Tenant's Initial Construction hereunder.

B.5 Early Access. After Landlord's delivery of the Leased Premises under Section 2.01 of the Lease and prior to the Term Commencement Date, Tenant may enter the Leased Premises for the performance of Tenant's Initial Construction commencing on the date that is the later of (i) Landlord's approval of Tenant's plans for Tenant's Initial Construction, (ii) Landlord's approval of Tenant's Contractor, and (iii) Landlord's receipt of copies of all necessary permits for Tenant's Initial Construction. Such early access to the Leased Premises shall be on all of the terms and conditions of the Lease, except the obligation to pay Gross Rent. Without limiting the generality of the foregoing, Tenant shall be responsible for any third party fees or costs (such as after-hours security, freight elevator operators, and the like) associated with Tenant's construction and move-in activities and reimburse Landlord for such fees and costs within thirty (30) days after invoice, and Tenant shall be responsible for any damage to the Leased Premises caused by Tenant or its employees, agents, contractors, subcontractors, material suppliers and laborers.

B.6 Common Corridor Work. Prior to the Rent Commencement Date, Landlord shall perform, at its sole cost and expense, the work necessary to extend the existing common corridor on the eleventh (11th) floor of the Building as shown on the attached fit plan, using Building standard materials and finishes.

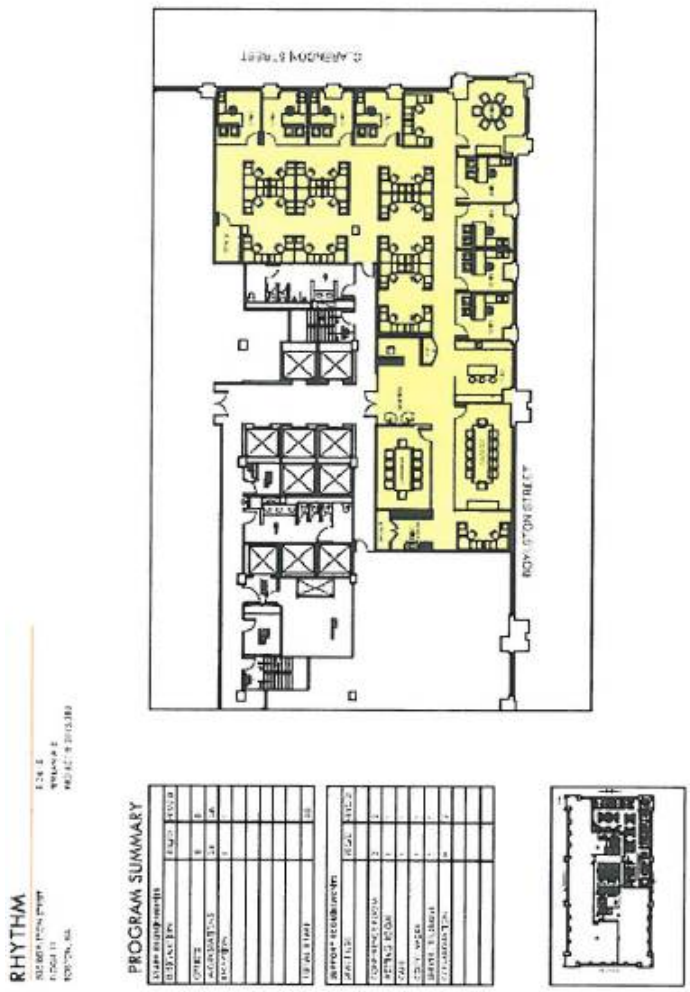

EXHIBIT B-l

Minimum Information Required

Floor Plans Showing:

1. Location and type of all partitions.

2. Location and type of all doors - indicate hardware and provide keying schedule.

3. Location and type of glass partitions, windows and doors - indicate framing if not Building Standard.

4. Location of telephone equipment accompanied by an approval of the telephone company.

5. Critical dimensions necessary for construction.

6. Location of all Building Standard electrical items - outlets, switches, telephone outlets (Building Standard lighting will be determined by Landlord’s architect).

7. Location and type of all non-Building Standard electrical items including lighting.

8. Location and type of equipment that will require special electrical requirements. Provide manufacturer’s specifications for use and operation.

9. Location, weight per square foot and description of any exceptionally heavy equipment or filing system exceeding 50 psf live load.

10. Requirements for special air conditioning or ventilation.

11. Type and color of floor covering.

12. Location, type and color or wall covering.

13. Location, type and color of Building Standard and non-Building Standard paint or finishes.

14. Location and type of plumbing.

15. Location and type of kitchen equipment.

Details Showing:

1. All millwork with verified dimensions and dimensions of all equipment to be built in.

2. Corridor entrance.

3. Bracing or support of special walls, glass partitions, etc., if desired. If not included with the space plan, the Landlord's architect will design all support or bracing required at Tenant's expense.

EXHIBIT B-2

Building Standard Improvements

Building Standard Improvements shall consist of:

A. Partitions

· All walls to extend 6" above finished ceiling, except demising walls and those for conference rooms are to extend from slab to the deck above.
· All walls to be insulated.
· All walls to be constructed using 2½" metal studs 24" on center with one layer 5/8" gypsum board on each side.
· All walls to be primed and painted with a sufficient number of coats of latex painted to achieve proper coverage.

B. Doors and Hardware

· Entrance: two (2) new, building-standard, 3'-0" W x 9'-0" H glass doors with building standard hardware, including door pull and magnetic lock. Card reader by Tenant, white or cream color.
· Interior: full height, solid core, mahogany veneer doors with stained finish, with an anodized, aluminum frame, Rayco-style or equivalent, and lever handle mortise latch set hardware from the Schlage L series.
· Back/Suite Egress: full height, solid core, mahogany veneer doors with split finish (stained on Tenant side to match interior and on multi-tenant corridor side to match other doors there) with welded, hollow metal frame, primed and painted black on common area side, and locking lever handle mortise latch set hardware from the Schlage L series.

C. Millwork

· Plastic Laminate: Wilson Art, Formica or equal.
· Coat Closet: metal coat rod and paint-grade wood hat shelf.

D. Glass & Glazing

· Sidelights: ½" tempered glass with polished edges, clear silicone joints, bottom channel and clean top head detail in sheetrock soffit.

E. Ceiling

· 2' x 2' x ¾" thick ceiling tile, Armstrong Ultima or the like, set in a 9/16" bolt-slot grid system with 1/8" reveal, Armstrong Silhouette XL or the like.

F. Window Treatment

· Horizontal aluminum one-inch, slat blinds for exterior windows.

G. Lighting

· Per Massachusetts energy code of one (1) watt per square foot.
· 2' x 2', direct/indirect, 2-lamp, florescent light fixture with anodized aluminum, perforated center basket or the like, with General Electric T-5 lamps.

H. Switching

· Per Massachusetts Energy code.
· Sensorswitch occupancy sensor model WSD-PDT in white, or equivalent.

I. Power

· 4 watts per square foot for plugs
· Outlets: standard duplex receptacle is wall-mounted 120-volt, 20-amp, with white plastic cover plate, Leviton catalog #16352-W or equivalent. Outlet type for copier to be coordinated with Tenant.
· Wiring: per code.

J. Life Safety Systems

· Sprinklers: per Massachusetts code. Building standard specification — flush ceiling mounted sprinkler heads, centered on ceiling tiles.

· Manual fire alarm pull stations, audible (horn) and visible (strobe) fire alarm notification devices, and smoke detectors: per Massachusetts code and building standard specification — Simplex devices, speaker should be white.
· Emergency Lighting: per code. See “Lighting” for building standard specification.
· Exit Signs: per code. Building standard specification - edge lit, LED.
· Spray Fireproofing: of exposed structural steel, as required, per code.
· Fire Extinguisher: per code, with or without cabinet.

K. Plumbing
· ADA Single Bowl Sink: Elkay #LRAD-2219L (1 hole).
· Faucet: Elkay LKE4160 with all accessories.
· Water heaters should be equipped with leak detection and auto shutdown of cold water feed.

L. Heating, Ventilating, Air Conditioning (HVAC)
· Per Massachusetts code codes applicable to a building constructed in the late 1980’s and within the parameters of the base building infrastructure, and per layout.
· Fan-powered terminal units (FPTU’s) should be specified to be Nailor with linear diffusers at perimeter and 2’x2’ diffusers for interior.
· Supplemental Cooling and Exhaust Fans: by Tenant.

M. Telecommunications & Data (Tel/Data)
· By Tenant.

EXHIBIT C

Building Rules and Regulations
for Five Hundred Boylston (the “Building”)

1. The sidewalks, doorways, halls, stairways, vestibules and other similar areas shall not be obstructed or used for any purpose other than ingress to and egress from Tenants’ respective leased premises, and for going from one part of the Building to another part.

2. Plumbing fixtures shall be used only for their designated purpose, and no substances of any kind shall be deposited therein which they are not designed to handle. Damage to any such fixture resulting from misuse by any Tenant or its employees or invitees shall be repaired at the expense of such Tenant.

3. Signs, advertisements, graphics, or notices visible in or from public corridors shall be subject to Landlord’s written approval. Nails, screws, and other attachments to the Building require prior written consent from Landlord. Upon the removal of sign, notice or graphic from a building door or public corridor the Tenant is responsible for returning the surface to its original condition.

4. Landlord will provide and maintain an alphabetical directory board for all office tenants of the Building in accordance with each Tenant’s lease on the first floor (main lobby) of the Building, the size, design and location to be determined by Landlord. No other directory shall be allowed.

5. All contractors and technicians rendering any installation service to tenants shall be subject to Landlord’s approval and supervision prior to performing services. This applies to all work performed in the Building, including, (but not limited to) installation of telephone, telegraph equipment and electrical devices, windows, ceilings, and any other physical portion of the Building.

6. Movement in to, inside or out of the Building of furniture, office equipment, or other bulky material which requires the use of elevators, stairways, or Building entrance and lobby shall be restricted to hours established by Landlord. All such movements shall be restricted to the Building’s freight elevators. Pre-arrangements with Landlord should be made regarding the time, method, and routing of movement, and tenants shall assume all risks of damages to articles moved and injury to persons or public resulting from such moves. Landlord shall not be liable for any acts or damages resulting from any such activity.

7. Any damage to the Building by the movement of a Tenant’s property, or done by a Tenant’s property while in the Building, shall be repaired at such Tenant’s expense.

8. Landlord shall have the power to reasonably prescribe the weight and position of safes and other heavy equipment, which shall in all cases, to distribute weight, stand on supporting devices approved by Landlord. In addition, Tenants shall obtain written approval of Landlord prior to installation or subsequent relocation of any safes or heavy equipment. Tenants shall be responsible for all costs associated with said installation or relocation, including, but not limited to engineering analysis and structural changes.

9. All routine deliveries to the premises shall be made between the hours of 6:00 a.m. and 6:00 p.m. weekdays (other than holidays) unless other arrangements are approved in

advance by the Building management office, and only shall be made through the freight elevators. Passenger elevators are to be used only for the movement of persons, unless an exception is approved by the Building management office. Courier use of passenger elevators shall be limited to Business Hours during Business Days unless otherwise approved by Landlord. Delivery hours are subject to change by Landlord. Tenants will adhere to any peak delivery restrictions implemented by the City of Boston. Delivery personnel/companies who do not adhere to building rules can be barred from the property by the Property Manager.

10. Corridor doors shall be kept closed.

11. Tenants shall cooperate with Landlord in maintaining their leased premises. Unless otherwise approved by Landlord office, Tenants shall not employ any person for the purpose of cleaning the leased premises other than the Building's cleaning and maintenance personnel.

12. Deliveries of water, soft drinks, newspapers, or other such items to any Tenant's leased premises shall be made only be suppliers approved by Landlord, and shall be restricted to hours established by Landlord and made by use of the freight elevators, if Landlord so directs.

13. Nothing shall be swept or thrown into the corridors, halls, elevator shafts, or stairways. No birds, fish, or animals of any kind shall be brought into or kept in, on or about any Tenant's leased premises.

14. Restaurants excluded, no cooking shall be done in any Tenant's leased premises except in connection with convenience lunch room or beverage service for employees and guests (on a non-commercial basis). All permitted cooking shall be done in a manner which complies with all of the provisions of the Tenant's lease and which does not produce fumes or odors. All cooking facilities shall be subject to approval of Landlord and must be approved by all applicable state and municipal authorities.

15. Food, soft drink or other vending machines shall not be placed within any Tenant's leased premises without Landlord's prior written consent.

16. No Tenant shall use or keep on its leased premises any kerosene, gasoline, or inflammable or combustible fluid or material other than limited quantities reasonably necessary for the operation and maintenance of office equipment. No Tenant shall use or keep any noxious gas or substances in its leased premises, or permit its leased premises to be used in a manner offensive or objectionable to Landlord or other occupants of the Building by reason of noise, odors, or vibrations, or interfere in any way with other tenants or those having business therein. All equipment causing vibrations shall be isolated.

17. Office Tenants shall not tamper with or attempt to adjust temperature control thermostats in their leased premises. Landlord shall make adjustments in thermostats on call from Tenants.

18. Tenants shall comply with all requirements necessary for the security of their leased premises and the Building, including the use of service passes issued by Landlord for after-hours movement of office equipment/packages, and signing security register in Building lobby after hours.

19. Landlord will furnish each Tenant with a reasonable number of initial keys for entrance doors into its leased premises, and may charge for additional keys thereafter. All such keys shall remain the property of Landlord. No additional locks will be allowed on any door of any leased premises without Landlord's prior written consent and Tenants shall not make any duplicate keys, except those provided by Landlord. Upon termination of this Lease, each Tenant shall surrender to Landlord all keys to its leased premises, and give to Landlord the combination of all locks for safes and vault doors, if any, in the leased premises.

20. Canvassing, peddling, soliciting and distribution of hand-bills in the Building are prohibited and each Tenant will cooperate to prevent these activities.

21. Tenants shall not make or permit any improper noises in the Building or otherwise interfere in any way with other Tenants or persons having business with them.

22. Landlord will not be responsible for lost or stolen personal property, money or jewelry from any Tenant's leased premises or public areas, regardless of whether such loss occurs when such area is locked against entry or not.

23. Building emergency stairs shall only be used for emergency purposes.

24. Tenant will work with Landlord in informing and enforcing building delivery rules with Tenant's delivery personnel, agents or invitees.

25. The building common areas including the garage and exterior are non-smoking areas. Tenants who permit smoking within their leased premises shall control the smoke and odor so it is not offensive or does not interfere with other building Tenants.

26. All Tenants will cooperate with Landlord and abide with local code in the testing and servicing of the Building life safety system.

27. Landlord reserves the right to modify or rescind any of these rules and regulations and to make future rules and regulations required for the safety, protection, and maintenance of the Building, the operation and preservation of good order thereof, and the protection and comfort of the Tenants and their employees and their visitors. Such rules and regulations, when made and written notice given to a Tenant, shall be binding upon such Tenant as if originally herein prescribed.

EXHIBIT D

LETTER OF CREDIT REQUIREMENTS

The letter of credit shall be for the amount specified in the Lease to which this Exhibit is attached (as renewed, replaced, and/or reduced pursuant to the Lease or this Exhibit, the "Letter of Credit"). The Letter of Credit (i) shall be irrevocable and shall be issued by a commercial bank reasonably acceptable to Landlord that either has an office in Boston, Massachusetts or New York City or permits draws to be made by overnight courier delivery, (ii) shall require only the presentation to the issuer of a certificate of the holder of the Letter of Credit stating that Landlord is entitled to draw on the Letter of Credit pursuant to the terms of the Lease, (iii) shall be payable to Landlord or its successors in interest as the Landlord and shall be transferable to any such successor or any lender holding a collateral assignment of Landlord's interest in the Lease, at no cost to Landlord or such transferee, (iv) shall be for an initial term of not less

than one (1) year and contain a provision that such term shall be automatically renewed for successive one-year periods unless the issuer shall, at least sixty (60) days prior to the scheduled expiration date, give Landlord notice of such nonrenewal, and (v) shall otherwise be in form and substance reasonably acceptable to Landlord. In the event that the issuer ceases to be reasonably acceptable to Landlord, due to a deterioration in its financial condition or change in status that threatens to compromise Landlord's ability to draw on the Letter of Credit, then Tenant shall provide a replacement Letter of Credit satisfying the terms of this Exhibit within thirty (30) days after notice of such event. Notwithstanding the foregoing, the term of the Letter of Credit for the final period shall be for a term ending not earlier than the date thirty (30) days after the last day of the Term.

