Use these links to rapidly review the document
TABLE OF CONTENTS
RHYTHM PHARMACEUTICALS, INC. INDEX TO FINANCIAL STATEMENTS

Table of Contents

As submitted confidentially to the Securities and Exchange Commission on December 9, 2015 as Amendment No. 1 to the confidential submission filing No. 377-01174

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)

855 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
Rhythm Pharmaceuticals, Inc.
855 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)

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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. See the definitions of "large accelerated filer," "accelerated filer" and "smaller reporting 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

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	$	$

(1) Includes additional 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.

Table of Contents

SUBJECT TO COMPLETION, DATED , 2015

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 intend to apply 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 13.

	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 162 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 .

MORGAN STANLEY *BofA MERRILL LYNCH* *PIPER JAFFRAY*

NEEDHAM

TABLE OF CONTENTS

Prospectus Summary	1
Risk Factors	13
Special Note Regarding Forward-Looking Statements	53
Market, Industry and Other Data	54
Use of Proceeds	56
Dividend Policy	57
Capitalization	58
Dilution	60
Selected Financial Data	62
Management's Discussion and Analysis of Financial Condition and Results of Operations	64
Business	79
Management	123
Executive and Director Compensation	131
Certain Relationships and Related Party Transactions	145
Principal Stockholders	147
Description of Capital Stock	149
Material United States Federal Income and Estate Tax Consequences to Non-U.S. Holders of our Common Stock	155
Shares Eligible for Future Sale	160
Underwriting	162
Legal Matters	169
Experts	169
Where You Can Find More Information	169
Index to Financial Statements	F-1

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 Restructuring."

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 body lacking satiety signals, which, in turn, leads to intense feelings of hunger and to obesity. Our development efforts are initially focused on two of these deficiencies, Prader-Willi Syndrome, or PWS, and pro-opiomelanocortin, or POMC, deficiency obesity, 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 initial proof of concept in our ongoing Phase 2 clinical trial in POMC deficiency obesity, a disorder of extreme and unrelenting appetite and obesity, in which setmelanotide dramatically reduced both weight and hunger. We are also conducting a Phase 2 clinical trial in PWS and we expect to report results from these clinical trials in the first half of 2016. These clinical trials expand upon previous setmelanotide clinical trials which enrolled over 200 general obese patients and demonstrated 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.

Our Product Pipeline

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

Setmelanotide for the Treatment of Obesity and Hyperphagia in PWS

PWS is a life-threatening, orphan disease with prevalence estimates ranging from approximately one in 8,000 to one in 52,000, and with at least 8,000 diagnosed patients in the United States. A hallmark of PWS is severe hyperphagia, an overriding physiological drive to eat, 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. Only one drug, a growth hormone, is approved for treating short stature in PWS. However, there is currently no approved treatment for the obesity and hyperphagia associated with PWS. Recent scientific studies identify deficiencies affecting the MC4 pathway as the likely cause of the obesity and associated symptoms of PWS, such as hyperphagia, and demonstrate that an MC4R agonist can directly impact these symptoms.

We have initiated a Phase 2 clinical trial to evaluate the effects of up to 10 weeks of treatment on weight reduction and PWS-specific food-related behavior in obese patients with PWS. We expect to enroll approximately 36 patients and report results from this trial in the first half of 2016. The U.S. Food and Drug Administration's, or FDA's, existing guidance on developing products for weight management addresses treatments for the population of general obesity patients, which requires treatment of large and diverse populations of general obese patients. In contrast, based on our consultations with the FDA, we believe we can pursue a faster path to approval of setmelanotide for our genetically-targeted patient populations, such as PWS patients, based on a clinical study program tailored in size, duration, and preclinical prerequisites appropriate for the smaller size and nature of these rare populations.

In September 2015, the FDA granted our orphan drug designation request for setmelanotide for the treatment of PWS. As described more fully under the caption "Business—Regulatory Matters," if a product with orphan drug designation receives the first FDA approval for that disease, the product will receive orphan drug exclusivity. The benefit of orphan drug exclusivity is that the FDA will not approve another sponsor's marketing application for the same drug for the same indication for seven years, except in certain limited circumstances.

Setmelanotide for the Treatment of Obesity and Hyperphagia in POMC Deficiency

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 believe that our addressable patient population for this disorder is approximately 100 to 500 patients worldwide. Like PWS, patients with POMC deficiency have unrelenting hyperphagia that begins in infancy and they develop severe, early onset obesity. POMC deficiency obesity results from two different homozygous genetic defects, both upstream (which refers to the relative position of the defect earlier in the pathway) of MC4R. Currently, there is no approved treatment for the obesity and hyperphagia associated with this genetic disorder.

We have initiated a Phase 2, open-label, clinical trial to evaluate the effects of up to 12 weeks of setmelanotide treatment on weight reduction and hunger in approximately six patients with POMC deficiency obesity. The initial patient in this trial lost 25.8 kg, or 56.9 lbs., over the first 13 weeks of treatment, immediately regained weight on withdrawal of drug, and resumed outstanding weight loss upon re-initiation of setmelanotide treatment in a long-term extension and has lost 51 kgs, or 112 lbs., over 42 weeks. Our second POMC patient has been treated for 10 weeks and has lost 17.8 kgs, or 39.2 lbs. We expect to report results from this trial in the first half of 2016. Based on our consultations with the FDA, we intend to pursue a faster path to approval of setmelanotide for POMC deficiency obesity, similar to the faster path we intend to seek in connection with the use of setmelanotide to treat obesity in PWS patients. In addition, we intend to apply for orphan drug designation for the use of setmelanotide for the treatment of POMC deficiency obesity.

Setmelanotide for the Treatment of Obesity and Hyperphagia in POMC Heterozygous and LepR Deficiency

We are also focusing on additional 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 intend to expand setmelanotide development to include two other upstream disorders, POMC heterozygous deficiency obesity, where patients only have one normal copy of the MC4 gene, and LepR deficiency obesity, where patients have a defective leptin receptor, for which there is also high unmet need and no approved or effective therapy. POMC heterozygous deficiency obesity results from the loss of function in one of two POMC genes. This condition is more prevalent than POMC deficiency obesity, affecting an estimated 2% of patients with severe, early onset obesity. We estimate that the addressable patient population may consist of approximately 4,000 patients in the United States.

LepR deficiency obesity is an ultra-rare orphan disease resulting in extreme hyperphagia and severe early onset obesity with an estimated prevalence of 1% of subjects with severe, early onset obesity. Like other deficiencies upstream in the MC4 pathway, LepR deficiency results in loss of function in the MC4 pathway. We estimate actual prevalence could be between 500 and 2,000 patients worldwide.

We intend to initiate Phase 2 clinical trials for both POMC heterozygous deficiency obesity and LepR deficiency obesity in the first half of 2016 to evaluate the effects of setmelanotide on hunger and weight in these disorders. We expect to report results from these trials in the first half of 2017. We also intend to pursue faster paths to approval for setmelanotide for both POMC heterozygous deficiency obesity and LepR deficiency obesity.

Setmelanotide: A First-in-Class Phase 2 MC4R Agonist

Setmelanotide is a potent, first-in-class, MC4R agonist peptide administered by daily SC injection. Setmelanotide is in Phase 2 clinical trials for the treatment of rare genetic disorders of obesity caused by MC4 pathway deficiencies. MC4R modulates a key pathway in humans that regulates energy homeostasis, which refers to the body's energy balance, 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 early onset

and severe obesity. The first generation MC4R agonists were small molecules that failed 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. Our previous setmelanotide clinical trials have enrolled over 200 general obese patients and demonstrated significant weight loss with good tolerability.

We have initiated two Phase 2 clinical trials of setmelanotide for the treatment of rare genetic disorders of obesity, one for POMC deficiency obesity and one for PWS. Based on FDA consultations to date, we believe we can seek indications for obesity caused by defects in the MC4 pathway with faster paths to approval because of the high unmet need and rare prevalence of these disorders. We expect to use the results of our Phase 2 clinical trials of setmelanotide in these indications as the foundation for proceeding directly to pivotal clinical trials. We also plan to initiate Phase 2 proof of concept trials in the first half of 2016 in POMC heterozygous deficiency obesity patients and in patients with LepR deficiency obesity, additional populations with genetically-defined deficiencies upstream in the MC4 pathway.

We believe our initial data in POMC deficiency obesity provides strong proof of concept that setmelanotide, when targeted for deficiencies in 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 still 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.

To date, most of our completed setmelanotide clinical trials have been in the general obese population. These trials have provided additional safety data as we focus on rare, genetic segments of obesity. In these trials, setmelanotide has generally achieved weight loss without adversely increasing blood pressure.

Company History

Our predecessor company was founded in November 2008 by former biopharmaceutical executives who have successfully developed, commercialized and in-licensed innovative pharmaceutical products and it commenced active operations in 2010. We subsequently expanded our senior management team to further broaden our team's experience in developing, registering and commercializing new drugs, and appointed our scientific advisory board, or SAB, members who 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 undisclosed public healthcare investment funds.

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;
- Advance setmelanotide for PWS and POMC deficiency obesity as our first indications in upstream MC4 pathway deficiencies;

- Expand setmelanotide development to additional upstream MC4 pathway deficiencies, including POMC heterozygous deficiency obesity and LepR deficiency obesity;
- Leverage the broad experience of our team in clinical and commercial drug development, and product acquisitions; and
- Commercialize setmelanotide for rare disease indications in core strategic markets.

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 13 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 September 30, 2015, we had an accumulated deficit of $44.5 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 our product candidate. We depend almost entirely on the success of setmelanotide, which is still in Phase 2 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.
- Our product candidate 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 our product candidate and 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 product candidate may be impaired.
- Our management could be distracted from their responsibilities to us as a result of the consulting services they provide to the Relamorelin Company, which may present conflicts, or the appearance of conflicts, with us.
- Since we have not operated as an independent company in the past, we may incur unforeseen expenses associated with doing so.

Corporate Restructuring and Other Information

We are a Delaware corporation organized in February 2013 under the name Rhythm Metabolic, Inc. Prior to our organization and the Corporate Restructuring 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 restructuring, which we refer to as the Corporate Restructuring, 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 Restructuring, 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 Restructuring 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 Restructuring 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 Restructuring, after which all clinical trials have been conducted by us.

In August 2015, we effected a 93,500-for-1 forward stock split of our then-outstanding common stock. Also in August 2015 and December 2015, we sold 25,000,000 shares and 15,000,000 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. Prior to consummation of this offering, the LLC entity will distribute its shares of our common stock to its members, which shares we anticipate will be exchanged by some of its members for newly-authorized shares of our series A-1 and series A-2 junior preferred stock,

convertible into our common stock on a one-to-one basis upon the closing of this offering. We refer to this distribution and exchange as the Distribution.

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 855 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 $1.0 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 manufacturing and development of setmelanotide through completion of our Phase 3 registration studies for the treatment of PWS; • approximately $ million for the manufacturing and development of setmelanotide through completion of our Phase 3 registration studies for the treatment of POMC deficiency obesity; and • the remainder for working capital purposes and other general corporate purposes.
Risk factors	See "Risk Factors" beginning on page 12 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 November 30, 2015 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 Distribution and the conversion of all of our outstanding preferred stock into 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;

- shares of common stock reserved for future issuance under our 2016 employee stock purchase plan; and
- shares of common stock issuable upon the exercise of stock options outstanding as of under our amended and restated 2015 equity incentive plan at a weighted average exercise price of $.

SUMMARY FINANCIAL DATA

The following summary financial data for the years ended December 31, 2013 and 2014 are derived from our audited financial statements included elsewhere in this prospectus. The summary financial data as of September 30, 2015 and for the nine months ended September 30, 2014 and 2015 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 nine-month period ended September 30, 2015 are not necessarily indicative of the results that may be expected for the fiscal year ending December 31, 2015 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 Restructuring."

Our historical results are not necessarily indicative of our future results, and our operating results for the nine-month period ended September 30, 2015 are not necessarily indicative of the results that may be expected for the fiscal year ending December 31, 2015 or any other interim periods or any future year or period.

	Year Ended December 31, 2013	Year Ended December 31, 2014	Nine Months Ended September 30,	
			2014	2015
			(unaudited)	
	(in thousands, except per share data)			
Statement of Operations and Comprehensive Loss Data:				
Operating Expenses:				
Research and development	$ 10,498	$ 5,280	$ 4,661	$ 3,530
General and administrative	1,701	1,213	1,070	1,400
Total operating expenses	12,199	6,493	5,731	4,930
Loss from operations	12,199	6,493	5,731	4,930
Net loss and comprehensive loss	$ (12,199)	$ (6,493)	$ (5,731)	$ (4,930)
Net loss attributable to common stockholders	$ (12,199)	$ (6,493)	$ (5,731)	$ (5,248)
Net loss attributable to common stockholders per common share, basic and diluted[(1)]	$ (0.13)	$ (0.07)	$ (0.06)	$ (0.06)
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[(1)]		$ (0.07)		$ (0.05)
Pro forma weighted average common shares outstanding, basic and diluted[(1)]		93,500,000		98,830,882

	As of September 30, 2015		
	Actual	Pro Forma(2)	Pro Forma As Adjusted(3)
	(unaudited in thousands)		
Balance Sheet Data:			
Cash and cash equivalents	$ 23,906		
Working capital	22,037		
Total assets	24,690		
Convertible preferred stock	24,476		
Accumulated deficit	(44,528)		
Total stockholders' equity (deficit)	$ (2,206)		

(1) See Notes 2 and 6 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 shares of series A-1 junior preferred stock and shares of series A-2 junior preferred stock in connection with the Distribution, the issuance of additional shares of series A preferred stock in December 2015 and the conversion of all of our outstanding preferred stock into 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 RESTRUCTURING

We are a Delaware corporation organized in February 2013 under the name Rhythm Metabolic, Inc. Prior to our organization and the Corporate Restructuring 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 restructuring, which we refer to as the Corporate Restructuring, 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 Restructuring, 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 Restructuring 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 Restructuring 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 Restructuring, 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., 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 August 2015, we effected a 93,500-for-1 forward stock split of our then-outstanding common stock. Also in August 2015 and December 2015, we sold 25,000,000 shares and 15,000,000 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. Prior to consummation of this offering, the LLC entity will distribute its shares of our common stock to its members, which shares we anticipate will be exchanged by some of its members for newly-authorized shares of our series A-1 and series A-2 junior preferred stock, convertible into our common stock on a one-to-one basis upon the closing of this offering. We refer to this distribution and exchange as the Distribution.

We have 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 provides us certain employee and consultant services. We have no employees, rather services are provided to us by the employees of the Relamorelin Company pursuant to this agreement. We share certain costs with the Relamorelin Company, including finance, accounting, research and development and operations. Following the Distribution and prior to consummation of this offering, these employees will become our employees and will enter into employment agreements with us and will continue to provide services to the Relamorelin Company in a consulting capacity. Following consummation of this offering, we may continue to share some services with the Relamorelin Company, as may be deemed appropriate by our management.

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 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.

We are a development stage 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 Restructuring. 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 research and development activities for our product candidate, setmelanotide. We have never generated any revenue from product sales. We have not obtained any regulatory approvals for our product candidate.

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 2 clinical development. 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 $12.2 million for the year ended December 31, 2013, and $6.5 million for the year ended December 31, 2014. As of September 30, 2015, we had an accumulated deficit of $44.5 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 our product candidate, 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 our product candidate;
- commercialize setmelanotide, if approved, by building a 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 a collaboration or partnership agreement, 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 our product candidate 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 require 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.

As of September 30, 2015, our cash and cash equivalents were approximately $23.9 million. We have received capital contributions from the Predecessor Company, the Relamorelin Company and the LLC entity from time to time as needed. In August 2015 and December 2015, we raised aggregate gross proceeds of $25.0 million and $15.0 million, respectively, through our issuance of series A preferred stock. 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 through at least the end of 2018. 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, our product candidate. 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 our product candidate. 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, and 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 our product candidate 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 our product candidate 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 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.

We have historically operated as a wholly-owned subsidiary of the LLC entity. The Relamorelin Company has assisted us by providing certain corporate functions pursuant to the Payroll Services Agreement. Following consummation of this offering, we may continue to share some services with the Relamorelin Company, as may be deemed appropriate by our management. See "Corporate Restructuring."

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 will incur for similar services in the future as an independent company; and

- our historical financial information does not reflect changes that we expect to incur in the future 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 indicated 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 Our Product Candidate

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 has only been studied for durations less than the expected duration of our pivotal Phase 3 clinical trials, and consequently there may be safety or efficacy issues in longer trials. It is possible that the effects seen in shorter term clinical trials will not be replicated at later time points or in larger clinical trials. For our POMC deficiency obesity studies, the number of patients studied is small, adding additional uncertainty. In addition, not all of our trials demonstrated statistically significant weight loss. There may be additional reasons why our early clinical trials are not predictive of later clinical trials including the limited patient populations of our target indications. Where such a small number of patients are available to study, even a single serious adverse event or poor efficacy outcome could have disappropriate effects in the viability of our program. We may also need to develop a genetic diagnostic test to help identify patients with genetic deficiencies affecting the MC4 pathway, a process that can be lengthy and cause additional delays in completing our clinical trials and present obstacles to obtaining approval. The FDA may require approval or clearance of a genetic diagnostic test, or the availability of a laboratory developed test, at the same time that the FDA approves the therapeutic product. Should the FDA determine in our case that a genetic diagnostic test for diagnosing patients for our therapies is needed, we may face significant delays or obstacles in obtaining approval of a new drug application, or NDA, for our product candidate.

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 or 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. If we fail to produce positive results in our planned Phase 3 clinical trials of setmelanotide, the development timeline and regulatory approval and commercialization prospects for our product candidate, 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 with any of these conditions is smaller than we estimate or if any approval that we obtain is based on a narrower definition of these patient populations, our revenue and ability to achieve profitability may be materially adversely affected.

Due to the rarity of some of our target indications, with the exception of the PWS Association patient registry, 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:

- *Prader Willi Syndrome.* The prevalence rates for PWS reported by published epidemiological studies in the United States and Europe vary, with estimates ranging from one in 8,000 to one in 52,000. We believe that there is an addressable population of approximately 8,000 patients in the United States, based on these epidemiological studies and supported by the number of patients that are currently registered with the PWS Association.

- *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 disorder is approximately 100 to 500 patients worldwide, 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 discussion 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 Heterozygous Deficiency Obesity and LepR Deficiency Obesity.* Our addressable patient population estimate for POMC heterozygous deficiency obesity is approximately 4,000 patients in the United States, and for LepR deficiency obesity is approximately 500 to 2,000 patients in the United States. These estimates are based on:

  - epidemiology studies on POMC heterozygous deficiency and LepR 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;

  - United States Census Bureau figures for adults and children, and Centers for Disease Control and Prevention, or CDC, prevalence numbers for severe adult obese patients (BMI>40 kg/m^2) and for severe early onset obese children (99^{th} percentile at ages 2 to 17 years old);

  - with wider availability of genetic testing expected for POMC heterozygous deficiency and LepR 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) the estimated prevalence from epidemiology studies of approximately 2% for POMC heterozygous and 1% for LepR deficiency, (y) 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 and (z) our estimated diagnosis rate of up to 40%.

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. 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.

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 commenced Phase 2 clinical trials for setmelanotide in 2015, which are ongoing, and we plan to commence additional Phase 2 clinical trials in 2016. We hope to initiate our first Phase 3 clinical trial in 2017. Successful initiation and completion of such clinical trials is a prerequisite to submitting an NDA to the FDA 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:

- the FDA may deny permission to proceed with our planned Phase 2 or 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 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;
- inadequate quantity or quality of our product candidate 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 validating the Patient Reported Outcome, or PRO, or the Observer Reported Outcome, or ORO, questionnaire for measuring subjective symptoms, which are likely to be a key endpoint in clinical trials;
- delays in validating any measures of hunger and related endpoints that may be utilized in a clinical trial, including delays caused by the need to translate the PRO and ORO or other measures of hunger into languages other than English;

- delays in validating and, if necessary, obtaining approval for any needed genetic diagnostic tests, for example, to identify patients with MC4 pathway deficiencies;
- delays in identifying and recruiting patients with any of the genetic causes of obesity in indications that we are targeting;
- the FDA or other regulatory agencies may disagree with our clinical trial designs, which may cause delays in initiating our clinical trials, or may disagree with our interpretation of data from clinical trials or change the requirements for approval even after it has reviewed and commented on the design for our clinical 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 due to the fact that we have not yet had discussions with the FDA regarding clinical trials for LepR 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 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, the IRBs at the sites where the IRBs 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 regulatory 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 regulatory 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 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.