Landlord shall be entitled to draw upon the Letter of Credit for its full amount or any portion thereof if (a) Tenant shall fail to perform any of its obligations under this Lease after the expiration of any applicable notice and cure period (or fail to perform any of its obligations under the Lease and transmittal of a default notice or running of any cure period is barred or tolled by applicable law), or (b) not less than 30 days before the scheduled expiration of the Letter of Credit, Tenant has not delivered to Landlord a new Letter of Credit in accordance with this Exhibit. Without limiting the generality of the foregoing, Landlord may, but shall not be obligated to, draw on the Letter of Credit from time to time in the event of a bankruptcy filing by or against Tenant and/or to compensate Landlord, in such order as Landlord may determine, for all or any part of any unpaid rent, any damages arising from any termination of this Lease in accordance with its terms, and/or any damages arising from any rejection of this Lease in a bankruptcy proceeding commenced by or against Tenant. Landlord may, but shall not be obligated to, apply the amount so drawn to the extent necessary to cure Tenant's failure to pay. Any amount drawn in excess of the amount applied by Landlord to cure any such failure shall be held by Landlord as a cash security deposit under Section 4.17 of the Lease for the performance by Tenant of its obligations under the Lease. After any such application by Landlord of the Letter of Credit or security deposit, Tenant shall reinstate the Letter of Credit to the amount originally required to be maintained under the Lease, upon demand (it being understood that such reinstatement obligation shall take into account both the then undrawn amount of the Letter of Credit and any unapplied cash security deposit then held by Landlord). If Tenant is then in compliance with all of its obligations under the Lease, within thirty (30) days after the expiration or sooner termination of the Term the Letter of Credit and any security deposit, to the extent not applied, shall be returned to the Tenant, without interest.

In the event of a sale of the Building or lease, conveyance or transfer of the Building, Landlord shall transfer the Letter of Credit or security deposit to the transferee. Upon such delivery of the letter of credit or security deposit to the transferee, the transferring Landlord shall be released by Tenant from all liability for the return of such security, and Tenant agrees to look to the transferee solely for the return of said security. The provisions hereof shall apply to every

transfer or assignment made of the security to such a transferee. Tenant further covenants that it will not assign or encumber or attempt to assign or encumber the Letter of Credit or the monies deposited herein as security, and that neither Landlord nor its successors or assigns shall be bound by any assignment, encumbrance, attempted assignment or attempted encumbrance.

EXHIBIT E

CLEANING SPECIFICATIONS

A. Daily Services — General (after 6:00 p.m. on Business Days)

1. Empty trash cans.
2. Dust all horizontal surfaces, desks, chairs, files, telephones, picture frames, etc. Computers will not be dusted.
3. Damp wash and wipe dry plastic or Formica desktops free of papers.
4. Clean and sanitize drinking fountains.
5. Spot clean all windows glass, including lobby doors for fingerprints and smudges
6. Dust mop and spot clean all tiled areas.
7. Vacuum carpeted traffic areas daily, wall to wall once per week.

B. Daily Services - Restrooms

1. Remove trash and clean receptacles.
2. Clean and sanitize lavatories, commodes, and urinals.
3. Clean out corners and edges.
4. Clean mirrors.
5. Spot clean wall tile and partitions.
6. Replenish supplies.
7. Sweep floor.
8. Mop and disinfect floor as necessary.

C. Daily Services - Elevators

1. Clean light lenses and replace burned out bulbs.
2. Spot clean walls.
3. Clean edges, corners, and tracks.
4. Vacuum carpet.

D. Daily Services - Street Level

1. Sweep all marble and/or granite public areas.
2. Clean all glass entrance ways and side panels.
3. Empty all ash urns.

4. Spot clean marble and/or granite walls.
5. Dust all horizontal edges.

E. Weekly Services - Stairways

1. Sweep from top to bottom.
2. Dust handrails and ledges.
3. Dust lights between floors.

F. Weekly Services - Marble/Granite Floors

1. Mop and/or wash all public areas.

G. Monthly Services - Tile Floors

1. Clean and wash all traffic lanes and other “high wear” areas.

H. Annual Services - General

1. Clean inside of all exterior windows.
2. Clean all fluorescent light fixture lenses.
3. Wash down all restroom walls and partitions.

I. Services as required

1. Spot clean carpeted areas.
2. Shampoo public areas outside tenant space.
3. Damp mop all tile floors.
4. Strip and recoat all tile floors.

J. Services - Building Exterior

1. Daily

    a. Police building perimeter for trash.
    b. Remove trash from tree wells and planters.

K. Services - Day Crew

1. Police and replenish supplies in all restrooms.
2. Vacuum all passenger elevators twice each day.
3. Clean and vacuum garage elevators.
4. Clean all ash urns twice each day.
5. Clean all glass entrance doors in main lobby.
6. Dust mop and/or damp mop all marble and/or granite floors in main lobby once each day.
7. Clean all windows on building perimeter at street level as needed.
8. Clean service area, hallway, and dock area.

PARKING ADDENDUM

Tenant shall have the right to use in the garage located within the Building a total of two (2) parking spaces, which shall be for unreserved spaces. If Tenant relinquishes any of such parking rights during the Term, Tenant shall no longer have a right to the parking relinquished and may obtain future parking solely upon a space-available basis. Rates charged by Landlord or its operator for such parking shall be the prevailing market rate for reserved or unreserved parking spaces, as the case may be, in such location as established by Landlord or its operator from time to time. The current rates are $675 per space per month for reserved spaces and $430 per space per month for unreserved spaces. Tenant’s right to use of the parking shall be subject to (i) timely payment of the parking rate as established from time to time, (ii) such further rules and regulations as Landlord or its operator may establish from time to time, and (iii) all applicable laws, ordinances, rules and regulations. Any additional month to month parking spaces that Tenant may from time to time request shall be at the prevailing market rate and subject to availability in accordance with Landlord’s customary practices in managing the garage at the Building.

Tenant shall encourage these spaces to be used by Multi-rider vehicles. A 10% discount will be provided on monthly parking rates for all registered carpools and vanpools.

Landlord has the right to lease the parking area to a third party operator (the “Parking Lessee”), in which case such Parking Lessee shall succeed to the rights and benefits, and assume and be fully responsible for the performance of Landlord’s obligations under this Addendum. If Landlord leases the parking space to a Parking Lessee, (i) Tenant shall pay the Parking Lessee directly for the use of the parking spaces and (ii) all references to “Landlord” in this Addendum shall, unless the context indicates otherwise, be read to mean the “Parking Lessee.”

RHYTHM PHARMACEUTICALS, INC.

CONSULTING AGREEMENT

This CONSULTING AGREEMENT (this "Agreement") is entered into as of June 12, 2017 ("Effective Date"), by and between Rhythm Pharmaceuticals, Inc. (the "Company"), a Delaware corporation, and Bart Henderson (the "Consultant").

1. Consulting Services.

(a) Subject to and upon the terms and conditions set forth in this Agreement, the Company hereby retains the Consultant, and the Consultant hereby agrees to be retained by the Company, to provide such consulting services as shall be determined and reasonably requested from time to time by or on behalf of the Company.

(b) The amount of time that Consultant shall devote to the performance of consulting services pursuant to this Agreement shall be mutually agreed upon by the Consultant and the Company. Unless otherwise agreed to by the Consultant and the Company in writing, the terms of compensation described in Section 2 hereof will apply.

(c) The Consultant shall provide consulting services under this Agreement at such times and locations as are mutually agreed upon by the Consultant and the Company. In rendering consulting services under this Agreement, the Consultant shall act solely as an independent contractor and this Agreement shall not be construed to create any employee/employer relationship between the Consultant and the Company.

(d) During the Term of this Agreement (as defined in Section 3 below), and except to the extent otherwise agreed upon in writing by the Consultant and the Company, the Consultant will keep separate and not co-mingle (i) his services for the Company, and (ii) any contact information obtained during his consulting relationship with the Company, with those provided, or pursuant, to his current employer and any other consulting arrangements.

(e) It is understood and agreed that, subject to the provisions of Section 1(d) and Section 7 hereof, the Consultant may be involved in any capacity in other businesses, endeavors and undertakings.

2. Compensation.

(a) Subject to, and in accordance with, the terms and conditions set forth in this Agreement, the Company shall, so long as the Consultant is providing consulting services to the Company under this Agreement, pay the Consultant a consulting fee in an amount equal to $400.00 per hour (the "Consulting Fee") spent rendering consulting services pursuant to this Agreement. For the first two months (June 12 — August 12, 2017), the number of hours per week will not exceed, and will be capped at no more than, 15 hours per week, and for the next two months (August 12, 2017 — October 12, 2017), the number of hours per week will not exceed, and will be capped at no more than, 10 hours per week. Notwithstanding the foregoing, the Consultant may exceed such hourly caps if the Consultant: (i) notifies the

Company in advance that the activities will exceed the determined hourly cap for the respective period, and (ii) receives prior written approval of the Company that the Consultant may exceed such cap(s).

(b) The Consultant shall invoice the Company for services rendered during the preceding calendar month no later than the 20th day of each calendar month, except for work completed June 12 — August 23, which will be invoiced no later than August 31. Each such monthly invoice shall set forth a reasonable description of the consulting services performed by the Consultant during the applicable month and the number of hours spent by the Consultant rendering such consulting services. The Company shall make payment of each such invoice within thirty (30) days of the date the Company receives such invoice, except for the portion of any such invoice that is disputed by the Company in good faith.

(c) The Company will not withhold any tax or Social Security payments due from the Consultant to any governmental taxing authority. The Consultant hereby agrees that he will timely pay all taxes and fees upon the income he has earned from the Company, and will indemnify and hold the Company harmless against the claims of any governmental taxing authority made in connection with the revenue derived by the Consultant under this Agreement.

(d) The Company shall reimburse the Consultant for any actual out-of-pocket expenses incurred by the Consultant while rendering consulting services under this Agreement so long as such expenses are reasonable and necessary, and appropriately documented and approved per the Company's standard practices. Without limiting the generality of the foregoing, any out-of-pocket travel expenses as well as any out-of-pocket expenses that, individually or in the aggregate, exceed $500.00, shall be reimbursed by the Company only if approved by the Company in advance of such out-of-pocket expenses being incurred by the Consultant.

(e) In consideration of the Consultant's prior service to the Company as a founder and former employee, and to the consulting arrangement contemplated by this Agreement, notwithstanding the terms of (i) the prior Employment Agreement, by and between the Company and the Consultant, dated as of November 16, 2016, (ii) the 2015 Equity Incentive Plan of the Company, as amended and in effect to date, (iii) any stock option agreements by and between the Company and the Consultant, and (iv) any compensatory unit vesting agreements by and between the Company's parent, Rhythm Holding Company, LLC (the "Parent") and the Consultant: (x) the Consultant will continue to vest in any restricted equity held in the Company and the Parent through and including December 31, 2017 on the same schedule as though the service relationship between the parties had not terminated, and (y) the Consultant will be able to exercise any vested options or compensatory units through and including October 1, 2018, notwithstanding any expiration of the Term of this Agreement prior to such dates. To clarify the foregoing, even if the Consultant is no longer providing services in any manner to the Company, he will continue to vest through December 31, 2017, and will have until October 1, 2018 to exercise any vested equity.

(f) Except for the Consulting Fee provided for under Section 2(a) hereof, any expense reimbursement in accordance with Section 2(d) hereof, and any equity vesting arrangements pursuant to Section 2(e) hereof, the Company shall have no obligation to provide any compensation to the Consultant with respect to any services rendered by the Consultant to the Company pursuant to this Agreement.

3. Term; Termination.

(a) This Agreement shall take effect as of the Effective Date and shall continue thereafter in full force and effect until October 12, 2017, unless either extended in accordance with the provisions of Section 3(b) hereof, or terminated in accordance with the provisions of Section 3(c) hereof (the "Term"). The Consultant shall begin providing consulting services to the Company on the Effective Date.

(b) This Agreement may be renewed by the Company for successive one-month periods (the "Renewal Period(s)") if the Company gives the Consultant at least fourteen (14) days' prior written notice of such renewal and the Renewal Period is agreed to by the Consultant and the Company in writing. The number of hours per week for each Renewal Period will not exceed, and will be capped at no more than, 10 hours per week. If the Agreement is extended under a Renewal Period, the only compensation for the Consultant's services during the Renewal Period will be as set forth in Section 2(a) hereof. For the avoidance of doubt, there will be no alterations to the vesting or exercise terms set forth in Section 2(e) hereof as a result of any extended Term or Renewal Period.

(c) This Agreement and the consulting services provided by the Consultant hereunder may be terminated at any time by either the Consultant or the Company for any reason or no reason by giving at least fourteen (14) days' prior written notice of termination to the other party. This Agreement and the consulting services provided by the Consultant hereunder shall terminate immediately upon the Consultant's death. The provisions of Sections 4, 5, 6, 7, 8 and 9 shall survive the termination of this Agreement.

(d) Upon expiration or termination of this Agreement, the Consultant agrees that he will not represent himself to third parties as continuing to have ongoing obligations to and with the Company, and will not hold himself out as having a role with the Company, nor have any authority to speak or act for or on behalf of the Company.

4. Confidential Information.

(a) For purposes of this Agreement, the term "Confidential Information" shall mean (i) confidential information, knowledge or data of the Company or any of its affiliates (each a "Related Company" and collectively the "Related Companies"), (ii) trade secrets of any Related Company, and (iii) any other information of any Related Company disclosed to the Consultant or to which the Consultant is given access prior to the termination of his consulting services to the Company. Without limiting the generality of the foregoing, the term Confidential Information shall include (A) all inventions, improvements, developments, ideas, processes, prototypes, plans, drawings, designs, models, formulations, specifications, methods, techniques, shop-practices, discoveries, innovations, creations,

technologies, formulas, algorithms, data, computer databases, reports, laboratory notebooks, papers, writings, photographs, source and object codes, software programs, other works of authorship, and know-how (including all records pertaining to any of the foregoing), whether or not reduced to writing and whether or not patented or patentable or registered or registrable under patent, copyright, trademark or similar statute (collectively, "Inventions"), that are owned by any Related Company or that are required to be assigned to the any Related Company by any person, including, without limitation, any employee or consultant of any Related Company, or that are licensed to any Related Company by any person, (B) information regarding any Related Company's plans for research and development or for new products, (C) engineering or manufacturing information pertaining to any Related Company or any of its operations or products, (D) information regarding regulatory matters pertaining to any Related Company, (E) information regarding any acquisition or strategic alliance effected by any Related Company or any proposed acquisition or strategic alliance being considered by any Related Company, (F) information regarding the status or outcome of any negotiations engaged in by any Related Company, (G) information regarding the existence or terms of any contract entered into by any Related Company, (H) information regarding any aspect of any Related Company's intellectual property position, (I) information regarding prices or costs of any Related Company, (J) information regarding any aspect of the business strategy of any Related Company, including, without limitation, marketing, selling and distribution strategies, (K) information regarding customers or suppliers of any Related Company, (L) information regarding the skills, compensation and other terms of employment or engagement of employees and consultants of any Related Company, (M) business plans, budgets, unpublished financial statements and unpublished financial data of any Related Company, (N) information regarding marketing and sales of any actual or proposed product or services of any Related Company, and (O) any other information that any Related Company may designate as confidential.

(b) The Consultant acknowledges that, except to the extent otherwise provided in this Section 4(b) or in Section 4(d) hereof, all Confidential Information disclosed to or acquired by the Consultant is a valuable, special, and unique asset of the Company and is to be held in trust by the Consultant for the Company's sole benefit. Except as otherwise provided in this Section 4(b) or in Section 4(d) hereof, the Consultant shall not, at any time during or after the Term, use for himself or others, or disclose or communicate to any person for any reason, any Confidential Information without the prior written consent of the Company. Notwithstanding anything in this Section 4(b) to the contrary, it is understood that, except to the extent otherwise expressly prohibited by the Company, (i) the Consultant may disclose or use Confidential Information in performing his consulting services to the Company but only to the extent required or necessary for the performance of such consulting services in the ordinary course and within the scope of his consulting services, and (ii) the Consultant may disclose any Confidential Information pursuant to a request or order of any court or governmental agency, provided that the Consultant promptly notifies the Company of any such request or order and provides reasonable cooperation (at the Company's expense) in the efforts, if any, of the Company to contest or limit the scope of such request or order.

(c) The Consultant acknowledges and agrees that the Company has received, and each Related Company may receive in the future, confidential or proprietary information

from third parties ("Third-Party Confidential Information") subject to a duty on the part of the Company or any other Related Company to maintain the confidentiality of such Third-Party Confidential Information and to use it only for certain limited purposes. During the Term and thereafter, the Consultant shall hold Third-Party Confidential Information in the strictest confidence and will not use or disclose to anyone any Third-Party Confidential Information, unless expressly authorized in writing by the Company or unless otherwise provided below in this Section 4(c) or in Section 4(d) hereof. Notwithstanding anything in this Section 4(c) to the contrary, it is understood that, except to the extent otherwise expressly prohibited by the Company, (i) the Consultant may disclose or use Third-Party Confidential Information in performing his consulting services for the Company but only to the extent required or necessary for the performance of such consulting services in the ordinary course and within the scope of his consulting services, and (ii) the Consultant may disclose any Third-Party Confidential Information pursuant to a request or order of any court or governmental agency, provided that the Consultant promptly notifies the Company of any such request or order and provides reasonable cooperation (at the Company's expense) in the efforts, if any, of the Company to contest or limit the scope of such request or order.