Changes in regulatory requirements, FDA guidance or unanticipated events during our clinical trials may force us to amend clinical trial protocols or the FDA 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 we believe these will not be required for rare genetic populations of obesity, any of these activities could result in additional clinical requirements for setmelanotide, increase our costs or delay approval of setmelanotide.

Amendments to our clinical trial protocols would require resubmission to the FDA and IRBs 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, prior to commencing a Phase 3 clinical trial for setmelanotide, we plan to validate and seek FDA concurrence with, or at least substantial input on, the Patient-Reported Outcome, or PRO, and Observer-Reported Outcome, or ORO, questionnaires for measuring subjective endpoints aimed at measuring 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, we plan to measure setmelanotide's ability to mitigate 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 setmelanotide's effect 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-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 regulatory authorities, may not consider the endpoints to provide evidence of clinically meaningful results or that results may be difficult for the FDA to interpret. If we experience delays in validation or do not receive agreement with our proposed PRO and ORO questionnaires based on the conceptual framework, content validity, reliability, other measures of validity, and ability to detect changes, we may not be able to proceed with Phase 3 clinical trials, and ultimately may not be able to obtain approval to market any of our products.

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.

Our target patient populations are small. We may not be able to initiate or continue clinical trials for setmelanotide or other product candidates that we may in the future develop if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA or similar regulatory authorities outside the United States. The pediatric population is an important patient

population for our product candidate and it may be even more challenging to commence studies in this population, and to locate and enroll pediatric patients. In addition, some of our competitors have ongoing clinical trials for product candidates that treat the same indications as setmelanotide, and patients who would otherwise be eligible for our clinical trials may instead enroll in clinical trials of our competitors' product candidates.

Patient enrollment is 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 our product candidate, which would cause the value of our company to decline and limit our ability to obtain additional financing.

Our product candidate 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 our product candidate 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 regulatory authorities.

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 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. 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, or SAE, 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 subcutaneous, or SC, injection, although there was no evidence of any serious respiratory or cardiac cause on careful examination. In addition, our interpretation of the safety data from our clinical trials is contingent upon the review and ultimate approval of the FDA or other regulatory authorities. The FDA or other regulatory authorities may not agree with our methods of analysis or our interpretation of the results. The long term effects of setmelanotide have not been tested in our clinical trials.

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 regulatory authorities may require the addition of a Risk Evaluation and Mitigation Strategy, or REMS, 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 our product candidate and could substantially increase the costs of commercializing our product candidate and significantly impact our ability to successfully commercialize our product candidate and generate revenues.

Although we have been granted orphan drug designation for setmelanotide in treating PWS, we may be unable to obtain orphan drug designation for other uses or to obtain exclusivity in any use. If our competitors are able to obtain orphan drug exclusivity for products that constitute the same drug and treat the same indications as our product candidate, we may not be able to have competing products approved by the applicable regulatory authority for a significant period of time.

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. If another sponsor receives such approval before we do (even where we have orphan drug designation for that use), we will be precluded from receiving marketing approval for our product for that use for the exclusivity period of seven years. 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. 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.

Although we have been granted orphan drug designation for setmelanotide in treating PWS, if we request orphan drug designation for setmelanotide for other uses, there can be no assurances 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 product does not guarantee that the FDA will accelerate regulatory review of, or ultimately approve, that product candidate, nor does it limit the ability of the FDA to grant orphan drug designation to product candidates of other companies that treat the same indications as setmelanotide prior to our product receiving exclusive marketing approval.

Even if we obtain orphan drug exclusivity for setmelanotide, that exclusivity may not effectively protect our product candidate 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.

We may be unable to obtain breakthrough therapy designation. Even if we do obtain such designation, 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 our product candidate 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." A 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 a 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 a breakthrough therapy is within the discretion of the FDA. Accordingly, even if we believe setmelanotide meets the criteria for designation as a breakthrough therapy, the FDA may disagree. In any event, the receipt of a 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 our product candidate for methods of delivery that would be acceptable to the FDA 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 may be necessary in order to translate the current formulations of setmelanotide into forms that will be acceptable to the FDA and/or to patients. While we plan to develop new and useful formulations of setmelanotide, we cannot estimate the probability of success, nor the resources and time needed to succeed. If we are unable 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 genetic deficiencies requires the identification of patients with unique genetic subtypes (for example, POMC genetic deficiency). This may require the development of genetic diagnostic tests that require substantial financial resources and regulatory approval. This testing may be a barrier to approval or to patients using our products and may raise ethical, legal and social issues related to the use of genetic information.

We intend to focus our development of setmelanotide as a treatment for obesity caused by certain genetic deficiencies affecting the MC4 pathway. For some genetic deficiencies affecting this pathway, for example PWS, no specific genetic diagnostic testing is expected to be required prior to initiation of therapy with setmelanotide. For other MC4 pathway deficiencies, this approach requires genetic diagnostic testing, identification, and recruitment of patients, which may require substantial financial resources as well as regulatory approvals for these genetic diagnostic tests. The development of these tests to accompany a clinical program can be difficult, and may delay our current timelines, or even prevent approval altogether. In addition, our estimates of the prevalence and incidence of these genetic deficiencies are based primarily on rates reported in scientific publications, and it is uncertain if these rates will be confirmed as subjects are screened for clinical trials. If these rates are lower than reported, recruitment and screening would be more costly and require additional time.

In order to assist in identifying this subset of patients, a genetic diagnostic test, which is a test or measurement that evaluates the presence of genetic variants in a patient, could be used. We anticipate that the development of a genetic diagnostic test concurrently with our product candidate will help us more accurately identify the patients who belong to the target subset. Use of a genetic diagnostic test in this way during clinical trials will result in product labeling, if the product candidate is approved, that limits use to only those patients who express the genetic variants identified by the genetic diagnostic test. We may need to rely on third-party collaborators to successfully develop and commercialize a genetic diagnostic test. If approved, this test may be subject to reimbursement limitations that could limit access to treatment. Finally, patients may have concerns about the collection and use of their genetic information which may limit adoption of testing.

We may be subject to regulation by the FDA, the Centers for Medicare and Medicaid Services, or CMS, and comparable foreign regulatory authorities, regarding the use of genetic diagnostic tests to identify patients with unique genetic subtypes, such as POMC genetic deficiency, who will be responsive to our products. We believe that if such tests are necessary, existing and available genetic diagnostic tests developed and administered by laboratories certified under the Clinical Laboratory Improvement Amendments, or CLIA, are sufficient to select appropriate patients and will be permitted by the FDA. Such tests are known as laboratory developed tests, or LDTs. For future product candidates, however, it could be necessary to develop *in vitro* diagnostic devices, which the FDA refers to as *in vitro* companion diagnostic devices, that provide information that is essential for the safe and effective use of the corresponding therapeutic product, and that require FDA clearance or approval. We may be dependent on the sustained cooperation and effort of any third-party collaborators with whom we may partner in the future to develop LDTs or even *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 such tests, if necessary, could delay or prevent approval of our product candidate.

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.

Risks Related to the Commercialization of Our Product Candidate

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 elsewhere. 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 European countries, 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.

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 any other

regulatory body, 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 product candidate 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 applicable regulatory authorities, 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. With the exception of PWS, which is more routinely identified, genetic diagnostic screening for deficiencies affecting the MC4 pathway is not routine. There is currently no readily available and approved genetic diagnostic test, nor are there guidelines to support genetic diagnostic screening. In addition, third-party payors may not reimburse patients for genetic diagnostic screening for deficiencies affecting the MC4 pathway. Broad acceptance of setmelanotide depends in part on the ability to identify and diagnose patients with these genetic defects, which may prove challenging. 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:

- setmelanotide's ability to treat obesity caused by certain genetic deficiencies affecting the MC4 pathway and, if required by any applicable regulatory 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;
- 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 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 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.

There are no currently approved pharmacological treatments for regulating hunger and hyperphagia-related behaviors of patients with PWS, POMC deficiency obesity, POMC heterozygous deficiency obesity or LepR deficiency obesity. Bariatric surgery is contraindicated in patients with PWS, and the severe obesity and hyperphagia associated with these other genetic disorders of obesity are also considered to be risk factors for bariatric surgery. We are aware that Zafgen, Inc. is conducting a clinical trial in PWS with belorinab, a MetAP2 inhibitor thought to affect the metabolism of fat. We are also aware of a clinical trial that was recently completed by Ferring Pharmaceuticals, Inc. to evaluate the use of carbetocin, an analogue of a brain peptide hormone oxytocin hypothesized to increase trust, reduce anxiety and improve behavior in patients with PWS. We also are aware of a clinical trial being conducted by Essentialis, Inc. to evaluate the safety and tolerability of controlled-release diazoxide in patients with PWS and to explore the

effects of diazoxide on hyperphagia-related behaviors and energy expenditure. In addition, in August 2015, Novo Nordisk announced it will initiate a Phase 3 clinical trial of Saxenda (liraglutide injection) for weight management in pediatric PWS patients. Also, Alize Pharma recently started a Phase 2 clinical trial in PWS of AZP-531, its unacylated ghrelin analog.

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.

The LLC entity maintains product liability insurance coverage for our clinical trials with a $10.0 million annual aggregate coverage limit. We intend to obtain similar product liability insurance coverage as an independent company. 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 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 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 Member States of the European Economic Area and comparable foreign regulatory authorities 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 comparable foreign regulatory authorities 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 comparable foreign regulatory agencies pursuant to inspections that would be conducted after we submit our NDAs or relevant foreign regulatory submission to the applicable regulatory agency. 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.

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 Peptisyntha SA, or Peptisyntha, under which Peptisyntha will provide certain process development and manufacturing services in connection with the manufacture of setmelanotide. Under our 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. We may need to engage additional third-party suppliers to manufacture our clinical drug supplies. 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 control the manufacturing process of, and are completely dependent on, our CMOs to comply with cGMPs for manufacture of both API and finished drug product. If our CMOs cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or applicable foreign regulatory agencies, they will not be able maintain a satisfactory manufacturing history. In addition, although we have no direct control over our CMOs' ability to maintain adequate quality control, quality assurance and qualified personnel, we are ultimately responsible for ensuring that our drug substances and finished product are manufactured in accordance with cGMPs. 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 an applicable foreign regulatory agency does not approve these facilities for the manufacture of our product candidate 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 applicable foreign regulatory agencies. We will need to submit information to the FDA and other regulatory authorities 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.

Any disputes that arise between us and the LLC entity, the Relamorelin Company and/or the Predecessor Company with respect to our past and ongoing relationships could harm our business operations.

Disputes may arise among the LLC entity, the Relamorelin Company and/or the Predecessor Company and us in a number of areas relating to our past and ongoing relationships, including:

- intellectual property, technology and business matters, including failure to make required technology transfers;
- labor, tax, employee benefit, indemnification and other matters arising from our separation from the LLC entity, the Relamorelin Company or the Predecessor Company;
- employee retention and recruiting;
- business combinations involving us;
- the nature, quality and pricing of transitional services the LLC entity, the Relamorelin Company or the Predecessor Company has agreed to provide us; and
- business opportunities that may be attractive to the LLC entity or the Relamorelin Company and us.

We may not be able to resolve any potential conflicts, and even if we do, the resolution may be less favorable than if we were dealing with an unaffiliated party.

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 or conflict 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 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 early 2013 from a third party bringing to our attention several patents and patent applications, both U.S. and non-U.S. 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 our setmelanotide product candidate.

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 our product candidate 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 2014 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 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.

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 almost entirely on the success of setmelanotide, which is still in Phase 2 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.

We currently have only one product candidate, setmelanotide, in clinical development, and our business depends almost 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 2 clinical development as a treatment for genetic deficiencies affecting the MC4 pathway, 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. Of the large number of drugs in development in the United States, only a small percentage will successfully complete the FDA regulatory approval process and will be commercialized. In addition, we have not discussed all of our proposed development programs with the FDA. 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 countries until we receive the requisite approval from such countries. MC4 has two Phase 2 clinical trials underway for the treatment of PWS and POMC deficiency

obesity. We will endeavor to work with the FDA to confirm that the FDA believes that one Phase 2 clinical trial is sufficient for these indications, but the FDA may require us to conduct additional Phase 2 clinical trials. The FDA or other regulatory authorities will also require that we conduct additional pivotal trials, and it is unclear if one or more Phase 3 trials will be required for approval in each indication, the need and length of placebo-controlled data in pivotal trials and the number of patients required for approval. We expect to seek an indication for obesity caused by genetic deficiencies affecting the MC4 pathway. If setmelanotide produces significant treatment effects in these patients, coupled with an acceptable safety profile, our overall clinical program may be less time consuming and require fewer patients than might a program for a broader obesity indication. In addition, the FDA has advised us that such a program would require development of a systematic and clearly defined approach to classifying patients' various mutations and selecting patients with mutations of clinical relevance.

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, if any, such that, if the clinical trials are successful, we can file an NDA in the United States by 2019. We have not finalized the design, timing and size of our Phase 3 trials with the FDA and therefore cannot assure you that they will start on time. In addition, obtaining approval of an NDA is a complex, lengthy, expensive and uncertain process, and the FDA may delay, limit or deny approval of setmelanotide for many reasons, including, among others:

- the FDA may disagree with our clinical trial design and 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 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 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 may disagree with the number, design, size, conduct or implementation of our clinical trials;
- the FDA may require that we conduct additional clinical trials or pre-clinical studies;
- the FDA 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 may find the data from preclinical studies and clinical trials insufficient to demonstrate that setmelanotide's clinical and other benefits outweigh its safety risks;
- the FDA may disagree with our interpretation of data from our preclinical studies and clinical trials;
- the FDA may not approve the formulation, labeling or specifications of setmelanotide;
- the FDA may not accept data generated at our clinical trial sites;
- if and when our NDA is submitted and reviewed by an advisory committee, the FDA 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 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;

- the FDA or the applicable 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 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 this product candidate, 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 approvals 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 regulatory authorities outside the United States on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the United States does not ensure approval by regulatory 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.

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 FDA requirements governing labeling, packaging, storage and promotion, and recordkeeping and submission of safety and other post-market information. The FDA has 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. 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 regulatory 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.

We are subject to healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, 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 future arrangements with third-party payors will expose us to broadly applicable fraud and abuse 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. Restrictions under applicable U.S. federal and state healthcare laws and regulations include the following:

- The federal healthcare anti-kickback statute prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made under federal healthcare programs such as Medicare and Medicaid.
- The federal False Claims Act imposes criminal and civil penalties, including those from civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease, or conceal an obligation to pay money to the federal government.
- The federal Health Insurance Portability and Accountability Act of 1996, as amended by the Health Information Technology for Economic and Clinical Health Act, imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program and also imposes obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information.

- The federal false statements statute prohibits knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services.

- The federal transparency requirements, sometimes referred to as the "Sunshine Act," under the Patient Protection and Affordable Care Act, require manufacturers of drugs, devices, biologics and medical supplies to report to the Department of Health and Human Services information related to physician payments and other transfers of value and physician ownership and investment interests.

- Analogous state laws and regulations, such as state anti-kickback and false claims laws and transparency laws, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers, and some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring drug manufacturers to report information related to payments to physicians and other healthcare providers or marketing expenditures and drug pricing.

Ensuring that our future business arrangements with third parties comply with applicable healthcare laws and regulations could be costly. 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 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, any of which could substantially disrupt our operations. If any of the physicians or other providers or entities with whom we expect to do business is found not to be in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

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, along with the manufacturing processes, post-approval clinical data, labeling, advertising and promotional activities for setmelanotide, we will be subject to continual requirements of and review by the FDA and other regulatory authorities. These requirements include, but are not limited to, 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, 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 regulatory agencies 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. 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.

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 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 our product candidate 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.

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, Bart Henderson, our President, Lex H.T. Van der Ploeg, Ph.D., our Chief Scientific Officer, and Fred T. Fiedorek, M.D., our Chief Medical Officer. We will enter into new letter agreements with Dr. Gottesdiener, Mr. Henderson, Dr. Van der Ploeg and Dr. Fiedorek but they may terminate their 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-man 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.

Four full-time employees and one part-time employee provide services to us, and in connection with becoming a public company, we expect to increase our number of employees and the scope of our operations. 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 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.

Following consummation of this offering, our executive officers will continue to be officers of the Relamorelin Company and the LLC entity and intend to provide consulting services to the Relamorelin Company, which may distract them from their focus on us.

Prior to consummation of this offering, Keith M. Gottesdiener, M.D., Bart Henderson, Lex H.T. Van der Ploeg, Ph.D. and Fred Fiedorek, M.D. will enter into employment letters with us and become our employees but will continue to provide services to the Relamorelin Company in a consulting capacity. Drs. Gottesdiener, Van der Ploeg and Fiedorek and Mr. Henderson will remain officers of the Relamorelin Company and the LLC entity but will not be contractually obligated to spend a specified number of hours per week providing consulting services to the Relamorelin Company, but their employment letters with us will permit them to render consulting services to the Relamorelin Company, provided that such consulting services do not prevent them from carrying out their duties and responsibilities to us. As a result, they may have responsibilities and time commitments that may distract them from their responsibilities to us, or may be faced with decisions that could have different implications for the two companies, such as the allocation of time and resources to each of us.

The direct or indirect ownership by our executive officers and certain of our directors of equity interests in the Relamorelin Company and the LLC entity, as well as the continued roles of certain of our directors with the Relamorelin Company and the LLC entity, may create, or may create the appearance of, conflicts of interest.

Because of their current or former positions with the Relamorelin Company and the LLC entity, all of our executive officers directly or indirectly own equity in the Relamorelin Company and the LLC entity. In addition, Todd Foley, Ed Mathers and Neil Exter, who are members of our board of directors, may, directly or indirectly, have equity interests in the Relamoralin Company and the LLC entity. Direct or indirect ownership by our executive officers and these directors of equity interests in the Relamorelin Company and the LLC entity creates, or may create the appearance of, conflicts of interest when these officers or directors are faced with decisions that could have different implications for the Relamorelin Company or the LLC entity than for us.

In addition, certain of our directors and officers are serving on the board of directors and/or as officers of the Relamorelin Company and the LLC entity. We expect that following the consummation of this offering these directors and officers will remain in their roles as directors and/or officers at these companies. Their continued service at these companies creates, or may create the appearance of, conflicts of interest when they are faced with decisions that could have different implications for the Relamorelin Company or the LLC entity than for us.

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 our 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 undisclosed healthcare investment funds, investments 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 our product candidate 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 through the completion of Phase 3 registration studies for setmelanotide for PWS and POMC deficiency 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, 2014, we had approximately $20.0 million of unused federal and state carryforwards of NOLs and approximately $0.9 million of unused federal and state carryforwards of tax credits.

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 $1.0 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 September 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, as described in the subsequent risk factor, is both costly and challenging.

If we are unable to implement and maintain effective internal controls over financial reporting in the future, we may fail to prevent or detect material misstatements in our financial statements, which may cause investors to lose confidence in the accuracy and completeness of our financial reports and the market price of our common stock may decline.

As a public company, we will be required to maintain internal controls over financial reporting and to report any material weaknesses in such internal controls. In addition, beginning with our 2016 annual report on Form 10-K to be filed in 2017, we will be required to file a report by management on the effectiveness of our internal controls over financial reporting pursuant to Section 404 of the Sarbanes-Oxley Act. This assessment will need to include disclosure of any material weaknesses identified by our management in our internal controls over financial reporting. A material weakness is a deficiency, or combination of deficiencies, in internal controls over financial reporting that results in more than a reasonable possibility that a material misstatement of annual or interim financial statements will not be prevented or detected on a timely basis. We are in the process of designing, implementing, and testing the internal controls over financial reporting required to comply with this obligation, which is a time-consuming, costly and complicated process.