(d) The Consultant's obligations under Section 4(b) and Section 4(c) hereof not to use, disclose or communicate Confidential Information or Third-Party Confidential Information to any person without the prior written consent of the Company shall not apply to any Confidential Information or Third-Party Confidential Information (i) that is or becomes publicly known (as demonstrated by written evidence provided by the Consultant) under circumstances involving no breach by the Consultant of this Agreement or (ii) that was or is approved for release by the Board of Directors of the Company or an authorized representative of the Company.

(e) The obligations of the Consultant under this Section 4 are without prejudice, and are in addition, to any other obligations or duties of confidentiality, whether express or implied or imposed by applicable law, that are owed to the Company or any other person to whom the Company owes an obligation of confidentiality.

5. No Improper Disclosure or Use of Materials.

(a) The Consultant shall not improperly use or disclose to, or for the benefit of, any Related Company any confidential information or trade secrets of (i) any former, current or future employer, (ii) any person to whom the Consultant has previously provided, currently provides or may in the future provide consulting services, or (iii) any other person to whom the Consultant owes an obligation of confidentiality. The Consultant shall not bring onto the premises of any Related Company any unpublished documents or any property belonging to any person referred to in the foregoing clauses (i)-(iii) of this Section 5(a) unless consented to in writing by such person. Without limiting the generality of the foregoing, the Consultant shall not disclose to any Related Company, and shall not use for the benefit of any Related Company, any information relating to or arising out of Consultant's work conducted at his present employer, or utilizing the funds, personnel, facilities, materials or other resources of his present employer, until such information has been published.

(b) The Consultant will promptly deliver to the Company, upon the termination of the Consultant's consulting services to the Company or, if earlier, upon the request of the Company, all documents and other tangible media (including all originals, copies, reproductions, digests, abstracts, summaries, analyses, notes, notebooks, drawings, manuals, memoranda, records, reports, plans, specifications, devices, formulas, storage media, including software, and computer printouts) in the Consultant's actual or constructive possession or control that contain, reflect, disclose or relate to any Confidential Information, Third-Party Confidential Information, Assigned Inventions (as defined in Section 6(a) below) or Proprietary Rights (as defined in Section 6(a) below). The Consultant will destroy any related computer entries on equipment or media not owned by any Related Company.

6. Inventions; Assignment.

(a) For purposes of this Agreement, the term "Assigned Inventions" (subject to the provisions of Section 6(c) hereof) shall mean any and all Inventions that (i) are made, conceived, invented, discovered, originated, authored, created, learned or reduced to practice by the Consultant, either alone or together with others, in the course of rendering his consulting services hereunder (regardless of whether or not such Inventions were made, conceived, invented, discovered, originated, authored, created, learned or reduced to practice by the Consultant at the Company's facilities or during regular business hours or utilizing resources of the Company), or (ii) arise out of or are based upon any Confidential Information or Third-Party Confidential Information. For purposes of this Agreement, the term "Proprietary Rights" shall mean any and all rights under or in connection with any patents, patent applications, copyrights, copyright applications, mask works, trade secrets and other intellectual property rights with respect to Assigned Inventions.

(b) The Consultant hereby agrees to hold any and all Assigned Inventions and Proprietary Rights in trust for the sole right and benefit of the Company and such other person or persons as the Company shall designate in writing, and the Consultant hereby assigns to the Company and such other person or persons as the Company shall designate in writing all of his right, title and interest in and to any and all Assigned Inventions and Proprietary Rights. The Consultant agrees to give the Company prompt written notice of any Assigned Invention or Proprietary Right and agrees to execute such instruments of transfer, assignment, conveyance or confirmation and such other documents as the Company may request to evidence, confirm or perfect the assignment of all of the Consultant's right, title and interest in and to any Assigned Invention or Proprietary Right pursuant to the foregoing provisions of this Section 6(b). The Consultant hereby waives and quitclaims to the Company any and all claims of any nature whatsoever that the Consultant may now or hereafter have for infringement of any Proprietary Rights assigned hereunder to the Company. The obligations of the Consultant under this Section 6(b) are without prejudice, and are in addition to, any other obligations or duties of the Consultant, whether express or implied or imposed by applicable law, to assign to the Company all Assigned Inventions and all Proprietary Rights.

(c) It is hereby understood and agreed that the Consultant is not assigning, and has not agreed to assign, to the Company pursuant to this Section 6, and that the term

"Assigned Inventions" shall not include, any right, title or interest in and to any Inventions, whether or not reduced to writing and whether or not patentable or registrable under patent, copyright, trademark or similar statutes, that are made, conceived, invented, discovered, originated, authored, created, learned or reduced to practice by the Consultant, either alone or together with others, in the course of his activities at his present employer or through the use of funds, personnel, laboratory facilities, research materials or other research resources of his present employer; provided, however, that such Inventions do not arise out of, nor are based upon, any Confidential Information or Third Party Confidential Information without proper authorization from the Company.

(d) At the request of the Company, the Consultant will assist the Company in every proper way to obtain and enforce in any country in the world Proprietary Rights relating to any or all Assigned Inventions. The Consultant's obligation under this Section 6(d) shall continue beyond the Term. If and to the extent that, at any time after the Term, the Company requests assistance from the Consultant with respect to obtaining and enforcing in any country in the world any Proprietary Rights relating to Assigned Inventions, the Company shall compensate the Consultant at a reasonable rate for the time actually spent by the Consultant on such assistance.

(e) Without the prior written consent of the Company, the Consultant shall not, at any time, file any patent or copyright application with respect to, or claiming, any Assigned Inventions.

(f) The obligations of the Consultant under this Section 6 are without prejudice, and are in addition, to any other obligations or duties, whether express or implied or imposed by applicable law, of the Consultant to assign Inventions to the Company.

7. No Conflicting Obligation.

(a) The Consultant hereby represents that he is free to enter into this Agreement and that his performance of all of the terms of this Agreement and of all of his duties as a consultant to the Company do not and will not breach (i) any agreement to keep in confidence information acquired by the Consultant in confidence or in trust, (ii) any agreement to assign to any third party inventions made by the Consultant, or (iii) any agreement not to compete against the business of any third party. Consultant further represents that he has not made and will not make any agreements in conflict with this Agreement.

(b) During the term of this Agreement and for a period of one (1) year following termination of Consultant's services pursuant to this Agreement, the Consultant (for his or her benefit or for the benefit of any other person, including any other person with which the Consultant may have a direct or indirect interest or relationship as an employee, consultant, advisor, equityholder or otherwise) shall not solicit or induce or attempt to induce any customer, vendor, contractor, employee, consultant or advisor of any Related Company to terminate, diminish, or materially alter his, her or its relationship with any Related Company.

(c) In the event that a court finds this Section 7, or any of its restrictions, to be unenforceable or invalid, the Consultant and the Company hereby agree that (i) this Section 7 will be automatically modified to provide the Company with the maximum protection of its business interests allowed by law and (ii) the Consultant shall be bound, and such court shall enforce, this Section 7 as so modified.

8. No Use of Name, Etc.; Non-Disparagement.

(a) Without the prior written consent of the Company, the Consultant shall not at any time use, for himself or on behalf of any other person, any name that is identical or similar to or likely to be confused with the name of any Related Company or any product or service produced or provided by any Related Company. The Company shall not use, and shall cause each other Related Company not to use, the name of the Consultant or that of the Consultant's past or present employer, or any adaptation thereof in any advertising, promotional or sales literature without prior written consent obtained from the Consultant.

(b) The Company and the Consultant acknowledge that the Consultant is the Founder, and former employee, President, and Treasurer of the Company. The Company agrees to acknowledge the Consultant as a Founder and former President of the Company, so long as such recognition continues to be in accordance with applicable rules and regulations of public companies if and when the Company goes public. The Consultant shall not hold himself out as currently representing the Company without the prior written consent of the Company, unless it is within the scope of the consulting services being provided for the Company. Matters and inquiries outside the scope of the consulting services and relating to the Company should be directed to the Chief Executive Officer of the Company or other appropriate Company personnel.

(c) The Consultant agrees not issue or cause to be issued or condone the issuance of any communication, written or otherwise, that disparages, criticizes, or otherwise reflects adversely or discourages any adverse action against the Company (or its products or services or employees), except if testifying truthfully under oath pursuant to any lawful court order or subpoena or otherwise communicating as is required or protected by law. The Company agrees not issue or cause to be issued or condone the issuance of any communication, written or otherwise, that disparages, criticizes, or otherwise reflects adversely or discourages any adverse action against the Consultant, except as required or protected by law.

9. Miscellaneous.

(a) This Agreement represents the entire Agreement of the parties with respect to the arrangements contemplated hereby. No prior agreement, whether written or oral, shall be construed to change, amend, alter, repeal or invalidate this Agreement. This Agreement may be amended only by a written instrument executed in one or more counterparts by the parties.

(b) No consent to or waiver of any breach or default in the performance of any obligations hereunder shall be deemed or construed to be a consent to or waiver of any other

breach or default in the performance of any of the same or any other obligations hereunder. Failure on the part of either party to complain of any act or failure to act of the other party or to declare the other party in default, irrespective of the duration of such failure, shall not constitute a waiver of rights hereunder and no waiver hereunder shall be effective unless it is in writing, executed by the party waiving the breach or default hereunder.

(c) This Agreement shall be binding upon and inure to the benefit of the parties hereto and their respective successors and permitted assigns. This Agreement may be assigned by the Company to any Affiliate of the Company and to a successor of its business to which this Agreement relates (whether by purchase or otherwise). "Affiliate of the Company" means any person or entity which, directly or indirectly, controls or is controlled by or is under common control with the Company and, for the purposes of this definition, "control" (including the terms "controlled by" and "under common control with") shall mean the possession, directly or indirectly, of the power to direct or cause the direction of the management and policies of another whether

through the ownership of voting securities or holding of office in another, by contract or otherwise. The Consultant may not assign or transfer any or all of his rights or obligations under this Agreement.

(d) Unless otherwise provided herein, any notice, report, payment or document to be given by one party to the other shall be in writing and shall be deemed given when delivered personally or mailed by certified or registered mail, postage prepaid (such mailed notice to be effective on the date which is three (3) business days after the date of mailing), or sent by nationally recognized overnight courier (such notice sent by courier to be effective one business day after it is deposited with such courier), or sent by email (such notice sent by email to be effective when sent, if confirmed by certified or registered mail or overnight courier as aforesaid), or sent by telefax (such notice sent by telefax to be effective when sent, if confirmed by certified or registered mail or overnight courier as aforesaid) addressed to the party at the address set forth on the signature page to this Agreement or to such other place as any party may designate as to itself by written notice to the other party. Either party may change its address for notices by means of a notice delivered in accordance with this Section 9(d).

(e) In connection with any initial public offering of the Company, the Consultant agrees to sign any lock-up agreement requested by the underwriters of the Company; provided that it is the same form of lock-up agreement that the Chief Executive Officer of the Company will sign.

(f) This Agreement shall be governed by and construed in accordance with the substantive laws of the Commonwealth of Massachusetts without reference to any choice or conflict of laws rule or provision that would result in the application of the substantive law of any other jurisdiction. Section headings of this Agreement are for reference only and shall not affect its interpretation. In the event that any provision of this Agreement should be held unenforceable by a court of competent jurisdiction, such court is hereby authorized to amend such provision so as to be enforceable to the fullest extent permitted by law, and all remaining provisions shall continue in full force without being impaired or invalidated in any way.

(g) The parties agree that any breach or threatened breach of Sections 4, 5, 6, 7 or 8 of this Agreement by the Consultant would cause irreparable harm to the Company; and that money damages will not provide an adequate remedy. In the event of a breach or threatened breach of Sections 4, 5, 6, 7 or 8 of this Agreement by the Consultant, the Company shall, in addition to any other rights and remedies it may have, be entitled to an injunction, without the need to post bond. The parties agree that any breach or threatened breach of Sections 4, 5, 6, 7 or 8 of this Agreement by the Company would cause irreparable harm to the Consultant; and that money damages will not provide an adequate remedy. In the event of a breach or threatened breach of Sections 4, 5, 6, 7 or 8 of this Agreement by the Company, the Consultant shall, in addition to any other rights and remedies it may have, be entitled to an injunction, without the need to post bond.

(h) In the event that the Company or conversely the Consultant enforces the provisions of Section 7(b) hereof through a court order, the Consultant, or conversely the Company agrees that the restrictions contained in Section 7(b) shall remain in effect for a period of one year from the effective date of such court order.

(i) This Agreement may be executed in counterparts, all of which together shall for all purposes constitute one agreement binding on each of the parties hereto notwithstanding that each such party shall not have signed the same counterpart.

(j) **THE CONSULTANT UNDERSTANDS THAT THIS AGREEMENT AFFECTS HIS RIGHTS TO CERTAIN INVENTIONS, AND RESTRICTS HIS RIGHTS TO DISCLOSE OR USE CONFIDENTIAL INFORMATION OR THIRD-PARTY CONFIDENTIAL INFORMATION.**

[*The remainder of this page is intentionally left blank.*]

IN WITNESS WHEREOF, the parties have signed this Agreement as of the date first above written, intending it to take effect as a sealed instrument.

RHYTHM PHARMACEUTICALS, INC.

By: /s/ Keith Gottesdiener
Name: Dr. Keith Gottesdiener
Title: Chief Executive Officer

Address:
500 Boylston Street, 11th Floor
Boston, MA 02116

Email:
kgottesdiener@rhythmtx.com

Phone Number:
(857) 264.4285

Telefax Number:
(857) 264.4299

CONSULTANT

/s/ Bart Henderson
(*sign above*)

Print name: Bart Henderson

Address:

Email:

Phone Number:
( )

Telefax Number:
( )

[*Signature Page to Consulting Agreement (Bart Henderson)*]

DEVELOPMENT AND MANUFACTURING SERVICES AGREEMENT

THIS DEVELOPMENT AND MANUFACTURING SERVICES AGREEMENT is made as of December 21, 2016 (the "Effective Date") by and between **RHYTHM PHARMACEUTICALS, INC.,** a Delaware corporation with offices at 500 Boylston Street, 11th Floor, Boston, MA 02116, USA ("Rhythm") and **RECIPHARM MONTS SAS,** a French corporation with an office at 18 route de Montbazon, 37 260 Monts, France ("Manufacturer").

RECITALS:

WHEREAS, Rhythm desires to engage Manufacturer to perform certain Development and/or Manufacturing Services (as those terms are defined below), on the terms and conditions set forth below, and Manufacturer desires to perform such Services for Rhythm.

AGREEMENT:

NOW, THEREFORE, in consideration of the foregoing premises and the Rhythm covenants of the parties set forth in this Agreement, the parties hereto agree as follows:

1. Definitions. Unless this Agreement expressly provides to the contrary, the following terms, whether used in the singular or plural, have the respective meanings set forth below:

1.1 "Affiliate" means, with respect to either Rhythm or Manufacturer, any corporation, company, partnership, joint venture and/or firm which controls, is controlled by or is under common control with Rhythm or Manufacturer, as the case may be. As used in the definition of Affiliate, "control" means (a) in the case of corporate entities, direct or indirect ownership of at least fifty percent (50%) of the stock or shares having the right to vote for the election of directors (or such lesser percentage that is the maximum allowed to be owned by a foreign corporation in a particular jurisdiction), and (b) in the case of non-corporate entities, the direct or indirect power to manage, direct or cause the direction of the management and policies of the non-corporate entity or the power to elect at least fifty percent (50%) of the members of the governing body of such non-corporate entity.

1.2 "Agreement" means this Development and Manufacturing Services Agreement, together with all Appendices attached hereto, as amended from time to time by the parties in accordance with Section 15.6, and all fully signed Work Orders entered into by the parties.

1.3 "API/Drug Substance" means the active pharmaceutical ingredient or drug substance identified on the applicable Work Order, or any intermediate or component of such active pharmaceutical ingredient or drug substance.

1.4 "Applicable Law" means all applicable UK, United States and European Union ordinances, rules, regulations, laws, guidelines, guidances, requirements and court orders of any kind whatsoever of any Authority, as amended from time to time including, without limitation, cGMP (if applicable) together with those of such additional jurisdictions as the parties may from time to time agree in writing.

1.5 "Authority" means any government regulatory authority responsible for granting approvals for the performance of Services under this Agreement or for issuing regulations pertaining to the Manufacture and/or use of Product in the intended country of use being at the date hereof the ANSM and the FDA, together with such additional government regulatory authorities as the parties may from time to time agree in writing.

1.6 "Batch" means a specific quantity of Product that is intended to be of uniform character and quality, within specified limits, and is produced during the same cycle of Manufacture as defined by the applicable Batch record.

1.7 "Batch Documentation" has the meaning set forth in Section 6.2.

1.8 "Certificate of Analysis" means a document signed by an authorized representative of Manufacturer, describing Specifications for, and testing methods applied to, Product, and the results of testing.