During the preparation of the financial statements for the nine months ended September 30, 2015 and 2014, we identified a $630,000 overstatement of our research and development expense previously reported for the six months ended June 30, 2014. The correction of this error decreased net loss and research and development expense by $630,000 for the six months ended June 30, 2014 and decreased basic and diluted net loss per common share by $0.01 per share for the same period. The error had no impact on our financial statements for the year ended December 31, 2014. This error was caused by a material weakness in our internal controls over financial reporting consisting of a lack of an effective control in place to properly reconcile accrued expenses and other liabilities to our underlying accounting records.

We have implemented, and are continuing to implement, measures designed to improve internal controls over financial reporting to remediate the control deficiency that led to this material weakness by, among other things, hiring qualified financial consultants with appropriate expertise to perform specific functions, and designing and implementing improved processes and internal controls, including an increased focus on performing effective account reconciliation reviews.

If we are unsuccessful in our efforts to remediate any material weakness in our internal controls over financial reporting, if we identify any additional material weaknesses in our internal controls over financial reporting or if we are unable to comply with the requirements of Section 404 in a timely manner, we will be unable to assert that our internal controls over financial reporting are effective, investors may lose confidence in the accuracy and completeness of our financial reports, the market price of our common stock could be negatively affected and we could be subject to sanctions or investigations by the SEC or other regulatory authorities, which would require additional financial and management resources.

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 our product candidate, if approved;
- the number of people in our target patient population;
- our plans to research, develop and commercialize our product candidate;
- 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 our product candidate;
- 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 our product candidate, and our ability to serve those markets;
- our expectations for the pricing of setmelanotide;
- the rate and degree of market acceptance of our product candidate, as well as the reimbursement coverage for our product candidate;
- regulatory developments in the United States and foreign countries;
- 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 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 some of our target indications, with the exception of the PWS Association patient registry, 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:

- *Prader Willi Syndrome*. The prevalence rates for PWS reported by published epidemiological studies in the United States and Europe vary, with estimates ranging from one in 8,000 to one in 52,000. We believe that there is an addressable population of approximately 8,000 patients in the United States, based on these epidemiological studies and supported by the number of patients that are currently registered with the PWS Association.

- *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 disorder is approximately 100 to 500 patients worldwide, 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 discussion 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 Heterozygous Deficiency Obesity and LepR Deficiency Obesity.* Our addressable patient population estimate for POMC heterozygous deficiency obesity is approximately 4,000 patients in the United States, and for LepR deficiency obesity is approximately 500 to 2,000 patients in the United States. These estimates are based on:

  - epidemiology studies on POMC heterozygous deficiency and LepR 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;

  - United States Census Bureau figures for adults and children, and Centers for Disease Control and Prevention, or CDC, prevalence numbers for severe adult obese patients (BMI>40 kg/m^2) and for severe early onset obese children (99^{th} percentile at ages 2 to 17 years old);

  - with wider availability of genetic testing expected for POMC heterozygous deficiency and LepR 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) the estimated prevalence from epidemiology studies of approximately 2% for POMC heterozygous and 1% for LepR deficiency, (y) 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 and (z) our estimated diagnosis rate of up to 40%.

See "Risk Factors—*Risks Related to the Development of Our Product Candidate—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 with any of these conditions is smaller than we estimate or if any approval that we obtain is based on a narrower definition of these patient populations, 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 September 30, 2015, we had cash and cash equivalents of approximately $23.9 million. In the past, we have received capital contributions from the Predecessor Company, the Relamorelin Company and the LLC entity from time to time as needed. In addition, we raised aggregate gross proceeds of $40.0 million in August 2015 and December 2015 from the sale of our series A preferred stock. We intend to use the net proceeds from this offering, together with our existing cash resources, as follows:

- approximately $ million to fund the manufacturing and development of setmelanotide through completion of our Phase 3 registration studies for the treatment of Prader Willi Syndrome;
- approximately $ million for the manufacturing and development of setmelanotide through completion of our Phase 3 registration studies for the treatment of POMC deficiency 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 13, 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.

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 capitalization as of September 30, 2015, as follows:

- on an actual basis;
- on a pro forma basis after giving effect to the issuance of additional shares of series A preferred stock in December 2015, the issuance of shares of series A-1 junior preferred stock and shares of series A-2 junior preferred stock in connection with the Distribution and the conversion of all outstanding shares of our preferred stock into shares of common stock upon the closing of this offering;
- 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 September 30, 2015		
	Actual	Pro Forma (unaudited)	Pro Forma As Adjusted
	(in thousands)		
Cash and cash equivalents	$ 23,906	$	$
Convertible preferred stock:			
Series A preferred stock; 40,000,000 shares authorized; 25,000,000 shares issued and outstanding actual; no shares issued and outstanding pro forma and pro forma as adjusted	24,476		
Stockholders' equity (deficit):			
Common stock, $0.001 par value; 150,000,000 shares authorized, 93,500,000 shares issued and outstanding actual; shares issued and outstanding pro forma; and shares issued and outstanding pro forma as adjusted	93		
Additional paid-in capital	42,229		
Accumulated deficit	(44,528)		
Total stockholders' equity (deficit)	(2,206)		
Total capitalization	$ 22,270		

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 September 30, 2015 was approximately $22.3 million, or $0.24 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 September 30, 2015.

Our pro forma net tangible book value as of September 30, 2015 was approximately $ million, or $ 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) our sale of 15,000,000 shares of series A preferred stock in December 2015 for gross proceeds of $15.0 million, (2) the issuance of shares of series A-1 junior preferred stock and shares of series A-2 junior preferred stock in connection with the Distribution, and (3) the conversion of all outstanding shares of our preferred stock into 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 September 30, 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 September 30, 2015, after giving effect to the pro forma adjustments and the offering described above. Our pro forma as adjusted net tangible book value as of September 30, 2015 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 September 30, 2015	$	
Increase per share attributable to pro forma adjustments described above		
Pro forma net tangible book value per share at September 30, 2015		
Increase per share attributable to new investors		
Pro forma as adjusted net tangible book value per share at September 30, 2015 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 September 30, 2015, 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 and an aggregate of shares of our common stock will be reserved for issuance under our 2016 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, 2013 and 2014 and the balance sheet data as of December 31, 2013 and 2014 are derived from our audited financial statements appearing elsewhere in this prospectus. The selected statements of operations data for the nine months ended September 30, 2014 and 2015 and the balance sheet data as of September 30, 2015 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. 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 "Corporate Restructuring."

Our historical results are not necessarily indicative of our future results, and our operating results for the nine-month period ended September 30, 2015 are not necessarily indicative of the results that may be expected for the fiscal year ending December 31, 2015 or any other interim periods or any future year or period.

	Year Ended December 31, 2013	Year Ended December 31, 2014	Nine Months Ended September 30, 2014	Nine Months Ended September 30, 2015
			(unaudited)	
	(in thousands, except share and per share data)			
Statement of Operations and Comprehensive Loss Data:				
Operating Expenses:				
Research and development	$ 10,498	$ 5,280	$ 4,661	$ 3,530
General and administrative	1,701	1,213	1,070	1,400
Total operating expenses	12,199	6,493	5,731	4,930
Loss from operations	(12,199)	(6,493)	5,731	4,930
Net loss and comprehensive loss	$ (12,199)	$ (6,493)	$ (5,731)	$ (4,930)
Net loss attributable to common stockholders	$ (12,199)	$ (6,493)	$ (5,731)	$ (5,248)
Net loss attributable to common stockholders per common share, basic and diluted[(1)]	$ (0.13)	$ (0.07)	$ (0.06)	$ (0.06)
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[(1)]		$ (0.07)		$ (0.05)
Pro forma weighted average common shares outstanding, basic and diluted[(1)]		93,500,000		98,830,882

(1) Unaudited pro forma net loss per share attributable to common stockholders is computed using the weighted-average number of shares of common stock outstanding after giving effect to the conversion of all shares of preferred stock into shares of common stock as if such conversion had occurred at the beginning of the period presented, or the date of original issuance, if

later, and includes preferred stock dividends. Accordingly, the pro forma basic and diluted net loss per share attributable to common stockholders excludes the effects of the cumulative preferred stock dividends.

	December 31,		September 30,
	2013	2014	2015
			(unaudited)
Balance Sheet Data:			
Cash and cash equivalents	$ 241	$ 152	$ 23,906
Working capital (deficit)	(1,350)	(358)	22,037
Total assets	505	194	24,690
Convertible preferred stock	—	—	24,476
Accumulated deficit	(33,105)	(39,598)	(44,528)
Total stockholders' equity (deficit)	$ (1,350)	$ (358)	$ (2,206)

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 two of these deficiencies, PWS and POMC deficiency obesity, 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, and that peptide therapeutics are uniquely suited for activating this target. We have demonstrated initial proof of concept in our ongoing Phase 2 clinical trial in POMC deficiency obesity, a disorder of extreme and unrelenting appetite and obesity, in which setmelanotide dramatically reduced both weight and hunger. We are also conducting a Phase 2 clinical trial in PWS, and we expect to report results from these clinical trials in the first half of 2016. These clinical trials expand upon previous setmelanotide clinical trials which enrolled over 200 general obese patients and demonstrated significant weight loss with good tolerability.

We have leveraged skilled experts, consultants, 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. At present, all employees are contracted with the Relamorelin Company but resources are shared with us through the Payroll Services Agreement. 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 venture capital 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 our product candidates. See "Risk Factors—*Risks Related to Our Financial Position and Need for Capital*" beginning on page 13 for additional information.

As of September 30, 2015, we had an accumulated deficit of $44.5 million. Our net losses were $12.2 million and $6.5 million, for the year ended December 31, 2013 and the year ended December 31, 2014, respectively, and $5.7 million and $4.9 million, for the nine months ended September 30, 2014 and 2015, respectively. 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 September 30, 2015, our existing cash and cash equivalents were approximately $23.9 million. In December 2015 we raised an additional $15 million in an equity financing. We expect that the net proceeds of this offering will enable us to fund our operating expenses through at least the end of 2018.

Corporate Background and Distribution

We are a Delaware corporation organized in February 2013 under the name Rhythm Metabolic, Inc. Prior to our organization and the Corporate Restructuring, we were part of the Predecessor Company which commenced active operations in 2010. As a result of the Corporate Restructuring, we became a wholly-owned subsidiary of the LLC entity. In August 2015 and December 2015, we sold shares of our series A preferred stock to investors pursuant to an equity financing. The LLC entity remains our largest stockholder, holding shares of our common stock representing, as of November 30, 2015, an approximately % equity interest in us with the balance being held by our series A investors.

Prior to consummation of this offering, as a part of the Distribution, the LLC entity will distribute its shares of our common stock to its members, which shares we anticipate will be exchanged by some of its members for newly-authorized shares of our series A-1 and series A-2 junior preferred stock, convertible into our common stock on a one-to-one basis upon the closing of this offering.

Pursuant to the Payroll Services Agreement, the Relamorelin Company provides us certain employee and consultant services. We have no employees, rather services are provided to us by the employees of the Relamorelin Company pursuant to this agreement. We share certain costs with the Relamorelin Company, including finance, accounting, research and development and operations. Following the Distribution and prior to consummation of this offering, these employees will become our employees and will enter into employment agreements with us and continue to provide services to the Relamorelin Company in a consulting capacity. Following consummation of this offering, we may continue to share some services with the Relamorelin Company, as may be deemed appropriate by our management. See "Corporate Restructuring."

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 allocated to us under the Payroll Services Agreement, 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 direct and allocated expenses from the Relamorelin Company for 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 and capitalized. 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 programs for setmelanotide.

Research and Development Summary	Year Ended December 31,		Nine Months Ended September 30,	
	2013	2014	2014	2015
	(in thousands)			
Setmelanotide Program	$ 10,498	$ 5,280	$ 4,661	$ 3,530

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 product candidate 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, for personnel which have been allocated from the Relamorelin Company. Other significant costs include rent which has been allocated from the Relamorelin Company, legal fees relating to patent and corporate matters and fees for accounting and consulting services.

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.

We have leveraged skilled experts, consultants, CROs, and contractors to manage our clinical operations, under the leadership and direction of our management. As of September 30, 2015, five employees provided services to us pursuant to our Payroll Services Agreement, three of whom hold Ph.D. or M.D. degrees. Of these employees, three were engaged in development activities and two were engaged in support administration, including business development and finance. We will expand our infrastructure to manage our clinical, finance and commercial operations with additional full-time employees.

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

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 Restructuring. At that time, we also entered into the Payroll Services Agreement. All employees are contracted with the Relamorelin Company, but are shared with us. Prior to consummation of this offering, the employees will enter into new agreements with us. We share costs with the Relamorelin Company, including finance, accounting, research and development and operations. These shared costs have been 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.

Series A Investor Right/Obligation & Series A Investor Call Option

Pursuant to the 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 have the obligation, or the Series A Investor Right/Obligation, to purchase additional shares of series A preferred stock as part of a second tranche of financing based the achievement of a specific milestone set forth in the series A preferred stock purchase agreement, or the Second Tranche Milestone. Additionally, subject to the terms and conditions set forth in the series A stock purchase agreement, the series A investors have the option, or the Series A Investor Call Option, to purchase additional shares of series A preferred stock in the event that the Second Tranche Milestone is not achieved.

We classify our Series A Investor Right/Obligation and Series A Investor Call Option as liabilities on our balance sheets as they are free-standing financial instruments. The Series A Investor Right/Obligation and the Series A Investor Call Option were initially recorded at fair value upon the issuance of series A preferred stock in August 2015, and they are subsequently remeasured to fair value at each balance sheet date. Changes in fair value of the Series A Investor Right/Obligation and the Series A Investor Call Option are recognized as a component of other income (expense), net in the statement of operations and comprehensive loss. We will continue to adjust the liabilities for changes in fair value until the earlier of the exercise of the Series A Investor Right/Obligation and Series A Investor Call Option or their expiration. Upon the closing of an initial public offering with a minimum price per share and gross

proceeds of at least $1.00 and $50 million, respectively, the series A preferred stock will automatically convert into shares of common stock on a 1-for-1 basis. The shares of series A preferred stock will be converted into common stock, at par value, with the remainder recorded to additional paid-in capital.

We use the Black-Scholes option-pricing model, which incorporates assumptions and estimates, to value the Series A Investor Call Option and assess these assumptions and estimates on a quarterly basis as additional information impacting the assumptions is 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 Option, risk-free interest rate, expected dividend yield and expected volatility of the price of the underlying preferred stock. We determine the fair value per share of the underlying preferred stock by taking into consideration the most recent sale of our 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 estimate 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 Option. 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 Option. A dividend yield of zero is assumed.

We have determined the fair value of the 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 through a backsolve calculation which assumes a 70 percent probability of closing, a discount rate of 17.1% and a second tranche closing date of November 30, 2015. The discount rate is estimated using the capital asset pricing model.

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 Restructuring, 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 Restructuring.

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 September 30, 2015, 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, 2013 and 2014 and the nine months ended September 30, 2014 and 2015, we had no amounts accrued for interest and penalties related to uncertain tax positions.

As of December 31, 2014, we had NOL carryforwards to reduce federal and state incomes taxes of approximately $17.0 million and $3.0 million, respectively. If not utilized, these carryforwards begin to expire in 2033. At December 31, 2014, we also had available research and development tax credits for federal and state income tax purposes of approximately $0.6 million and $0.3 million, respectively. The federal and state credits begin to expire in 2033 and 2028, respectively.

Utilization of the NOL 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 NOLs 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 we adopted the 2015 equity incentive plan, which we expect to amend and restate prior to consummation of this offering. We have reserved 16,500,000 shares of common stock under the 2015 equity incentive plan. The first grants issued by us under the 2015 equity incentive plan were issued in the fourth quarter of 2015.

The stock compensation expense allocated to us from the LLC entity was $127,000 and $66,000 for the years ended December 31, 2013 and 2014, respectively, and $59,000 and $65,000 for the nine months ended September 30, 2014 and 2015, respectively.

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

	Year Ended December 31,		Nine Months Ended September 30,	
	2013	2014	2014	2015
	(in thousands)		(unaudited)	
Research and development	$ 37	$ 23	$ 21	$ 45
General and administrative	90	43	38	20
Total	$ 127	$ 66	$ 59	$ 65

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.

At September 30, 2015, the total LLC entity unrecognized compensation expense related to unvested restricted common unit awards, including estimated forfeitures, was $0.56 million, and we expect to recognize our portion over a weighted-average period of approximately 1.6 years.

Determination of the fair value of common units

The LLC entity operates as a private company with no active public market for its common units. Therefore, the LLC entity board of directors estimated the fair value of the LLC entity's common units at various dates, with input from management, considering the LLC entity's most recently available third-party valuations of common units and its assessment of additional objective and subjective factors that it believed were relevant and which may have changed from the date of the most recent valuation through the date of the applicable grant or award.

The LLC entity determined the estimated per share fair value of its 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, the LLC entity considered all objective and subjective factors that it believed to be relevant for each valuation conducted, including the LLC 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 the LLC entity's common and preferred units;
- the prices at which the LLC entity sold its preferred units to outside investors in arm's length transactions, and the rights, preferences and privileges of those preferred units relative to common units;
- The LLC entity's results of operations, financial position and the status of the LLC entity's research and preclinical development efforts;
- the material risks related to the LLC 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 the LLC entity;
- the likelihood of achieving a liquidity event for the holders of 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 the LLC entity's common units prepared in accordance with methodologies outlined in the Practice Aid.

Valuation methodologies

The LLC entity's valuations of common units 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 venture capital 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, the Company's 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 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, a common unit only has value if the funds available for distribution to 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 units, is used to determine the value of the equity and the corresponding value of the 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 the LLC 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 the LLC entity, three types of future-event scenarios were considered: an initial public offering, a sale and dissolution. The LLC 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, the LLC 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, the LLC 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 March 31, 2014

The LLC entity performed a contemporaneous valuation of its common units on March 31, 2014 to coincide with its preparation for a potential initial public offering. Pursuant to the American Institute of Certified Public Accountants Practice Aid, the PWERM is appropriate when the time to a liquidity event is short, making the range of possible future outcomes relatively easy to predict. Given the proximity to a potential initial public offering, the LLC entity chose to use the PWERM. The LLC entity considered three scenarios: an equity financing, a preferred equity financing followed by a favorable sale, and an unfavorable sale with no preferred equity financing.

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

The LLC entity performed a 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 the equity of the Company 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 Series A Investor Right/Obligation and 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 Series A Investor Right/Obligation and 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.

Results of Operations

Comparison of years ended December 31, 2013 and December 31, 2014

The following table summarizes our results of operations for the years ended December 31, 2013 and 2014, together with the changes in those items in dollars and as a percentage:

	Year Ended December 31,		Change	
	2013	2014	$	%
	(in thousands)			
Statement of Operations Data:				
Operating Expenses:				
Research and development	$ 10,498	$ 5,280	$ (5,218)	(50)%
General and administrative	1,701	1,213	(488)	(29)%
Total operating expenses	12,199	6,493	(5,706)	(47)%
Loss from operations	(12,199)	(6,493)	5,706	47%
Net loss and comprehensive loss	$ (12,199)	$ (6,493)	$ 5,706	47%

Research and development expense. Research and development expense decreased by $5.2 million to $5.3 million in 2014 from $10.5 million in 2013, a decrease of 50%. The decrease was primarily due to a decrease in external services in 2014 as a series of large Phase 2 clinical trials for setmelanotide were substantially completed in 2013 and the first half of 2014. The next Phase 2 clinical trials for setmelanotide were initiated in the last quarter of 2014.

General and administrative expense. General and administrative expense decreased by $488,000 to $1.2 million in 2014 from $1.7 million in 2013, a decrease of 29%. The decrease in general and administrative expense was primarily attributable to a decrease in required support activities for setmelanotide trials as a series of large Phase 2 clinical trials for setmelanotide were substantially completed in 2013 and the first half of 2014. As a result, the overall proportion of general and administrative expense allocated to us was reduced in the second half of 2014.