1.9 "Certificate of Compliance" means a document, signed by an authorized representative of Manufacturer, certifying that a particular Batch was Manufactured in accordance with cGMP (if applicable), all other Applicable Law, and the Specifications.

1.10 "cGMP" means current good manufacturing practices and regulations applicable to the Manufacture of Product that are promulgated by any Authority.

1.11 "Change Order" has the meaning set forth in Section 5.3.

1.12 "Confidential Information" has the meaning set forth in Section 10.

1.13 "Delivery " means availability of a Batch at the Facility following Rhythm's acceptance in accordance with Section 6.3.

1.14 "Develop" or "Development" means the studies and other activities conducted by Manufacturer under this Agreement to develop, implement and/or validate all or any part of a Manufacturing Process including, without limitation, analytical tests and methods, formulations and dosage forms and stability.

1.15 "Equipment" means any equipment or machinery, including Rhythm Equipment, used by Manufacturer in the Development and/or Manufacturing of Product, or the holding, processing, testing, or release of Product.

1.16 "Facility" means the facility(ies) of Manufacturer identified in the applicable Work Order.

1.17 "FDA" means the United States Food and Drug Administration, and any successor agency having substantially the same functions.

1.18 "FDCA" means the United States Federal Food, Drug and Cosmetic Act, 21 U.S.C. §321 et seq., as amended from time to time.

1.19 "*force majeure*" has the meaning set forth in Section 15.2.

1.20 "Improvements" means all Technology and discoveries, inventions, developments, modifications, innovations, updates, enhancements, improvements, writings or rights (whether or not protectable under patent, trademark, copyright or similar laws) that are conceived, discovered, invented, developed, created, made or reduced to practice in the performance of Services under this Agreement.

1.21 "IND" means an Investigational New Drug application filed with the FDA in accordance with Applicable Law.

1.22 "Manufacture" and "Manufacturing" means any steps, processes and activities necessary to produce Product including, without limitation, the manufacturing, processing, primary packaging, labeling (except for investigational materials for clinical trials), quality control testing, stability testing, release, storage or supply of Product.

1.23 "Manufacturer Indemnitees" has the meaning set forth in Section 12.2.

1.24 "Manufacturer Technology" means the Technology of Manufacturer (a) existing prior to the Effective Date, or (b) developed or obtained by or on behalf of Manufacturer independent of this Agreement and without reliance upon the Confidential Information of Rhythm.

1.25 "Manufacturing Process" means any and all processes and activities (or any step in any process or activity) used or planned to be used by Manufacturer to Manufacture Product, as evidenced in the Batch Documentation or master Batch Documentation.

1.26 "New Drug Application" means a New Drug Application filed with the FDA in accordance with Applicable Law.

1.27 "Product" means any API/Drug Substance or drug product comprised of API/Drug Substance in each case as specified in the applicable Work Order, including, if applicable, bulk packaging and/or labeling as provided in such Work Order.

1.28 "Quality Agreement" has the meaning set forth in Section 2.2.

1.29 "Records" has the meaning set forth in Section 5.4(a).

1.30 "Representative" has the meaning set forth in Section 3.1.

1.31 "Reprocess" and "Reprocessing" means introducing a Product back into the process and repeating appropriate manipulation steps that are part of the established Manufacturing Process. Continuation of a process step after an in-process control test show the process to be incomplete is not considered reprocessing.

1.32 "Rework" and "Reworking" means subjecting a Product to one or more processing steps that are different from the established Manufacturing Process.

1.33 "Rhythm Equipment" means the Equipment, if any, identified on the applicable Work Order as being provided by Rhythm or purchased or otherwise acquired by Manufacturer at Rhythm's expense.

1.34 "Rhythm Indemnitees" has the meaning set forth in Section 12.1.

1.35 "Rhythm Materials" means the materials identified in the applicable Work Order as being provided by Rhythm, including labels (if any) for Product.

1.36 "Rhythm Technology" means (a) Rhythm Materials and any intermediates, components, or derivatives of Rhythm Materials, (b) Product and any intermediates, components, or derivatives of Product, (c) Specifications, and (d) the Technology of Rhythm or its Affiliates (i)

existing prior to the Effective Date, or (ii) developed or obtained by or on behalf of Rhythm or its Affiliates independent of this Agreement and without reliance upon the Confidential Information of Manufacturer.

1.37 "Services" means the Development, Manufacturing and/or other services described in a Work Order entered into by the parties.

1.38 "Specifications" means the list of tests, references to any analytical procedures and appropriate acceptance criteria which are numerical limits, ranges or other criteria for tests described in order to establish a set of criteria to which Product at any stage of Manufacture should conform to be considered acceptable for its intended use that are provided by or approved by Rhythm, as such specifications are amended or supplemented from time to time by the parties in writing.

1.39 "Technology" means all methods, techniques, trade secrets, copyrights, know-how, data, documentation, regulatory submissions, specifications and other intellectual property of any kind (whether or not protectable under patent, trademark, copyright or similar laws).

1.40 "Work Order" means a written work order referencing this Agreement, substantially in the form attached hereto as Appendix A. for the performance of Services by Manufacturer under this Agreement.

2. Engagement of Manufacturer.

2.1 Services and Work Orders. From time to time, Rhythm may wish to engage Manufacturer to perform Services for Rhythm. Such Services will be set forth in a Work Order. Each Work Order will be appended to this Agreement, will include the material terms for the project, and may include the scope of work, specified Services, Specifications, deliverables, timelines, milestones (if any), quantity, budget, payment schedule and such other details and special arrangements as are agreed to by the parties with respect to the activities to be performed under such Work Order. No Work Order will be effective unless and until it has been agreed to and signed by authorized representatives of both parties. Documents relating to the relevant project, including without limitation Specifications, proposals, quotations and any other relevant documentation, will only be effective if attached to the applicable Work Order and incorporated in the Work Order by reference. Each fully signed Work Order will be subject to the terms of this Agreement and will be incorporated herein and form part of this Agreement. Manufacturer will perform the Services specified in each fully signed Work Order, as amended by any applicable Change Order(s), and in accordance with the terms and conditions of such Work Order and this Agreement. Notwithstanding the foregoing, nothing in this Agreement will obligate either party to enter into any Work Order under this Agreement.

2.2 Quality Agreement. If appropriate or if required by Applicable Law, the parties will also agree upon a Quality Agreement containing quality assurance provisions for the Manufacture of Product ("Quality Agreement"), which agreement will also be attached to the applicable Work Order and incorporated by reference in the Work Order.

2.3 Conflict Between Documents. If there is any conflict, discrepancy, or inconsistency between the terms of this Agreement and any Work Order, Quality Agreement, purchase order, or other document or form used by the parties, the terms of this Agreement will control.

3. Project Performance.

3.1 Representatives. Each party will appoint a representative having primary responsibility for day-to-day interactions with the other party for the Services (each, a "Representative"), who will be identified in the applicable Work Order. Each party may change its Representative by providing written notice to the other party in accordance with Section 15.3; provided that Manufacturer will use reasonable efforts to provide Rhythm with at least forty-five (45) days prior written notice of any change in its Representative for the Services. Except for notices or communications required or permitted under this Agreement, which will be subject to Section 15.3, or unless otherwise mutually agreed by the parties in writing, all communications between Manufacturer and Rhythm regarding the conduct of the Services pursuant to such Work Order will be addressed to or routed directly through the parties' respective Representatives.

3.2 Communications. The parties will hold project team meetings via teleconference or in person, on a periodic basis as agreed upon by the Representatives. Manufacturer will make written reports to Rhythm as specified in the applicable Work Order.

3.3 Subcontracting. Manufacturer may not subcontract with any third party including, but not limited to, any Affiliate of Manufacturer, to perform any of its obligations under this Agreement without the prior written consent of Rhythm. Manufacturer will be solely responsible for the performance of any permitted subcontractor, and for costs, expenses, damages, or losses of any nature arising out of such performance as if such performance had been provided by Manufacturer itself under this Agreement. Manufacturer will cause any such permitted subcontractor to be bound by, and to comply with, the terms of this Agreement, as applicable, including without limitation, all confidentiality, quality assurance, regulatory and other obligations and requirements of Manufacturer set forth in this Agreement.

3.4 Duty to Notify. Manufacturer will promptly notify Rhythm if at any time during the term of this Agreement Manufacturer has reason to believe that it will be unable to perform or complete the Services in a timely manner. Compliance by Manufacturer with this Section 3.4 will not relieve Manufacturer of any other obligation or liability under this Agreement.

4. Materials and Equipment.

4.1 Supply of Materials. Unless the parties otherwise agree in a Work Order, Manufacturer will supply, in accordance with the relevant approved raw material specifications, all materials to be used by Manufacturer in the performance of Services under a Work Order other than the Rhythm Materials specified in such Work Order. Rhythm or its designees will provide Manufacturer with the Rhythm Materials. Manufacturer agrees (a) to account for all Rhythm Materials, (b) not to provide Rhythm Materials to any third party without the express prior written consent of Rhythm, (c) not to use Rhythm Materials for any purpose other than conducting the Services, including, without limitation, not to analyze, characterize, modify or reverse engineer any Rhythm Materials or take any action to determine the structure or composition of any Rhythm Materials unless required pursuant to a signed Work Order, and (d) to destroy or return to Rhythm all unused quantities of Rhythm Materials according to Rhythm's written directions.

4.2 Ownership of Materials. Rhythm will at all times retain title to and ownership of the Rhythm Materials, Product, any intermediates and components of Rhythm Materials or Product, and any work in process at each and every stage of the Manufacturing Process. Manufacturer will provide within the Facility an area or areas where the Rhythm Materials, Product, any intermediates and components of Rhythm Materials or Product, and any work in process are segregated and stored

in accordance with the Specifications and cGMP (if applicable), and in such a way as to be able at all times to clearly distinguish such materials from products and materials belonging to Manufacturer, or held by it for a third party's account. Manufacturer will ensure that Rhythm Materials, Product, any intermediates and components of any Rhythm Materials or Product, and any work in process are free and clear of any liens or encumbrances. Manufacturer will at all times take such measures as are required to protect the Rhythm Materials, Product, any intermediates and components of any Rhythm Materials or Product, and any work in process from risk of loss or damage at all stages of the Manufacturing Process. Manufacturer will immediately notify Rhythm if at

any time it believes any Product or Rhythm Materials, or any intermediates and components of any Rhythm Materials or Product, have been damaged, lost or stolen.

4.3 Supply of Equipment. Unless otherwise agreed in a Work Order, Manufacturer will supply all Equipment necessary to perform the Services, except that Rhythm will supply the Rhythm Equipment, if any. The Rhythm Equipment will not be used by Manufacturer except in performance of Services under the applicable Work Order. Title to the Rhythm Equipment will remain with Rhythm and Manufacturer will ensure that the Rhythm Equipment is properly labeled as Rhythm property and remains free and clear of any liens or encumbrances. At Rhythm's written request, the Rhythm Equipment will be returned to Rhythm, or to Rhythm's designee, at Rhythm's expense. Manufacturer will be responsible, at its own cost, for maintenance of the Rhythm Equipment. To the extent Rhythm provides spare parts for the Rhythm Equipment, such spare parts will remain the property of Rhythm and will be used by Manufacturer only for maintenance of the Rhythm Equipment. Manufacturer will immediately notify Rhythm if at any time it believes any Rhythm Equipment has been damaged, lost or stolen.

5. Development and Manufacture of Product.

5.1 Resources; Applicable Law. Manufacturer will comply with all Applicable Law in performing Services.

5.2 Facility.

(a) Performance of Services. Manufacturer will perform all Services at the Facility, provide all staff necessary to perform the Services in accordance with the terms of the applicable Work Order and this Agreement, and hold at such Facility all Equipment, Rhythm Equipment, Rhythm Materials and other items used in the Services. Manufacturer will not change the location of such Facility or use any additional facility for the performance of Services under this Agreement without at least one hundred fifty (150) days prior written notice to, and prior written consent from, Rhythm, which consent will not be unreasonably withheld or delayed (it being understood and agreed that Rhythm may withhold consent pending satisfactory completion of a quality assurance audit and/or regulatory impact assessment of the new location or additional facility, as the case may be). Manufacturer will maintain, at its own expense, the Facility and all Equipment required for the Manufacture of Product in a state of repair and operating efficiency consistent with the requirements of cGMP (if applicable) and all Applicable Law.

(b) Validation. Manufacturer will be responsible for performing all validation of the Facility, Equipment and cleaning and maintenance processes employed in the Manufacturing Process in accordance with cGMP (if applicable), Manufacturer's SOPs, the applicable Quality Agreement (if any), Applicable Law, and in accordance with any other validation procedures established by Rhythm and made known in writing to Manufacturer. Manufacturer will also be responsible for ensuring that all such validated processes are carried out in accordance with their terms.

(c) Licenses and Permits. Manufacturer will be responsible for obtaining, at its expense, any Facility or other licenses or permits, and any regulatory and government approvals necessary for the performance of Services by Manufacturer under this Agreement. At Rhythm's request, Manufacturer will provide Rhythm with copies of all such approvals and submissions to Authorities, and Rhythm will have the right to use any and all information contained in such approvals or submissions in connection with regulatory approval and/or commercial development of Product.

(d) Access to Facility. Manufacturer will permit Rhythm or its duly authorized representatives, upon reasonable advance written notice, to observe and consult with Manufacturer during the performance of Services under this Agreement, including without limitation the Manufacturing of any Batch of Product. Manufacturer also agrees that Rhythm and its duly authorized agents will have continuous access, during operational hours and during active Manufacturing, to inspect the Facility and Manufacturing Process, with reasonable scope and frequency, to ascertain compliance by Manufacturer with the terms of this Agreement, including, without limitation, inspection of (i) the Equipment and materials used in the performance of Services, (ii) the holding facilities for such materials and Equipment, and (iii) all Records relating to such Services and the Facility. Rhythm will also have the right, at its expense, to conduct "mock" pre-approval audits upon reasonable notice to Manufacturer, and Manufacturer agrees to cooperate with Rhythm in such "mock audits." A "mock audit" will not be conducted more than once a year during maximum 2 days with 2 persons. The cost of any other audits shall be quoted and agreed.

5.3 Changes to Work Orders. Manufacturing Process and Specifications.

(a) Changes to Work Orders. If the scope of work of a Work Order changes, then the applicable Work Order may be amended as provided in this Section 5.3(a). If a required modification to a Work Order is identified by Rhythm or by Manufacturer, the identifying party will notify the other party in writing as soon as reasonably possible. Manufacturer will provide Rhythm with a change order containing a description of the required modifications and their effect on the scope, fees (including remuneration for waste and scrap if any) and timelines specified in the Work Order ("Change Order"), and will use reasonable efforts to do so within ten (10) business days of receiving or providing such notice, as the case may be. No Change Order will be effective unless and until it has been signed by authorized representatives of both parties. If Rhythm does not approve such Change Order, and has not terminated the Work Order, but requests the Work Order to be amended to take into account the modification, then the parties will use reasonable efforts to agree on a Change Order that is mutually acceptable. If practicable, Manufacturer will continue to work under the existing Work Order during any such negotiations, provided such efforts would facilitate the completion of the work envisioned in the proposed Change Order, but will not commence work in accordance with the Change Order until it is authorized in writing by Rhythm.

(b) Process/Specifications Changes. Any change or modification to the Manufacturing Process or Specifications for any Product must be approved in advance by Rhythm and will be made in accordance with the change control provisions of the applicable Quality Agreement. In the event that the parties' compliance with Applicable Law (including but not limited to any change thereto or change in interpretation thereof by any Authority) requires any change to the Product or Manufacturing Process, the parties shall negotiate in good faith with respect to an appropriate amendment to this Agreement and associated documentation (including any applicable Work Order and applicable Quality Agreement) to implement such change.

5.4 Record and Sample Retention.

(a) Records. Manufacturer will keep complete and accurate records (including, without limitation, reports, accounts, notes, data, and records of all information and results obtained from performance of Services) of all work done by it under this Agreement, in form and substance as specified in the applicable Work Order, the applicable Quality Agreement, and this Agreement (collectively, the "Records"). All such Records will be the property of Rhythm. Manufacturer will not transfer, deliver or otherwise provide any such Records to any party other than Rhythm, without the prior written approval of Rhythm. Records will be available at reasonable times for inspection, examination and copying by or on behalf of Rhythm. All original Records of the Development and Manufacture of Product under this Agreement will be retained and archived by Manufacturer in accordance with cGMP (if applicable) and Applicable Law, but in no case for less than a period of five (5) years following completion of the applicable Work Order. Upon Rhythm's request, Manufacturer will promptly provide Rhythm with copies of such Records. Five (5) years after completion of a Work Order, all of the aforementioned records will be sent to Rhythm or Rhythm's designee; provided, however, that Rhythm may elect to have such records retained in Manufacturer's archives for an additional period of time at a reasonable charge to Rhythm.