Comparison of nine months ended September 30, 2014 and September 30, 2015

The following table summarizes our results of operations for the nine months ended September 30, 2014 and 2015, together with the changes in those items in dollars and as a percentage:

	Nine Months Ended September 30,		Change	
	2014	2015	$	%
	(in thousands)			
Statement of Operations Data:				
Operating Expenses:				
Research and development	$ 4,661	$ 3,530	$ (1,131)	(24)%
General and administrative	1070	1,400	330	30%
Total operating expenses	5,731	4,930	(801)	(14)%
Loss from operations	(5,731)	(4,930)	801	14%
Net loss and comprehensive loss	$ (5,731)	$ (4,930)	$ 801	14%

Research and development expense. Research and development expense decreased by $1.1 million to $3.5 million for the nine months ended September 30, 2015 from $4.7 million for the nine months ended September 30, 2014, a decrease of 24%. Included in the expenses for the nine months ended September 30, 2015 are $0.9 million non-cash expenses related to the modification of warrants made in connection with a

license agreement. The decrease in research and development expense was primarily attributable to a decrease in CRO costs as a series of large Phase 2 clinical trials for setmelanotide were substantially completed in the first half of 2014. For the remainder of 2015, we expect our research and development costs to increase as we initiate additional new clinical trials for setmelanotide and hire additional personnel in the clinical operations department.

General and administrative expense. General and administrative expense increased by $330,000 to $1.4 million for the nine months ended September 30, 2015 from $1.1 million for the nine months ended September 30, 2014, an increase of 30%. The increase in general and administrative expense was primarily attributable to an increase in accounting fees and recruitment costs. For the remainder of 2015, we expect a slight increase in general and administrative expense associated with hiring in the finance department.

Liquidity and Capital Resources

As of September 30, 2015, our existing cash and cash equivalents were approximately $23.9 million. We have received capital contributions from the Predecessor Company, the Relamorelin Company and the LLC entity from time to time as needed. In August 2015 and December 2015, we received aggregate gross proceeds of $25.0 million from the sale of our series A preferred stock.

Cash flows

The following table provides information regarding our cash flows for the years ended December 31, 2013 and December 31, 2014, and the nine months ended September 30, 2014 and September 30, 2015:

	Year Ended December 31,			Nine Months Ended September 30,		
	2013	2014	Change	2014 (unaudited)	2015 (unaudited)	Change
	(in thousands)					
Net cash provided by (used in):						
Operating activities	$ (10,643)	$ (7,508)	$ 3,135	$ (6,742)	$ (3,316)	$ 3,426
Financing activities	10,884	7,419	(3,465)	6,785	27,070	20,285
Net increase (decrease) in cash and cash equivalents	$ 241	$ (89)	$ (330)	$ 43	$ 23,754	$ 23,711

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 $10.6 million for the year ended December 31, 2013, and consisted primarily of a net loss of $12.1 million adjusted for non-cash items, which consisted of stock-based compensation. The significant items in the change in operating assets and liabilities include an increase in accounts payable, accrued expenses and other current liabilities of $202,000 and a decrease of approximately $1.2 million in prepaid expenses and other current assets.

Net cash used in operating activities was $7.5 million for the year ended December 31, 2014, and consisted primarily of a net loss of $6.4 million adjusted for non-cash items, which consisted of stock-based compensation. The significant items in the change in operating assets and liabilities include a decrease in accounts payable, accrued expenses and other current liabilities of $1.3 million offset by a decrease of approximately $222,000 in prepaid expenses and other current assets.

Net cash used in operating activities was $6.7 million for the nine-month period ended September 30, 2014, and consisted primarily of a net loss of $5.7 million adjusted for non-cash items, which consisted of

stock-based compensation. The significant items in the change in operating assets and liabilities include a decrease in accounts payable, accrued and other current liabilities expenses of $1.3 million and a decrease of approximately $220,000 in prepaid expenses and other current assets.

Net cash used in operating activities was $3.3 million for the nine-month period ended September 30, 2015, and consisted primarily of a net loss of $3.9 million adjusted for non-cash items, which consisted of stock-based compensation and warrant amendment expense. The significant items in the change in operating assets and liabilities include an increase in accounts payable, accrued expenses and other current liabilities of $1.4 million and an increase of approximately $0.8 million in prepaid expenses and other current assets.

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 $10.9 million for the year ended December 31, 2013, consisting of $6.0 million of cash transfers and $4.9 million of shared costs and costs paid on our behalf.

Net cash provided by financing activities was $7.4 million for the year ended December 31, 2014, consisting of $5.7 million of cash transfers and $1.7 million of shared costs and costs paid on our behalf.

Net cash provided by financing activities was $6.8 million for the nine months ended September 30, 2014, consisting of $5.7 million of cash transfers and $1.1 million of shared costs and costs paid on our behalf.

Net cash provided by financing activities was $27.1 million for the nine months ended September 30, 2015, consisting of $25 million of proceeds from the issuance of series A preferred stock, $1.6 million of cash transfers and $500,000 of shared costs and costs paid on our behalf.

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 through at least the end of 2018. 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 and December 2015, respectively, we issued 25,000,000 and 15,000,000, shares of series A preferred stock, respectively, at a price of $1.00 per share, resulting in gross proceeds of $40.0 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.

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 agreement with Ipsen 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.

We are not a party to the lease for the facility shared with the Relamorelin Company.

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.

Internal Controls and Procedures

During the preparation of the financial statements for the nine months ended September 30, 2015 and 2014, we identified a $630,000 overstatement of our research and development expense previously reported for the six months ended June 30, 2014. The correction of the error decreased net loss and research and development expense by $630,000 for the six months ended June 30, 2014 and decreased basic and diluted net loss per common share by $0.01 per share for the same period. The error had no impact on our financial statements for the year ended December 31, 2014. This error was caused by a material weakness in our internal controls over financial reporting consisting of a lack of an effective control in place to properly reconcile accrued expenses and other liabilities to our underlying accounting records. For additional information, see the risk factor "*If we are unable to implement and maintain effective internal controls over financial reporting in the future, we may fail to prevent or detect material misstatements in our financial statements, which may cause investors to lose confidence in the accuracy and completeness of our financial reports and the market price of our common stock may decline*" on page 52 of this prospectus.

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 $1.0 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 September 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.

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 body lacking satiety signals, which, in turn, leads to intense feelings of hunger and to obesity. Our development efforts are initially focused on two of these deficiencies, Prader-Willi Syndrome, or PWS, and pro-opiomelanocortin, or POMC, deficiency obesity, 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 initial proof of concept in our ongoing Phase 2 clinical trial in POMC deficiency obesity, a disorder of extreme and unrelenting appetite and obesity, in which setmelanotide dramatically reduced both weight and hunger. We are also conducting a Phase 2 clinical trial in PWS, and we expect to report results from these clinical trials in the first half of 2016. These clinical trials expand upon previous setmelanotide clinical trials which enrolled over 200 general obese patients and demonstrated 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—specifically PWS, POMC deficiency obesity and leptin receptor, or LepR, deficiency obesity—or genes that are downstream of MC4R or affect MC4R itself. We are focusing setmelanotide clinical development on patients with 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. Setmelanotide, which is administered by subcutaneous, or SC, injection, is currently in Phase 2 clinical trials for two genetic disorders of obesity, PWS and POMC deficiency obesity.

PWS is a life-threatening, orphan disease with prevalence estimates ranging from approximately one in 8,000 to one in 52,000, and with at least 8,000 diagnosed patients in the United States. A hallmark of PWS is severe hyperphagia, an overriding physiological drive to eat, 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. Only one drug, a growth hormone, is approved for treating short stature in PWS, however there is currently no approved treatment for the obesity and hyperphagia associated with PWS. Recent scientific studies identify deficiencies affecting the MC4 pathway as the cause of the obesity and associated symptoms of PWS, such as hyperphagia, and suggest that an MC4R agonist can directly impact these symptoms. We have initiated a Phase 2 clinical trial to evaluate the effects of up to 10 weeks of treatment on weight reduction and PWS-specific food-related behavior in obese patients with PWS. We expect to enroll approximately 36 patients and report results from this trial in the first half of 2016. The U.S. Food and Drug Administration's, or FDA's, existing guidance on developing products for weight management addresses treatments for the population of general obesity patients, which requires treatment of large and diverse populations of general obese patients. In contrast, based on our consultations with the FDA, we believe we can pursue a faster path to approval of setmelanotide for our genetically-targeted patient populations, such as PWS patients, based on a clinical study program tailored in size, duration, and preclinical prerequisites appropriate for the smaller size and nature of these rare populations.

In September 2015, the FDA granted our orphan drug designation request for setmelanotide for the treatment of PWS. As described more fully under the caption "Business—Regulatory Matters," if a product with orphan drug designation receives the first FDA approval for that disease, the product will receive orphan drug exclusivity. The benefit of orphan drug exclusivity is that the FDA will not approve another sponsor's marketing application for the same drug for the same indication for seven years, except in certain limited circumstances.

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 believe that our addressable patient population for this disorder is approximately 100 to 500 patients worldwide. Like PWS, patients with POMC deficiency have unrelenting 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. Currently, there is no approved treatment for the obesity and hyperphagia associated with this genetic disorder. We have initiated a Phase 2, open-label, clinical trial to evaluate the effects of up to 12 weeks of setmelanotide treatment on weight reduction and hunger in approximately six patients with POMC deficiency obesity. The initial patient in this trial lost 25.8 kg, or 56.9 lbs., over the first 13 weeks of treatment, immediately regained weight on withdrawal of drug, and resumed outstanding weight loss upon re-initiation of setmelanotide treatment in a long-term extension and has lost 51 kgs, or 112 lbs., over 42 weeks. Our second POMC patient has been treated for 10 weeks and has lost 17.8 kgs, or 39.2 lbs. We expect to report results from this trial in the first half of 2016. Based on our consultations with the FDA, we intend to pursue a faster path to approval of setmelanotide for POMC deficiency obesity, similar to the faster path we intend to seek in connection with the use of setmelanotide to treat obesity in PWS patients. In addition, we intend to apply for orphan drug designation for the use of setmelanotide for the treatment of POMC deficiency obesity.