(b) Sample Retention. Manufacturer will take and retain, (i) for such period and in such quantities as may be required by cGMP (or other applicable Authority), and (ii) for such additional period and in such additional quantities as may be required by the applicable Quality Agreement, samples of Product from the Manufacturing Process produced under this Agreement. Further, upon Rhythm's written request, Manufacturer will submit such samples to Rhythm, except to the extent that Manufacturer is required by applicable cGMP to retain possession of any such samples pursuant to the preceding clause (i).

5.5 Regulatory Matters,

(a) Regulatory Approvals. Rhythm will be responsible for obtaining, at its expense, all regulatory and governmental approvals and permits necessary for Rhythm's use of any Product Developed and/or Manufactured under this Agreement, including, without limitation, IND, ANDA, and NDA submissions and any analogous submissions filed with the appropriate Authority of a country other than the United States. Manufacturer will be responsible for providing Rhythm with all supporting data and information relating to the Development and/or Manufacture of Product necessary for obtaining such approvals, including, without limitation, all Records, raw data, reports, authorizations, certificates, methodologies, Batch Documentation, raw material specifications, SOPs, standard test methods, Certificates of Analysis, Certificates of Compliance and other documentation in the possession or under the control of Manufacturer relating to the Development and Manufacture of Product (or any intermediate, or component of Product).

(b) Regulatory Inspections. Manufacturer will permit Rhythm or its agents to be present and participate in any visit or inspection by any Authority of the Facility (to the extent it relates in any way to any Product) or the Manufacturing Process. Manufacturer will to the extent the same relates to or affects the Development and/or Manufacture of Product give as much advance notice as possible to Rhythm of any such visit or inspection described in the preceding sentence. Manufacturer will provide Rhythm with a copy of any report or other written communication received from such Authority in connection with such visit or inspection, and any written communication received from any Authority relating to any Product, the Facility (if it relates to or affects the Development and/or Manufacture of Product) or the Manufacturing Process, within twenty-four (24) hours after receipt, and will consult with, and require approval from, Rhythm before responding to each such communication; provided, that the copies of such communications

and responses so provided to Rhythm by Manufacturer may be redacted as necessary to remove customer names and product or manufacturing information unrelated to the Development and/or Manufacture of Product. Rhythm shall provide its responses in a timely manner to enable Manufacturer to comply with any timeframes for response to imposed by such Authority. Manufacturer will provide Rhythm with a copy of its final responses within five (5) business days after submission.

5.6 Waste Disposal. The generation, collection, storage, handling, transportation, movement and release of hazardous materials and waste generated in connection with the Services will be the responsibility of Manufacturer at Manufacturer's sole cost and expense. Without limiting other applicable requirements, Manufacturer will prepare, execute and maintain, as the generator of waste, all licenses, registrations, approvals, authorizations, notices, shipping documents and waste manifests required under Applicable Law.

5.7 Safety Procedures. Manufacturer will be solely responsible for implementing and maintaining health and safety procedures for the performance of Services and for the handling of any materials or hazardous waste used in or generated by the Services. Manufacturer, in consultation with Rhythm, will develop safety and handling procedures for API/Drug Substance and Product as specified in the Specifications; provided, however, that Rhythm will have no responsibility for Manufacturer's health and safety program.

6. Testing and Acceptance Process.

6.1 Testing by Manufacturer. The Product Manufactured under this Agreement will be Manufactured in accordance with the Manufacturing Process approved by Rhythm, and with cGMP (unless otherwise expressly stated in the applicable Work Order). Each Batch of Product will be sampled and tested by Manufacturer against the Specifications, and the quality assurance department of Manufacturer will review the documentation relating to the Manufacture of the Batch and will assess if the Manufacture has taken place in compliance with cGMP (if applicable) and the Manufacturing Process.

6.2 Provision of Records. If, based upon such tests and documentation review, a Batch of Product conforms to the Specifications and was Manufactured according to cGMP (if applicable) and the Manufacturing Process, then a Certificate of Compliance will be completed and approved by the quality assurance department of Manufacturer. This Certificate of Compliance, a Certificate of Analysis, the Specifications, and a complete and accurate copy of the Batch records (collectively, the "Batch Documentation") for each Batch of Product will be delivered to Rhythm by a reputable overnight courier or by registered or certified mail, postage prepaid, return receipt required to verify delivery date. Upon request, at reasonable frequency, Manufacturer will also deliver to Rhythm all raw data, reports, authorizations, certificates, methodologies, raw material specifications, SOPs, standard test methods, and other documentation in the possession or under the control of Manufacturer relating to the Manufacture of each Batch of Product. If Rhythm requires additional copies of such Batch Documentation, these will be provided by Manufacturer to Rhythm at cost.

6.3 Review of Batch Documentation; Acceptance. Rhythm will review the Batch Documentation for each Batch of Product and may test samples of the Batch of Product against the Specifications. Rhythm will notify Manufacturer in writing of its acceptance or rejection of such Batch within six (6) weeks of receipt of the complete Batch Documentation relating to such Batch. During this review period, the parties agree to respond promptly to any reasonable inquiry or request for a correction or change by the other party with respect to such Batch Documentation. Rhythm has no obligation to accept a Batch if such Batch does not comply with the Specifications

and/or was not Manufactured in compliance with cGMP (if applicable) and the Manufacturing Process. Within eight (8) working days following Rhythm's delivery of written notice of acceptance of a Batch, Rhythm shall provide to Manufacturer the information required by Section 7(a) and (b) and arrange for collection of the Batch by it or its designee.

6.4 Disputes. In case of any disagreement between the parties as to whether Product conforms to the applicable Specifications or cGMP (if applicable), the quality assurance representatives of the parties will attempt in good faith to resolve any such disagreement and Rhythm and Manufacturer will follow their respective SOPs to determine the conformity of the Product to the Specifications and cGMP (if applicable). If the foregoing discussions do not resolve the disagreement in a reasonable time (which will not exceed thirty (30) days), a representative sample of such Product will be submitted to an independent testing laboratory mutually agreed upon by the parties for tests and final determination of whether such Product conforms with such Specifications. The laboratory must meet cGMP (if applicable), be of recognized standing in the industry, and consent to the appointment of such laboratory will not be unreasonably withheld or delayed by either party. Such laboratory will use the test methods contained in the applicable Specifications. The determination of conformance by such laboratory with respect to all or part of such Product will be final and binding on the parties absent manifest error. The fees and expenses of the laboratory incurred in making such determination will be paid by the party against whom the determination is made.

6.5 Product Non-Compliance and Remedies. If a Batch of Product fails to conform to the Specifications or was not Manufactured in compliance with cGMP (if applicable) and the Manufacturing Process, then Manufacturer will, at Rhythm's sole option:

(a) refund in full the fees and expenses paid by Rhythm for such Batch, including, but not limited to, the cost of Rhythm Materials used in the Manufacture of such Batch; or

(b) at Manufacturer's cost and expense, including, but not limited to, the cost of Rhythm Materials used in the Manufacture of such Batch, Manufacture a new Batch of Product as soon as reasonably possible; or

(c) where deemed possible by Manufacturer Rework or Reprocess the Product, at Manufacturer's cost and expense, so that the Batch can be deemed to have been Manufactured in compliance with cGMP (if applicable) and the Manufacturing Process, and to conform to Specifications.

The parties agree that the table in Schedule 1 is indicative of the responsibility for such a failure, Moreover, the parties will meet to discuss, evaluate and analyze the reasons for and implications of the failure to comply with cGMP (if applicable) and/or the Manufacturing Process and will decide whether to proceed with or to amend the applicable Work Order via a Change Order, or to terminate such Work Order.

6.6 Disposition of Non-Conforming Product. The ultimate disposition of non-conforming Product will be the responsibility of Rhythm's quality assurance department.

7. Delivery. Manufacturer agrees not to release or Deliver Product to Rhythm or its designee until it has received a written acceptance from Rhythm in accordance with Section 6.3, and approval from Rhythm or Rhythm's designee to release. Manufacturer will ensure that each Batch will be delivered to Rhythm or Rhythm's designee, (a) on the Delivery date designated by

Rhythm in accordance with Section 6.3, and (b) in accordance with the instructions for shipping and packaging specified by Rhythm in the applicable Work Order or as otherwise agreed to by the parties in writing. Delivery terms will be EXW Recipharm Monts site (Incoterms 2010). All required information to permit shipment and a bill of lading will be furnished to Rhythm with respect to each shipment.

8. Fees and Payments.

8.1 Price. The price of Product and/or the fees and expenses for the performance of Services will be set forth in the applicable Work Order.

8.2 Invoice. Manufacturer will invoice Rhythm according to the invoice schedule in the applicable Work Order, referencing in each such invoice the Work Order(s) to which such invoice relates. Notwithstanding the foregoing, Manufacturer will not issue a final invoice for a Batch of Product until such time as such Batch has been delivered to Rhythm in accordance with Section 7. Payment of undisputed invoices will be due thirty (30) days after receipt of the invoice and reasonable supporting documentation by Rhythm.

(a) Where the parties intend that Manufacturer will bear the VAT cost of the importing of excipients into France on behalf of Rhythm, Manufacturer shall invoice the amount of such anticipated VAT (as determined by Manufacturer in good faith) (plus an administration fee of 5%) to Rhythm three (3) weeks in advance of the anticipated payment date of such VAT. Rhythm shall pay such invoice as soon as reasonably practicable so as to assure that Manufacturer has received cleared funds prior to making the payment of such VAT. Upon determination of the actual amount of such VAT due and payable, Manufacturer shall promptly (i) pay such amount to the applicable taxing authority; (ii) provide documentation reasonably acceptable to Rhythm with respect to both the actual amount of such VAT and Manufacturer's payment thereof; and (iii) refund to Rhythm the excess amount (if any) previously paid by Rhythm pursuant to the first two sentences of this Section 8.2(a) over such actual amount of such VAT paid by Manufacturer, or, if such actual amount of such VAT paid by Manufacturer exceeds such amounts previously paid by Rhythm, invoice Rhythm for the amount of such deficiency (any such invoice shall be due thirty (30) days after receipt of such invoice and reasonable supporting documentation by Rhythm).

8.3 Payments. Rhythm will make all payments pursuant to this Agreement by check or wire transfer to a bank account designated in writing by Manufacturer. All payments under this Agreement will be made in Euros.

8.4 Financial Records. Manufacturer will keep accurate records of all Services performed and invoice calculations, and, upon the request of Rhythm, will permit Rhythm or its duly authorized agents to examine such records during normal business hours for the purpose of verifying the correctness of all such calculations.

8.5 Taxes. Duty, sales, use or excise taxes imposed by any governmental entity that apply to the provision of Services will be borne by Rhythm (other than taxes based upon the income of Manufacturer).

9. Intellectual Property Rights.

9.1 Rhythm Technology. All rights to and interests in Rhythm Technology will remain solely in Rhythm and no right or interest therein is transferred or granted to Manufacturer under this Agreement. Manufacturer acknowledges and agrees that it does not acquire a license or any

other right to Rhythm Technology except for the limited purpose of carrying out its duties and obligations under this Agreement and that such limited, non-exclusive, license will expire upon the completion of such duties and obligations or the termination or expiration of this Agreement, whichever is the first to occur.

9.2 Manufacturer Technology. All rights to and interests in Manufacturer Technology will remain solely in Manufacturer and, except as otherwise set forth in this Agreement, no right or interest therein is transferred or granted to Rhythm under this Agreement. Manufacturer hereby grants to Rhythm a non-exclusive, perpetual, irrevocable, royalty-free, transferable and sublicensable license to Rhythm and its Affiliates to use and modify Manufacturer Technology to develop, Manufacture, have Manufactured, distribute, offer for sale, sell, and otherwise dispose of Product.

9.3 Improvements. Manufacturer agrees (a) to promptly disclose to Rhythm all patentable Improvements, and (b) that all Improvements will be the sole and exclusive property of Rhythm, and are hereby assigned to Rhythm (or its designee), and (c) that any such assignment to Rhythm (or its designee) shall be made without additional compensation to Manufacturer. Manufacturer will take such steps as Rhythm may reasonably request (at Rhythm's expense) to vest in Rhythm (or its designee) ownership of the Improvements.

9.4 Patent Filings. Rhythm will have the exclusive right and option, but not the obligation, to prepare, file, prosecute, maintain and defend, at its sole expense, any patents that claim or cover the Improvements.

9.5 Technology Transfer. If Rhythm elects to Manufacture Product, or to have Product Manufactured by a third party, then Manufacturer will provide to Rhythm or its designee, all Manufacturing information, including, without limitation, documentation, technical assistance, materials and cooperation by appropriate employees of Manufacturer as Rhythm or its designee may reasonably require in order to Manufacture Product. Rhythm will compensate Manufacturer for such assistance at the hourly-rate(s) set forth in the applicable Work Order, or such other reasonable rate(s) as the parties may agree in writing.

10. Confidentiality.

10.1 Confidential Information. During the Term and continuing thereafter, each party will keep confidential and not disclose to others or use for any purpose other than as necessary to fulfill its obligations or in the reasonable exercise of rights granted to it under this Agreement, all "Confidential Information". As used in this Agreement, "Confidential Information" means any scientific, technical, trade or business information which is given by one party or its Affiliates or their respective employees or representatives to the other, either under a Confidentiality Agreement entered into by the parties in anticipation of this Agreement or under this Agreement, and which is treated by the disclosing party as confidential or proprietary or a trade secret, or is which is developed by one party for the other under the terms of this Agreement. Confidential Information of Manufacturer includes, but is not limited to, Manufacturer Technology. Confidential Information of Rhythm includes, but is not limited to, Rhythm Technology and Improvements. The restrictions of this Section 10.1 will not apply to any portion of the Confidential Information which (a) is known to the recipient at the time of disclosure and is not subject to another confidentiality obligation to the discloser or its Affiliates, as reasonably documented by recipient's written records; (b) later becomes public knowledge through no fault of the recipient; (c) is received from a third party having the lawful right to disclose the information; or (d) is independently developed by or on behalf of recipient without use of or reliance upon discloser's Confidential Information.

Information will not be deemed to be part of the "public domain" by reason solely that it is known to only a few of those people to whom it might be of commercial interest, and a combination of two (2) or more portions of the Confidential Information shall not be deemed to be generally available to the public by reason solely of each separate portion being so available.

10.2 Permitted Disclosure. A party may disclose Confidential Information of the other party to (a) its Affiliates, and to its and their directors, employees, consultants, and agents in each case who have a specific need to know such Confidential Information and who are bound by a like obligation of confidentiality and restriction on use and (b) the extent such disclosure is required to comply with Applicable Law, the rules of any stock exchange or listing entity, or to defend or prosecute litigation; provided, however, that the recipient provides prior written notice of such disclosure to the discloser and takes reasonable and lawful actions to avoid or minimize the degree of such disclosure, including upon the discloser's request, seeking confidential treatment of such Confidential Information. Moreover, Rhythm may disclose Confidential Information of Manufacturer relating to the Development and/or Manufacture of Product to entities with whom Rhythm has (or may have) a marketing and/or development collaboration or to *bona fide* actual or prospective underwriters, investors, lenders or other financing sources or to potential acquirors of the business to which this Agreement relates, and who in each case have a specific need to know such Confidential Information and who are bound by a like obligation of confidentiality and restrictions on use,

10.3 Return of Confidential Information. This Agreement does not constitute the conveyance of ownership with respect to or a license to any Confidential Information, except as otherwise provided in this Agreement. Upon the expiration or termination of this Agreement for any reason, each party agrees, except as otherwise provided in this Agreement, to return to the other party all documentation or other tangible evidence or embodiment of Confidential Information belonging to the other party and not to use such Confidential Information, unless otherwise agreed. Notwithstanding the foregoing, one archival copy may be maintained by the recipient and kept confidential and segregated from the recipient's regular files.

10.4 Public Statements. Manufacturer will not make any public statements or releases concerning this Agreement or the transactions contemplated by this Agreement, or use Rhythm's name in any form of advertising, promotion or publicity, without obtaining the prior written consent of Rhythm.

11. Representations and Warranties.

11.1 Manufacturer's Representations and Warranties. Manufacturer represents and warrants to Rhythm that:

(a) it has the full power and right to enter into this Agreement and that there are no outstanding agreements, assignments, licenses, encumbrances or rights of any kind held by other parties, private or public, that are inconsistent with the provisions of this Agreement;

(b) the execution and delivery of this Agreement by Manufacturer has been authorized by all requisite corporate action and this Agreement is and will remain a valid and binding obligation of Manufacturer, enforceable in accordance with its terms, subject to laws of general application relating to bankruptcy, insolvency and the relief of debtors;

(c) the Services will be performed with requisite care, skill and diligence, in accordance with Applicable Law and industry standards, and by individuals who are appropriately trained and qualified;

(d) it has and shall continue to have written agreements with its directors, officers, employees, agents, permitted subcontractors and representatives to effectuate the terms of this Agreement, including without limitation Sections 9 and 10 hereof, and shall enforce such agreements to provide Rhythm with the benefits thereof;

(e) the conduct and the provision of the Services will not violate any patent, trade secret or other proprietary or intellectual property rights of any third party and it will promptly notify Rhythm in writing should it become aware of any claims asserting such violation;

(f) it shall not knowingly use or incorporate any invention, discovery, technology, know-how and/or other intellectual property that is not owned by, or otherwise assignable by, Manufacturer in the performance of the Services without the prior written consent of Rhythm;

(g) at the time of delivery to Rhythm, the Product Manufactured under this Agreement (i) will have been Manufactured in accordance with cGMP (if applicable) and all other Applicable Law, the Manufacturing Process, the applicable Quality Agreement, and Specifications, and (ii) will not be adulterated or misbranded under the FDCA or other Applicable Law; and

(h) Manufacturer, its Affiliates, approved subcontractors, and each of their respective officers and directors, as applicable, and any person used by Manufacturer, its Affiliates or approved subcontractors to perform Services under this Agreement (i) have not been debarred and are not subject to a pending debarment, and will not use in any capacity in connection with the Services any person who has been debarred or is subject to a pending debarment pursuant to section 306 of the FDCA, 21 U.S.C. § 335a, (ii) are not ineligible to participate in any federal and/or state healthcare programs or federal procurement or non-procurement programs (as that term is defined in 42 U.S.C. 1320a-7b(f)), (iii) are not disqualified by any government or regulatory agencies from performing specific services, and are not subject to a pending disqualification proceeding, and (iv) have not been convicted of a criminal offense related to the provision of healthcare items or services and are not subject to any such pending action. Manufacturer will notify Rhythm immediately if Manufacturer, its Affiliates, approved subcontractors, or any of their respective officers or directors, as applicable, or any person used by Manufacturer, its Affiliates or approved subcontractors to perform Services under this Agreement is subject to any of the foregoing, or if any action, suit, claim, investigation, or proceeding relating to the foregoing is pending, or to the best of Manufacturer's knowledge, is threatened.

11.2 Rhythm Representations and Warranties. Rhythm represents and warrants to Manufacturer that:

(a) it has the full power and right to enter into this Agreement and that there are no outstanding agreements, assignments, licenses, encumbrances or rights held by other parties, private or public, that are inconsistent with the provisions of this Agreement; and

(b) the execution and delivery of this Agreement by Rhythm has been authorized by all requisite corporate action and this Agreement is and will remain a valid and binding obligation of Rhythm, enforceable in accordance with its terms, subject to laws of general application relating to bankruptcy, insolvency and the relief of debtors.

11.3 Disclaimer of Other Representations and Warranties. EXCEPT AS EXPRESSLY SET FORTH IN THIS AGREEMENT, NEITHER PARTY MAKES ANY REPRESENTATIONS OR EXTENDS ANY WARRANTIES OF ANY KIND, EITHER EXPRESS OR IMPLIED, INCLUDING, BUT NOT LIMITED TO, WARRANTIES OF MERCHANTABILITY, FITNESS FOR A PARTICULAR PURPOSE, OR NON-INFRINGEMENT.

12. Indemnification.

12.1 Indemnification by Manufacturer. Manufacturer agrees to indemnify, defend and hold harmless Rhythm, its Affiliates and its and their respective officers, directors, employees, subcontractors, and agents (collectively, the "Rhythm Indemnitees") against any and all losses, damages, liabilities or expenses (including reasonable attorneys fees and other costs of defense) (collectively, "Losses") in connection with any and all actions, suits, claims or demands that may be brought or instituted against any Rhythm Indemnitee by any third party alleging the infringement of third-party rights by Rhythm's use, in supplying the Products, of any process, method, Specification or information process or method, other than one supplied to Manufacturer by Rhythm.

12.2 Indemnification by Rhythm. Rhythm agrees to indemnify, defend and hold harmless Manufacturer, its Affiliates and its and their respective officers, directors, employees, subcontractors, and agents (collectively, the "Manufacturer Indemnitees") against any and all Losses in connection with any and all actions, suits, claims or demands that may be brought or instituted against any Manufacturer Indemnitee by any third party to the extent they arise out of or relate to the use of the Product (except to the extent that such Losses are within the scope of the indemnification obligation of Manufacturer under Section 12.1),

12.3 Indemnification Procedures. Each party shall notify the other party within thirty (30) days of receipt of any claims made for which the other party might be liable under Section 12.1 or 12.2, as the case may be. Subject to Section 12.4, the indemnifying party will have the sole right to defend, negotiate, and settle such claims. The indemnified party will be entitled to participate in the defense of such matter and to employ counsel at its expense to assist in such defense; provided, however, that the indemnifying party will have final decision-making authority regarding all aspects of the defense of any claim. The party seeking indemnification will provide the indemnifying party with such information and assistance as the indemnifying party may reasonably request, at the expense of the indemnifying party. The parties understand that no insurance deductible will be credited against losses for which a party is responsible under this Section 12.

12.4 Settlement. Neither party will be responsible or bound by any settlement of any claim or suit made without its prior written consent; provided, however, that the indemnified party will not unreasonably withhold or delay such consent. If a settlement contains an absolute waiver of liability for the indemnified party, and each party has acted in compliance with the requirements of Section 12.3, then the indemnified party's consent will be deemed given. Notwithstanding the foregoing, Manufacturer will not agree to settle any claim on such terms or conditions as would impair Rhythm's ability or right to Manufacture, market, sell or otherwise use Product, or as would impair Manufacturer's ability, right or obligation to perform its obligations under this Agreement.

12.5 Limitation of Liability.

(a) NEITHER PARTY WILL BE LIABLE TO THE OTHER UNDER ANY LEGAL THEORY (WHETHER TORT, CONTRACT OR OTHERWISE) FOR SPECIAL, INDIRECT, INCIDENTAL, CONSEQUENTIAL OR PUNITIVE DAMAGES ARISING OUT OF OR RELATED TO THIS AGREEMENT OR THE EXERCISE OF ITS RIGHTS HEREUNDER, INCLUDING LOST PROFITS ARISING FROM OR RELATING TO ANY BREACH OF THIS AGREEMENT, HOWEVER CAUSED, EVEN IF THE PARTY HAS BEEN ADVISED OF THE POSSIBILITY OF SUCH DAMAGES, EXCEPT AS A RESULT OF A BREACH OF THE CONFIDENTIALITY AND NON-USE OBLIGATIONS IN SECTION 10. NOTHING IN THIS SECTION 12.5 IS INTENDED TO LIMIT OR RESTRICT THE INDEMNIFICATION RIGHTS OR OBLIGATIONS OF EITHER PARTY.

(b) Subject to Section 12.5(a), 12.5(c) and 12.6, the total liability of Manufacturer to Rhythm with respect to Services to be performed and Product supplied pursuant to this Agreement shall not exceed 100% of the amounts paid or payable by Rhythm to Manufacturer in respect of such Product under a Work Order, plus any applicable interest and/or legal fees. For avoidance of doubt, the limitation of liability contained in this Section 12.5(b) shall not apply to any indemnity obligations of Manufacturer pursuant to Section 12.1.

(c) The total liability of Manufacturer to Rhythm with respect to any inability of Manufacturer to return any API/Drug Substance and/or Rhythm Materials (a) supplied to Manufacturer by Rhythm, and (b) not incorporated into finished Product delivered to Rhythm hereunder, shall not exceed 50,000 Euros.

12.6 Exception to Limitations. Nothing in this Agreement shall exclude or limit the liability of a Party, to the extent such liability may not be excluded or limited, as a matter of law.

13. Insurance.

13.1 Manufacturer Insurance. Manufacturer will secure and maintain in full force and effect throughout the term of this Agreement (and for at least five (5) years thereafter for claims made coverage), the following minimum insurance coverage with financially sound and nationally reputable insurers:

(a) *Commercial General Liability,* including coverage for contractual liability assumed by Manufacturer and coverage for Manufacturer's independent contractor(s), with a general aggregate limit of not less than Two Million United States Dollars ($2,000,000);

(b) *Public and Products Liability,* exclusive of the coverage provided by the Commercial General Liability policy, with at least Two Million United States Dollars ($2,000,000) per occurrence and an aggregate limit of Two Million United States Dollars ($2,000,000);

(c) *"All Risk" Property,* valued at replacement cost, covering loss or damage to the Facility and Rhythm's property and materials in the care, custody, and control of Manufacturer; and

(d) *Contingent Motor Liability and Employer's Liability,* in such amounts and under such terms as are customary for similar companies providing like services.

13.2 Evidence of Insurance. Manufacturer will furnish to Rhythm a certificate from an insurance carrier (having a minimum AM Best rating of A Stable) demonstrating the insurance requirements set forth above. The insurance certificate will confirm each of the following:

(a) Rhythm and its Affiliates are named as an additional insured with respect to matters arising from this Agreement;

(b) such insurance is primary and non-contributing to any liability insurance carried by Rhythm.

In addition, Manufacturer shall provide written notice to Rhythm within 20 days following any material change or cancellation of any of its insurance coverages referenced in Section 13.1.

13.3 Insurance Information. Manufacturer will comply, at Rhythm's expense, with reasonable requests for information made by Rhythm's insurance provider representative(s), including permitting such representative(s) to inspect the Facility during operational hours and upon reasonable notice to Manufacturer. In regard to such inspections, the representative(s) will adhere to such guidelines and policies pertaining to safety and non-disclosure as Manufacturer may reasonably require.

14. Term and Termination.

14.1 Term. This Agreement will take effect as of the Effective Date and, unless earlier terminated pursuant to this Section 14, will expire on the later of (a) three (3) years from the Effective Date, or (b) the completion of Services under all Work Orders executed by the parties prior to the third anniversary of the Effective Date. The term of this Agreement may be extended by Rhythm continuously for additional two (2) year periods upon written notice to Manufacturer at least thirty (30) days prior to the expiration of the then current term.

14.2 Termination by Rhythm. Rhythm will have the right, in its sole discretion, to terminate this Agreement or any Work Order (a) upon sixty (60) days prior written notice to Manufacturer, or (b) immediately upon written notice if (i) in Rhythm's reasonable judgment, Manufacturer is or will be unable to perform the Services in accordance with the agreed upon timeframe and/or budget set forth in the applicable Work Order, or (ii) Manufacturer fails to obtain or maintain any material governmental licenses or approvals required in connection with the Services.

14.3 Termination by Either Party. Either party will have the right to terminate this Agreement or any signed Work Orders that are pending by written notice to the other party, upon the occurrence of any of the following:

(a) the other party files a petition in bankruptcy, or enters into an agreement with its creditors, or applies for or consents to the appointment of a receiver or trustee, or makes an assignment for the benefit of creditors, or becomes subject to involuntary proceedings under any bankruptcy or insolvency law (which proceedings remain undismissed for sixty (60) days);

(b) the other party fails to start and diligently pursue the cure of a material breach of this Agreement within thirty (30) days after receiving written notice from the other party of such breach; or

(c) a *force majeure* event that will, or continues to, prevent performance (in whole or substantial part) of this Agreement or any pending Work Order for a period of at least ninety (90) days. In the case of a *force majeure* event relating solely to a pending Work Order, the right to terminate will be limited to such Work Order.

14.4 Effect of Termination. Manufacturer will, upon receipt of a termination notice from Rhythm, promptly cease performance of the applicable Services and will take all reasonable steps to mitigate the out-of-pocket expenses incurred in connection therewith. In particular, Manufacturer will use all commercially reasonable efforts to:

(a) immediately cancel, to the greatest extent possible, any third party obligations;

(b) promptly inform Rhythm of any irrevocable commitments made in connection with any pending Work Order(s) prior to termination;

(c) to the greatest extent possible promptly return to the vendor for a refund all unused, unopened materials in Manufacturer's possession that are related to any pending Work Order; provided, that Rhythm will have the option, but not the obligation, to take possession of any such materials;

(d) promptly inform Rhythm of the cost of any remaining unused, unreturnable materials ordered pursuant to any pending Work Order(s) according to minimum order quantity of Manufacturer's suppliers, and either deliver such materials to Rhythm (or its designee) or properly dispose of them, as instructed by Rhythm; and

(e) perform only those services and activities mutually agreed upon by Rhythm and Manufacturer as being necessary or advisable in connection with the close-out of any pending Work Order(s).

14.5 Return of Materials/Confidential Information. Upon the expiration or termination of this Agreement, each party will promptly return all Confidential Information of the other party that it has received pursuant to this Agreement as required by Section 10.3 and otherwise comply with the obligations set forth in Section 10.3. Manufacturer will also promptly return at Rhythm's expense all Rhythm Materials, Rhythm Equipment, retained samples, data, reports and other property, information and know-how in recorded form that was provided by Rhythm, or developed in the performance of the Services, that are owned by or licensed to Rhythm.

14.6 Inventories. Upon expiration or termination of this Agreement or a pending Work Order, Rhythm (a) shall purchase from Manufacturer any existing inventories of Product ordered under this Agreement that conforms to the Specifications and is Manufactured in accordance with cGMP (if applicable) and the Manufacturing Process, at the price for such Product set forth in the applicable Work Order, and (b) shall purchase any such Product in process held by Manufacturer as of the date of the termination, at a price to be mutually agreed (it being understood that such price will reflect, on a pro rata basis, work performed and non-cancelable out-of-pocket expenses actually incurred by Manufacturer with respect to the Manufacture of such in-process Product). Following any such purchase, if so directed by Rhythm in writing, Manufacturer shall dispose of such material at Rhythm's cost.

14.7 Payment Reconciliation. Within thirty (30) days after the close-out of a Work Order, Manufacturer will provide to Rhythm a written itemized statement of all work performed by it in connection with the terminated Work Order, an itemized breakdown of the costs associated with that work (including any outstanding costs for purchases under Section 14.6 or for Rhythm Equipment, and any irrevocable commitments made by Manufacturer in connection with any pending Work Order(s) prior to termination), and a final invoice for that Work Order. If Rhythm

has pre-paid to Manufacturer more than the amount in a final invoice then Manufacturer agrees to promptly refund that money to Rhythm, or to credit the excess payment toward another existing or future Work Order, at the election of Rhythm.

14.8 Survival. Expiration or termination of this Agreement for any reason will not relieve either party of any obligation accruing prior to such expiration or termination. Further, the provisions of Sections 1, 2.3, 4 (except for the first two sentences of Section 4.1 and the first sentence of Section 4.3), 5.2(c), 5.2(d), 5.4 through 5.7, 6, 9, 10, 12, 13, 14.4 through 14.8 and 15, and the provisions of any applicable Quality Agreement, will survive any termination or expiration of this Agreement.

15. Miscellaneous.

15.1 Independent Contractor. All Services will be rendered by Manufacturer as an independent contractor for federal, state and local income tax purposes and for all other purposes. Manufacturer will not in any way represent itself to be a partner or joint venturer of or with Rhythm. This Agreement does not create an employer-employee relationship between Rhythm on the one hand and Manufacturer or any employee, subcontractors, Affiliate of Manufacturer, or any Manufacturer personnel on the other. Manufacturer is acting under this Agreement as an independent contractor with full power and authority to determine the means, manner and method of performance of Manufacturer's duties. Manufacturer shall be responsible for and shall withhold and/or pay any and all applicable federal, state or local taxes, payroll taxes, workers' compensation contributions, unemployment insurance contributions, or other payroll deductions from the compensation of Manufacturer's employees and other Manufacturer personnel. Manufacturer understands and agrees that it is solely responsible for such matters and that it will indemnify Rhythm and hold Rhythm harmless from all claims and demands in connection with such matters.

15.2 *Force Majeure*. Except as otherwise expressly set forth in this Agreement, neither party will have breached this Agreement for failure or delay in fulfilling or performing any term of this Agreement when such failure or delay is caused by or results from causes beyond the reasonable control of the affected party, including, without limitation, fire, floods, embargoes, shortages, epidemics, quarantines, war, acts of war (whether war be declared or not), insurrections, riots, civil commotion, strikes, acts of God or acts, omissions, or delays in acting, by any governmental authority ("*force majeure*"). The party affected by any event *of force majeure* will promptly notify the other party, explaining the nature, details and expected duration of the *force majeure* event. Such party will also notify the other party from time to time as to when the affected party reasonably expects to resume performance in whole or in part of its obligations under this Agreement, and to notify the other party of the cessation of any such event. A party affected by an event *of force majeure* will use its reasonable efforts to remedy, remove, or mitigate such event and the effects of it with all reasonable dispatch. If a party anticipates that an event of *force majeure* may occur, such party will notify the other party of the nature, details and expected duration of the *force majeure* event. Upon termination of the event of *force majeure*, the performance of any suspended obligation or duty will promptly recommence.

15.3 Notices. All notices must be in writing and sent to the address for the recipient set forth in this Agreement below or in a subsequent notice as the recipient may specify in writing under this procedure. All notices must be given (a) by personal delivery, with receipt acknowledged, or (b) by first class, prepaid certified or registered mail, return receipt requested, or (c) by prepaid international express delivery service. Notices will be effective upon receipt or at a later date stated in the notice.

If to Manufacturer, to:

Recipharm Monts SAS
18 route de Montbazon
37 260 Monts
France
Attention: General Manager

With a copy to :
Recipharm AB
Lagervägen 7,
SE-136 50 Jordbro,
Sweden
Attention : Legal

If to Rhythm, to:

Rhythm Pharmaceuticals, Inc.
500 Boylston Street, 11th Floor
Boston, MA 02116
USA
Attention: President

15.4 Assignment. This Agreement may not be assigned or otherwise transferred by either party without the prior written consent of the other party; provided, however, that Rhythm may, without such consent, but with notice to the Manufacturer, assign this Agreement, in whole or in part, (a) in connection with the transfer or sale of all or substantially all of its assets or the line of business or Product to which this Agreement relates, (b) to a successor entity or acquirer in the event of a merger, consolidation or change of control, or (c) to any Affiliate. Any purported assignment in violation of the preceding sentence will be void. Any permitted assignee will assume the rights and obligations of its assignor under this Agreement.

15.5 Entire Agreement. This Agreement, including the attached Appendices and any fully-signed Work Orders, each of which are incorporated herein, constitute the entire agreement between the parties with respect to the specific subject matter of this Agreement and all prior agreements, including but not limited to the Confidentiality Agreement between the parties dated 2016 January 5 (the "CDA")„with respect thereto are superseded; provided, that all Confidential Information exchanged under the CDA shall remain subject to continuing obligations of non-use, non-disclosure and return, as set forth herein and therein..

15.6 No Modification. This Agreement and and/or any Work Order or Quality Agreement may be changed only by a writing signed by authorized representatives of both parties.

15.7 Severability; Reformation. If for any reason a court of competent jurisdiction finds any provision of this Agreement or any portion of such a provision to be invalid or unenforceable, such provision will be reformed to the extent required to make the provision valid and enforceable to the maximum extent permitted by law.

15.8 Governing Law. The validity, interpretation, and enforcement of this Agreement, matters arising out of or related to this Agreement or its making, performance or breach, and related

matters shall be governed by the laws of England, and all rights and remedies shall be governed by such laws without reference to choice of law doctrine. The parties expressly reject any application to this Agreement of (a) the United Nations Convention on Contracts for the International Sale of Goods, and (b) the 1974 Convention on the Limitation Period in the International Sale of Goods, as amended by that certain Protocol, done at Vienna on April 11, 1980.

15.9 Waiver. No waiver of any term, provision or condition of this Agreement in any one or more instances will be deemed to be or construed as a further or continuing waiver of any other term, provision or condition of this Agreement. Any such waiver, extension or amendment will be evidenced by an instrument in writing executed by an officer authorized to execute waivers, extensions or amendments.

15.10 Counterparts. This Agreement may be executed in any number of counterparts, each of which will be deemed an original and all of which together will constitute one and the same instrument.

15.11 Headings. This Agreement contains headings only for convenience and the headings do not constitute or form a part of this Agreement, and should not be used in the construction of this Agreement.

15.12 No Benefit to Third Parties. The representations, warranties, covenants and agreements set forth in this Agreement are for the sole benefit of the parties hereto and their successors and permitted assigns, and they will not be construed as conferring any rights on any other persons.

Schedule 1

Main Reason for Failure	Recipharm Batch Cost	Cost of Components	Cost of MPEG	Cost API
Stability Out of Specification, with all SOPS/process followed	Rhythm	Rhythm	Rhythm	Rhythm
Batch fails assay or other chemical test, with all SOPS/process followed	Rhythm	Rhythm	Rhythm	Rhythm
Fails due to Rhythm Equipment operated by Recipharm	Recipharm	Recipharm	Rhythm	Rhythm
Fails Sterility, from facility, utilities, water, components, disposable/Recipharm eqt	Recipharm	Recipharm	Recipharm	Recipharm
Recipharm non compliant with SOPs or cGMPs	Recipharm	Recipharm	Recipharm	Recipharm

[Signature page follows]

IN WITNESS WHEREOF, the parties hereto have caused this Agreement to be executed by their duly authorized representatives as of the date first above written.

RHYTHM PHARMACEUTICALS, INC.

By /s/ Bart Henderson

Print Name Bart Henderson

Title President

Date 12/27/16

RECIPHARM MONTS SAS

By /s/ Michel SAUDEMON

Print Name Michel SAUDEMON

Title General Manager

Date 2016, December 23rd

By /s/ Kjell JOHANSSON

Print Name Kjell JOHANSSON

Title President, Manuf. Services EU

Date 5/1-2017

APPENDIX A

SAMPLE WORK ORDER

THIS WORK ORDER is by and between **RHYTHM PHARMACEUTICALS, INC.,** ("Rhythm") and **RECIPHARM MONTS SA** ("Manufacturer"), and upon execution will be incorporated into the Development and Manufacturing Services Agreement between Rhythm and Manufacturer dated December 21, 2016 (the "Agreement"). Capitalized terms in this Work Order will have the same meanings as set forth in the Agreement.

Rhythm hereby engages Manufacturer to provide Services, as follows:

1. **API/Drug Substance and Product.**

Describe the specific API/Drug Substance(s) and Product(s).

2. **Services.** Manufacturer will render to Rhythm the following Services:

Describe the specific Services to be conducted by Manufacturer or attach Manufacturer's proposal.

3. **Facilit(ies).** The Services described above will be rendered at the following facilities of Manufacturer:

Include Facility address(es).

4. **Rhythm Materials.** Rhythm will provide to Manufacturer the following materials to be used by Manufacturer to perform the Services:

Describe specific materials, including without limitation API, being provided by Rhythm to Manufacturer.

5. **Rhythm Equipment.**

Include any equipment that will be provided by Rhythm to Manufacturer to be used by Manufacturer in performance of the Services.

6. **Manufacturer Representative.** *Name and Title*

7. **Rhythm Representative.** *Name and Title*

8. **Compensation.** The total compensation due Manufacturer for Services under this Work Order is ***INSERT WRITTEN AMOUNT (INSERT NUMERICAL AMOUNT).*** Manufacturer will invoice Rhythm for all amounts due under this Work Order. Such amounts will be invoiced in United States Dollars to the attention of ***[INSERT NAME]*** as follows: ***[INSERT INVOICE SCHEDULE].*** All undisputed payments will be made by Rhythm within thirty (30) days of its receipt of an invoice and reasonable supporting documentation. Payments will be made in United States Dollars.

9. **[Quality Agreement.** The provisions of the Quality Agreement, attached hereto as Attachment 1, are incorporated herein by reference.]

All other terms and conditions of the Agreement will apply to this Work Order.

WORK ORDER AGREED TO AND ACCEPTED BY:

RHYTHM PHARMACEUTICALS, INC.		**RECIPHARM MONTS SA**	
By	_____	By	_____
Print Name	_____	Print Name	_____
Title	_____	Title	_____
Date	_____	Date	_____
		By	_____
		Print Name	_____
		Title	_____
		Date	_____

Exhibit 10.16

Rhythm Pharmaceuticals, Inc.
500 Boylston Street — 11th Floor
Boston, MA 02116
Main Telephone: 617-585-2090
www.rhythmtx.com

July 17, 2017

Hunter Smith
17 Myanos Road
New Canaan, CT 06840

Dear Hunter:

On behalf of Rhythm Pharmaceuticals, Inc., (the "Company" or "Rhythm"), I am pleased to set forth below the terms of your employment with the Company.

Employment. You will be employed as Chief Financial Officer, beginning on July 31, 2017 (the "Start Date"), or sooner, if available, reporting to Keith Gottesdiener, CEO. You will be responsible for performing the duties associated with the position above or as the Company may otherwise assign to you. Your primary place of employment will be in the Company's offices located in Boston, Massachusetts; however, you will be expected to travel as may be necessary to fulfill your responsibilities. In the course of your employment with Company, you will be subject to, and required to comply with, all company policies and all applicable laws and regulations.

Base Salary. During your employment, your salary will be $380,000 annualized, subject to all required and elected taxes and other withholdings. Your salary may be adjusted from time to time in accordance with normal business practice and in the sole discretion of the Company.

Annual Target Cash Incentive. Following the end of each fiscal year and subject to the approval by the Company's Board of Directors, you will be eligible to earn a performance and retention bonus, based on your performance and the Company's performance, each during the applicable fiscal year, and your continued employment in good standing on the date of incentive distribution. Your annual incentive opportunity is a target of 30% of your annualized base salary, which will be increased to 35% if and when Rhythm successfully completes an initial public offering.

Equity Grant. As soon as reasonably practicable following your Start Date, and subject to approval by the Board of Directors of the Company, the Company shall grant to you a stock option (the "Option") under the Company's 2015 Equity Incentive Plan, as it may be amended from time to time (the "Plan"), to purchase 1,850,000 shares (the "Option Shares") of the Company's common stock, $0.001 par value per share (the "Common Stock"), at an exercise price equal to fair market value of the Common Stock, as determined by the Board of Directors of the Company, on the date of the grant of the Option (the "Grant Date"). Promptly after the Grant Date, the Company and you shall execute and deliver to each other the

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Company's then standard form of stock option agreement, evidencing the Option and the terms thereof. The Option shall be subject to, and governed by, the terms and provisions of the Plan and your stock option agreement. In the event of a conflict related to the Option between the terms in this letter and the terms of the Plan, the terms of this letter will supersede.

Subject to the terms and conditions set forth below in this letter and unless the Board of Directors of the Company shall otherwise determine on the Grant Date, the Option shall vest as follows: the 1,850,000 Option Shares will be exercisable for twenty-five percent (25%) of the remaining Option Shares subject to such Option as of the first anniversary of your Start Date, and the remainder of the Option Shares subject to such Option shall become exercisable thereafter in a series of thirty-six (36) equal monthly installments until such Option shall have become fully vested and exercisable.

Upon termination of your employment with the Company, you may exercise each Option, to the extent then outstanding and exercisable, but only until the earlier to occur of (i) the expiration of the term of such Option and (ii) the expiration of the limited period of time set forth in the Plan and/or your stock option agreement for the exercise of such Option following termination of your employment with the Company.

Any Option Shares you acquire pursuant to the exercise of any of the Options shall be subject to the terms, restrictions on transfer and voting provisions set forth in the Plan, your stock option agreements and any other agreement to which you shall become, or are required to become, a party pursuant to the terms of the Plan.

You may be awarded additional equity grants from time to time in accordance with normal business practice and in the sole discretion of the Company's Board of Directors. The terms of any equity grant will be consistent with any plan under which they are granted and the terms of the applicable agreement under which the award(s) are granted.

Sign-on Bonus and Travel and Relocation Expenses. Rhythm will agree to reimburse you for up to $125,000 in travel, commuting, lodging and other expenses (including moving your family to Boston if you decide to do so), and for appropriate relocation expenses. At the end of two years of employment, if less than $125,000 has been expensed for these purposes, Rhythm will provide the balance to you in the form of a cash sign-on bonus.

Benefits. You may participate in any and all benefit programs that the Company establishes and makes available to its employees from time to time, subject to the terms and conditions of those programs. The Company's benefits programs are subject to change at any time in the Company's sole discretion.

Vacation. You will be entitled to annual paid vacation of four (4) weeks. Your accrual and use of vacation time will be pursuant to any vacation or time off policy the Company may establish or modify from time to time. The Company's vacation policy is subject to change at any time in the Company's sole discretion.

Outside Board Duties. You currently serve as an independent director of the NYSE listed multinational Genessee & Wyoming Inc. ("Genessee"), and as a member of its Governance/Nominating Committee. You may remain as a director of Genessee, provided that your duties in such director role shall not in any

way interfere with your role and duties as CFO of, and commitments to, the Company which shall supersede and take priority in any and all respects. Moreover, you agree that you will not be permitted to take on any additional director, board observer, advisory, consulting, or other such roles or commitments without the express prior written consent of the CEO of the Company.

Severance. If the Company terminates your employment without Cause (as defined below) or you resign your employment for Good Reason (as defined below) (in either event, a "Qualifying Termination"), subject to your execution of a reasonable release acceptable to the Company (the "Release"), the expiration of any revocation period provided in the Release and your continued compliance with the terms of the NDA (as defined below), the Company will pay you an amount equal to your then-current base salary rate for a period of six (6) months (the "Regular Severance Amount"). However, if such a Qualifying Termination occurs up to the date that you complete one year of employment, Regular Severance Amount will be equal to an amount equal to your then current base salary rate for a period of twelve (12) months.

If there is a Qualifying Termination within the three (3) months immediately preceding or the twelve (12) months immediately following a "Sale of the Company Transaction" (as such term is defined in the Plan, as amended and in effect from time to time), subject to your execution of a Release following your Separation from Service (as defined below), the expiration of any revocation period provided in the Release and your continued compliance with the terms of the NDA, in lieu of any Regular Severance Amount, the Company will pay you an amount equal to your then-current base salary rate for a period of six (6) months (the "Sale of the Company Severance Amount") plus an amount equal to 100% of your annual target cash incentive.

Any severance amount to which you may be entitled under this letter will be paid in substantially equal installments in accordance with the Company's ordinary payroll practices, beginning on the first payroll date following the date that is either (i) 60 days after the date of your Separation from Service, or (ii) in the case of a Separation from Service that is a Qualifying Termination that occurs within the three (3) months immediately preceding a Sale of the Company Transaction, 60 days after the date of such Sale of the Company Transaction. To be eligible for either the Regular Severance Amount or the Sale of the Company Severance Amount, as applicable, you must execute and deliver the Release to the Company and allow it to become effective within 30 days of your Separation from Service or, if later, a Sale of the Company Transaction giving rise to a Sale of the Company Severance Amount entitlement.

In addition, if following your Separation from Service, you are eligible for and timely elect continued medical insurance coverage pursuant to COBRA, the Company will reimburse you for the applicable premiums for you and your eligible dependents during the period commencing on the date of your Separation from Service and ending on the earlier to occur of (a) the final day of the Severance Period and (b) the date you otherwise become ineligible for continued coverage under COBRA. Notwithstanding the foregoing, if the Company determines that it cannot provide such reimbursement of premiums to you without potentially violating applicable law, the Company shall not be obligated to make any such payments or reimbursements to you.

If the Qualifying Termination occurs within the three (3) months immediately preceding or the twelve (12) months immediately following a Sale of the Company Transaction, then all of the equity awards granted to you and then held by you will then be vested.

The foregoing provisions of this paragraph shall apply notwithstanding anything express or implied to the contrary in any agreement or award between you and the Company, or in any plan of the Company, that is applicable to such outstanding equity award.

Notwithstanding anything herein to the contrary, in the event that any compensation or benefit that constitutes "nonqualified deferred compensation" within the meaning of Section 409A of the Internal Revenue Code of 1986, as amended (the "Code"), becomes payable upon the occurrence of a Sale of the Company Transaction, such compensation or benefit shall not be paid unless such Sale of the Company Transaction constitutes a "change in control event" within the meaning of Section 409A of the Code.

If any payment or benefit you would receive under this letter, when combined with any other payment or benefit you receive pursuant to the termination of your employment with the Company ("Payment") would (i) constitute a "parachute payment" within the meaning of Section 280G of the Code, and (ii) but for this sentence, be subject to the excise tax imposed by Section 4999 of the Code (the "Excise Tax"), then such Payment shall be either (x) the full amount of such Payment or (y) such lesser amount (with your choice of whether to reduce cash payments or stock option compensation or both) as would result in no portion of the Payment being subject to the Excise Tax, whichever of the foregoing amounts, taking into account the applicable federal, state and local employment taxes, income taxes and the Excise Taxes results in your receipt, on an after-tax basis, of the greater amount of the Payment notwithstanding that all or some portion of the Payment may be subject to the Excise Tax.

Definitions

Separation from Service. For purposes of this letter, "Separation from Service" means a "separation from service" within the meaning of Section 409A of the Code. Each installment payment provided under this letter shall at all times be considered a separate and distinct payment for purposes of Section 409A of the Code. Notwithstanding anything in this letter to the contrary, to the extent required to avoid a prohibited distribution under Section 409A of the Code, the benefits provided under this letter will not be provided to you until the earlier of (a) the expiration of the six-month period measured from the date of your Separation from Service with the Company or (b) the date of your death. Upon the first business day after expiration of the relevant period, all payments delayed pursuant to the preceding sentence will be paid in a lump sum and any remaining payments due will be paid as otherwise provided herein.

Cause. "Cause" shall mean the occurrence of any of the following events by the individual: (i) commission of any crime involving the Company, or any crime involving fraud, breach of trust, or physical or emotional harm to any person, moral turpitude or dishonesty; (ii) any unauthorized use or disclosure of the Company's proprietary information (other than any such use or disclosure that is not intentional and is not material); (iii) any intentional misconduct or

gross negligence that has a material adverse effect on the Company's business or reputation; (iv) any material breach by you of any agreement between you and the Company that is not cured within thirty (30) days after receipt of written notice from the Company describing any such breach; or (v) repeated and willful failure to perform the duties, functions and responsibilities of the individual's position after a written warning from the Company.

Good Reason. "Good Reason" shall mean your resignation from all positions you then hold with the Company if: (A) without your written consent (i) there is a material diminution in the nature or scope of your authorities, duties, title, or authority; (ii) there is a material reduction of your base salary; provided,

however, that a material reduction in your base salary pursuant to a salary reduction program affecting all or substantially all of the employees of the Company and that does not adversely affect you to a greater extent than other similarly situated employees shall not constitute Good Reason; or (iii) you are required to relocate your primary work location to a facility or location that would increase your one way commute distance by more than thirty-five (35) miles from your primary work location as of immediately prior to such change, (B) you provide written notice outlining such conditions, acts or omissions to the Company's General Counsel within thirty (30) days immediately following such material change or reduction, (C) such material change or reduction is not remedied by the Company within thirty (30) days following the Company's receipt of such written notice and (D) your resignation is effective not later than thirty (30) days after the expiration of such thirty (30) day cure period. "Good Reason" shall also mean your resignation, at your sole discretion, on the one year anniversary of a Sale of the Company Transaction from all positions you then hold with the Company or its successor if by that date (i) you have not entered into a written letter or agreement with the Company or such successor that provides for your continued employment with the Company or such successor, and (ii) if at that one year anniversary of a Sale of the Company Transaction, another Chief Financial Officer has any control and/or oversight, directly or indirectly, over the Company (or what used to be the Company prior to such transaction). For purposes of clarification, any Qualifying Termination that occurs on the first anniversary of a Sale of the Company Transaction shall be deemed and treated as occurring within the twelve (12) months immediately following a Sale of the Company Transaction for all purposes of this letter of employment.

Invention, Non-Disclosure, Non-Competition and Non-Solicitation Obligations. In exchange for your employment with the Company pursuant to the terms and conditions herein, you acknowledge and reaffirm your obligations set forth in the Employee Confidentiality, Assignment of Inventions, Non-Competition and Non-Solicitation Agreement (the "NDA") you have executed for the benefit of the Company, which obligations remain in full force and effect.

At-Will Employment. This letter shall not be construed as an agreement, either express or implied, to employ you for any stated term, and shall in no way alter the Company's policy of employment at-will. Similarly, nothing in this letter shall be construed as an agreement, either express or implied, to pay you any compensation or grant you any benefit beyond the end of your employment with the Company, except as otherwise explicitly set forth in this letter. This letter supersedes all prior understandings, whether written or oral, including, without limitation, your current employment agreement, with respect to the subject matter of this letter.

Hunter, I look forward to working with you as part of the Rhythm team. Please indicate your acceptance of this letter of employment by signing a copy of this offer letter and returning it to us by Wednesday, July 19, 2017.

Sincerely,

/s/ Keith M. Gottesdiener
Keith M. Gottesdiener
Chief Executive Officer

The foregoing correctly sets forth the terms of my at-will employment with Rhythm. I am not relying on any representations other than those set forth above.

/s/ Hunter Smith	July 18, 2017
Hunter Smith	Date

Exhibit 10.17

Rhythm Pharmaceuticals, Inc.
500 Boylston Street — 11th Floor
Boston, MA 02116
Main Telephone: 617-585-2090
www.rhythmtx.com

July 5, 2017

Nithya Desikan
82 Bay State Road
Belmont, MA 02478

Dear Nithya:

On behalf of Rhythm Pharmaceuticals, Inc., formerly known as Rhythm Metabolic, Inc. (the "Company" or "Rhythm"), I am pleased to set forth below the terms of your employment with the Company.

Employment. You will be employed as Chief Commercial Officer, beginning on July 23, 2017 (the "Start Date"), or sooner, if available, reporting to Keith Gottesdiener, CEO. You will be responsible for performing the duties associated with the position above or as the Company may otherwise assign to you. Your primary place of employment will be in the Company's offices located in Boston, Massachusetts; however, you will be expected to travel as may be necessary to fulfill your responsibilities. In the course of your employment with Company, you will be subject to, and required to comply with, all company policies and all applicable laws and regulations.

Base Salary. During your employment, your salary will be $360,000 annualized, subject to all required and elected taxes and other withholdings. Your salary may be adjusted from time to time in accordance with normal business practice and in the sole discretion of the Company.

Annual Target Cash Incentive. Following the end of each fiscal year and subject to the approval by the Company's Board of Directors, you will be eligible to earn a performance and retention bonus, based on your performance and the Company's performance, each during the applicable fiscal year, and your continued employment in good standing on the date of incentive distribution. Your annual incentive opportunity is a target of 30% of your annualized base salary, which will be increased to 35% if and when Rhythm successfully completes an initial public offering.

Equity Grant. As soon as reasonably practicable following your Start Date, and subject to approval by the Board of Directors of the Company, the Company shall grant to you a stock option (the "Option") under the Company's 2015 Equity Incentive Plan, as it may be amended from time to time (the "Plan"), to purchase 1,850,000 shares (the "Option Shares") of the Company's common stock, $0.001 par value per share (the "Common Stock"), at an exercise price equal to fair market value of the Common Stock, as determined by the Board of Directors of the Company, on the date of the grant of the Option (the "Grant Date"). Promptly after the Grant Date, the Company and you shall execute and deliver to each other the

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Company's then standard form of stock option agreement, evidencing the Option and the terms thereof. The Option shall be subject to, and governed by, the terms and provisions of the Plan and your stock option agreement. In the event of a conflict related to the Option between the terms in this letter and the terms of the Plan, the terms of this letter will supersede.

Subject to the terms and conditions set forth below in this letter and unless the Board of Directors of the Company shall otherwise determine on the Grant Date, the Option shall vest as follows: (i) 300,000 of the Option Shares subject to such Option will be exercisable on the Start Date, and (ii) the remaining 1,550,000 Option Shares will be exercisable for twenty-five percent (25%) of the remaining Option Shares subject to such Option as of the first anniversary of your Start Date, and the remainder of the Option Shares subject to such Option shall become exercisable thereafter in a series of thirty-six (36) equal monthly installments until such Option shall have become fully vested and exercisable.

Upon termination of your employment with the Company, you may exercise each Option, to the extent then outstanding and exercisable, but only until the earlier to occur of (i) the expiration of the term of such Option and (ii) the expiration of the limited period of time set forth in the Plan and/or your stock option agreement for the exercise of such Option following termination of your employment with the Company.

Any Option Shares you acquire pursuant to the exercise of any of the Options shall be subject to the terms, restrictions on transfer and voting provisions set forth in the Plan, your stock option agreements and any other agreement to which you shall become, or are required to become, a party pursuant to the terms of the Plan.

You may be awarded additional equity grants from time to time in accordance with normal business practice and in the sole discretion of the Company's Board of Directors. The terms of any equity grant will be consistent with any plan under which they are granted and the terms of the applicable agreement under which the award(s) are granted.

Sign-on Bonus. Rhythm will provide you with a cash sign-on bonus of $100,000.

Benefits. You may participate in any and all benefit programs that the Company establishes and makes available to its employees from time to time, subject to the terms and conditions of those programs. The Company's benefits programs are subject to change at any time in the Company's sole discretion.

Vacation. You will be entitled to annual paid vacation of four (4) weeks. Your accrual and use of vacation time will be pursuant to any vacation or time off policy the Company may establish or modify from time to time. The Company's vacation policy is subject to change at any time in the Company's sole discretion.

Severance. If the Company terminates your employment without Cause (as defined below) or you resign your employment for Good Reason (as defined below) (in either event, a "Qualifying Termination"), subject to your execution of a reasonable release acceptable to the Company (the "Release"), the expiration of any revocation period provided in the Release and your continued compliance with the terms of the NDA (as defined below), the Company will pay you an amount equal to your then-current base salary rate for a period of six (6) months (the "Regular Severance Amount"). However, if such a

Qualifying Termination occurs up to the date that you complete one year of employment, Regular Severance Amount will be equal to an amount equal to your then current base salary rate for a period of twelve (12) months.

If there is a Qualifying Termination within the three (3) months immediately preceding or the twelve (12) months immediately following a "Sale of the Company Transaction" (as such term is defined in the Plan, as amended and in effect from time to time), subject to your execution of a Release following your Separation from Service (as defined below), the expiration of any revocation period provided in the Release and your continued compliance with the terms of the NDA, in lieu of any Regular Severance Amount, the Company will pay you an amount equal to your then-current base salary rate for a period of six (6) months (the "Sale of the Company Severance Amount") plus an amount equal to 100% of your annual target cash incentive.

Any severance amount to which you may be entitled under this letter will be paid in substantially equal installments in accordance with the Company's ordinary payroll practices, beginning on the first payroll date following the date that is either (i) 60 days after the date of your Separation from Service, or (ii) in the case of a Separation from Service that is a Qualifying Termination that occurs within the three (3) months immediately preceding a Sale of the Company Transaction, 60 days after the date of such Sale of the Company Transaction. To be eligible for either the Regular Severance Amount or the Sale of the Company Severance Amount, as applicable, you must execute and deliver the Release to the Company and allow it to become effective within 30 days of your Separation from Service or, if later, a Sale of the Company Transaction giving rise to a Sale of the Company Severance Amount entitlement.

In addition, if following your Separation from Service, you are eligible for and timely elect continued medical insurance coverage pursuant to COBRA, the Company will reimburse you for the applicable premiums for you and your eligible dependents during the period commencing on the date of your Separation from Service and ending on the earlier to occur of (a) the final day of the Severance Period and (b) the date you otherwise become ineligible for continued coverage under COBRA. Notwithstanding the foregoing, if the Company determines that it cannot provide such reimbursement of premiums to you without potentially violating applicable law, the Company shall not be obligated to make any such payments or reimbursements to you.

If the Qualifying Termination occurs within the three (3) months immediately preceding or the twelve (12) months immediately following a Sale of the Company Transaction, then all of the equity awards granted to you and then held by you will then be vested.

The foregoing provisions of this paragraph shall apply notwithstanding anything express or implied to the contrary in any agreement or award between you and the Company, or in any plan of the Company, that is applicable to such outstanding equity award.

Notwithstanding anything herein to the contrary, in the event that any compensation or benefit that constitutes "nonqualified deferred compensation" within the meaning of Section 409A of the Internal Revenue Code of 1986, as amended (the "Code"), becomes payable upon the occurrence of a Sale of the Company Transaction, such compensation or benefit shall not be paid unless such Sale of the Company Transaction constitutes a "change in control event" within the meaning of Section 409A of the Code.

If any payment or benefit you would receive under this letter, when combined with any other payment or benefit you receive pursuant to the termination of your employment with the Company ("Payment") would (i) constitute a "parachute payment" within the meaning of Section 280G of the Code, and (ii) but for this sentence, be subject to the excise tax imposed by Section 4999 of the Code (the "Excise Tax"), then such Payment shall be either (x) the full amount of such Payment or (y) such lesser amount (with your choice of whether to reduce cash payments or stock option compensation or both) as would result in no portion of the Payment being subject to the Excise Tax, whichever of the foregoing amounts, taking into account the applicable federal, state and local employment taxes, income taxes and the Excise Taxes results in your receipt, on an after-tax basis, of the greater amount of the Payment notwithstanding that all or some portion of the Payment may be subject to the Excise Tax.

Definitions

Separation from Service. For purposes of this letter, "Separation from Service" means a "separation from service" within the meaning of Section 409A of the Code. Each installment payment provided under this letter shall at all times be considered a separate and distinct payment for purposes of Section 409A of the Code. Notwithstanding anything in this letter to the contrary, to the extent required to avoid a prohibited distribution under Section 409A of the Code, the benefits provided under this letter will not be provided to you until the earlier of (a) the expiration of the six-month period measured from the date of your Separation from Service with the Company or (b) the date of your death. Upon the first business day after expiration of the relevant period, all payments delayed pursuant to the preceding sentence will be paid in a lump sum and any remaining payments due will be paid as otherwise provided herein.

Cause. "Cause" shall mean the occurrence of any of the following events by the individual: (i) commission of any crime involving the Company, or any crime involving fraud, breach of trust, or physical or emotional harm to any person, moral turpitude or dishonesty; (ii) any unauthorized use or disclosure of the Company's proprietary information (other than any such use or disclosure that is not intentional and is not material); (iii) any intentional misconduct or gross negligence that has a material adverse effect on the Company's business or reputation; (iv) any material breach by you of any agreement between you and the Company that is not cured within thirty (30) days after receipt of written notice from the Company describing any such breach; or (v) repeated and willful failure to perform the duties, functions and responsibilities of the individual's position after a written warning from the Company.

Good Reason. "Good Reason" shall mean your resignation from all positions you then hold with the Company if: (A) without your written consent (i) there is a material diminution in the nature or scope of your authorities, duties, title, or authority; (ii) there is a material reduction of your base salary; provided, however, that a material reduction in your base salary pursuant to a salary reduction program affecting all or substantially all of the employees of the Company and that does not adversely affect you to a greater extent than other similarly situated employees shall not constitute Good Reason; or (iii) you are required to relocate your primary work location to a facility or location that would increase your one way commute distance by more than thirty-five (35) miles from your primary work location as of immediately prior to such change, (B) you provide written notice outlining such conditions, acts or omissions to the Company's General Counsel within thirty (30) days immediately following such material change or reduction, (C) such material change or reduction is not remedied by the Company within thirty (30) days following the Company's receipt of such written notice and (D) your resignation is effective not later than

thirty (30) days after the expiration of such thirty (30) day cure period. "Good Reason" shall also mean your resignation on the one year anniversary of a Sale of the Company Transaction from all positions you then hold with the Company or its successor if by that date you have not entered into a written letter or agreement with the Company or such successor that provides for your continued employment with the Company or such successor. For purposes of clarification, any Qualifying Termination that occurs on the first, anniversary of a Sale of the Company Transaction shall be deemed and treated as occurring within the twelve (12) months immediately following a Sale of the Company Transaction for all purposes of this letter of employment.

Invention, Non-Disclosure, Non-Competition and Non-Solicitation Obligations. In exchange for your employment with the Company pursuant to the terms and conditions herein, you acknowledge and reaffirm your obligations set forth in the Employee Confidentiality, Assignment of Inventions, Non-Competition and Non-Solicitation Agreement (the "NDA") you have executed for the benefit of the Company, which obligations remain in full force and effect

At-Will Employment. This letter shall not be construed as an agreement, either express or implied, to employ you for any stated term, and shall in no way alter the Company's policy of employment at-will. Similarly, nothing in this letter shall he construed as an agreement, either express or implied, to pay you any compensation or grant you any benefit beyond the end of your employment with the Company, except as otherwise explicitly set forth in this letter. This letter supersedes all prior understandings, whether written or oral. including, without limitation. your current employment agreement, with respect to the subject matter of this letter.

Nithya, I look forward to working with you as part of the Rhythm team. Please indicate your acceptance of this letter of employment by signing a copy of this offer letter and returning it to us by Friday, July 7, 2017.

Sincerely,

/s/ Keith M. Gottesdiener
Keith M. Gottesdiener
Chief Executive Officer

The foregoing correctly sets forth the terms of my at-will employment with Rhythm, I am not relying on any representations other than those set forth above.

/s/ Nithya Desikan	7/5/17
Nithya Desikan	Date

Exhibit 10.20

Summary of Non-Employee Director Compensation Policy

Under the Company's non-employee director compensation policy, all non-employee directors will be paid an annual retainer fee of $35,000 and such additional fees as are set forth in the following table. All payments will be made quarterly in arrears.

Non-Employee Director	Annual Fee
Lead Director	$ 25,000
Non-Executive Chair	$ 30,000
Chairman of the audit committee	$ 15,000
Member of the audit committee (other than chairman)	$ 7,500
Chairman of the compensation committee	$ 10,000
Member of the compensation committee (other than chairman)	$ 5,000
Chairman of the governance and nominating committee	$ 8,000
Member of the governance and nominating committee (other than chairman)	$ 4,000

Under the policy, each individual who is initially appointed or elected to the board of directors will be eligible to receive an option to purchase up to 200,000 shares of our common stock under the Plan on the date he or she first becomes a non-employee director. These option grants will vest annually over a three-year period from the date of grant, subject to continued service as a non-employee director through that vesting date. In addition, on the date of the annual meeting of stockholders, each continuing non-employee director who has served on the board of directors for a minimum of six months will be eligible to receive an option grant to purchase up to 100,000 shares of our common stock, which will vest in full upon the earlier of the first anniversary of the date of grant or the date of the next annual meeting of stockholders. The exercise price for each of these option grants will be equal to the fair market value of our common stock on the date of grant. These new director grants and annual grants will be subject to approval by our board of directors at the time of grant. The share numbers set forth herein will be appropriately adjusted for any split or recapitalization of the Company's securities.

Exhibit 23.1

Consent of Independent Registered Public Accounting Firm

We consent to the reference to our firm under the caption "Experts" and to the use of our report dated May 23, 2017, in the Registration Statement (Form S-1) and related Prospectus of Rhythm Pharmaceuticals, Inc. for the registration of shares of its common stock.

/s/ Ernst & Young LLP

Boston, Massachusetts
September 5, 2017

QuickLinks

Exhibit 23.1