We are also focusing on additional 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 intend to expand setmelanotide development to include two other upstream disorders, POMC heterozygous deficiency obesity and LepR deficiency obesity, for which there is also high unmet need and no approved or effective therapy. POMC heterozygous deficiency obesity results from the loss of function in one of two POMC genes. This condition is more prevalent than POMC deficiency obesity, affecting an estimated 2% of patients with severe, early onset obesity. We

estimate that the addressable patient population may consist of approximately 4,000 patients in the United States. LepR deficiency obesity is an ultra-rare orphan disease resulting in extreme hyperphagia and severe early onset obesity, with an estimated prevalence of 1% of subjects with severe, early onset obesity. Like other deficiencies upstream in the MC4 pathway, LepR deficiency results in loss of function in the MC4 pathway. We estimate actual prevalence could be between 500 and 2,000 patients worldwide.

We intend to initiate Phase 2 clinical trials for both POMC heterozygous deficiency obesity and LepR deficiency obesity in the first half of 2016 to evaluate the effects of setmelanotide on hunger and weight in these disorders. We expect to report results from these trials in the first half of 2017. We also intend to pursue faster paths to approval for setmelanotide for both POMC heterozygous deficiency obesity and LepR deficiency obesity.

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 undisclosed public healthcare investment funds.

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 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 PWS and POMC deficiency obesity as our first indications in upstream MC4 pathway deficiencies.** We are conducting two Phase 2 clinical trials in patients with upstream genetic deficiencies affecting the MC4 pathway, one for the treatment of patients with PWS, and one for the treatment of patients with POMC deficiency obesity. We believe these trials will be sufficient to enable initiation of Phase 3 registration studies. Based on FDA consultations to date, we intend to pursue indications for both PWS and POMC deficiency obesity.

- **Expand setmelanotide development to additional upstream MC4 pathway deficiencies, including POMC heterozygous deficiency obesity and LepR deficiency obesity.** We believe we can leverage our mechanistic understanding of and experience with PWS and POMC deficiency obesity to advance development of setmelanotide for other upstream MC4 pathway deficiencies. Accordingly, we intend to initiate Phase 2 clinical trials in the first half of 2016 for the rare genetic disorders, POMC heterozygous deficiency obesity and LepR deficiency obesity.

- **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.

- **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.

Our Product Pipeline

The following chart depicts key information regarding the development of our product candidate, 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, recent advances in genetic studies have identified several diseases that are the result of genetic defects affecting the MC4 pathway, most notably PWS. 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

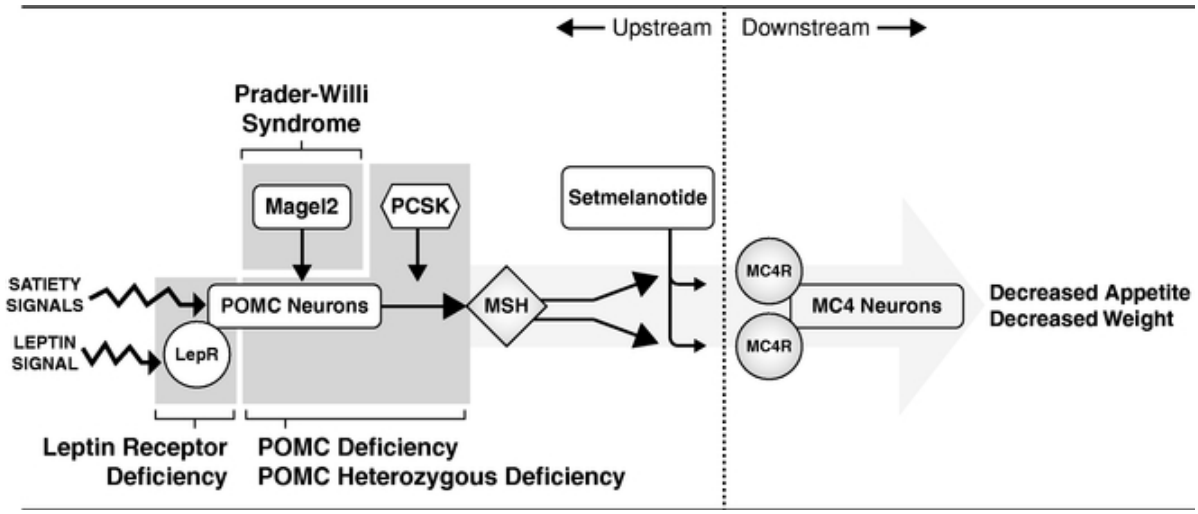
The MC4 pathway serves a critical role in the control of food intake and energy balance. Its activity decreases appetite and caloric intake, and increases energy expenditure, with MC4R acting as the final step in the signaling pathway. This important hypothalamic, or lower brainstem, pathway has been 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.

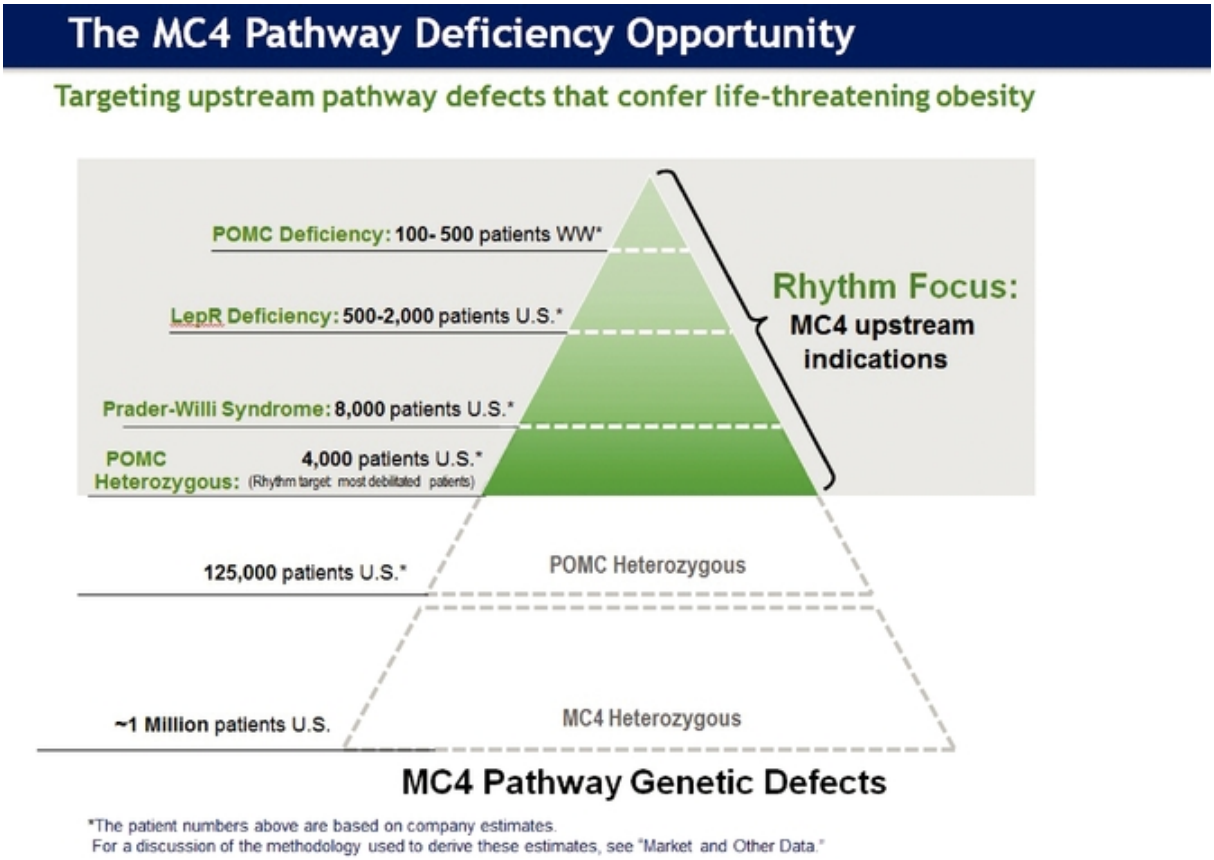
We are focused on developing setmelanotide for genetic disorders that result in defects in this pathway that are upstream of MC4R. Setmelanotide has the potential to restore lost function in this pathway by activating the intact MC4 pathway below the genetic defect. In this way, we believe setmelanotide 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 the estimated number of patients within these indications.



Obesity Caused by Upstream Genetic Deficiencies Affecting the MC4 Pathway

Prader-Willi Syndrome

PWS, a form of genetic MC4 pathway deficiency, is an orphan 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 the disease is severe hyperphagia, which leads to severe obesity as well as behavioral and metabolic complications. PWS patients also exhibit intellectual disability and delayed growth.

The genetics of PWS are complex, involving several 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, impairs the function of POMC neurons, which are key components of the MC4 pathway. Studies have suggested a link between defects in MAGEL2 in humans with obesity, hyperphagia, autism spectrum disorders, reduced intellectual ability and most other aspects of behavior and metabolism associated with PWS. Unraveling the function of the MAGEL2 gene in MAGEL2 deficient mice revealed functionally defective POMC neurons which otherwise would promote satiety by activating MC4. We believe this inherent defect in POMC neurons can be bypassed, as MAGEL2 deficient mice are responsive to therapeutic activation of MC4R, resulting in control of appetite. These published findings support the rationale for the treatment of PWS patients with an MC4R agonist.

For PWS patients, obesity and hyperphagia are the greatest threats to their health and these patients often die at a young age from related complications. Hyperphagia has a significant negative impact on the

patients' quality of life as well as causing obesity and a range of associated co-morbidities. Normal satiety, or the feeling of fullness after eating, does not exist in a person with PWS. The physiological drive to eat is so powerful and overwhelming that most PWS patients will go to great lengths to eat large quantities of food, in some cases even if it is spoiled, indigestible or unpalatable to others.

Hyperphagia impairs PWS patients' ability to live independently, requiring costly and constant supervision to prevent overeating. Without supervision, PWS patients are likely to die prematurely as a result of choking, stomach rupture or tissue necrosis, or from complications caused by morbid obesity, such as heart failure and respiratory failure. While a small number of PWS patients are cared for in costly group homes, the majority of PWS patients are cared for in their family homes until at least age 30 and their caregivers undertake substantial efforts to create physical barriers to eating. These efforts result in extremely stressful environments as caregivers often place locks and alarms on cabinets and refrigerators that contain food to impede PWS patients' efforts to obtain food at all times. The typical annual cost of treating a PWS patient can exceed $100,000, excluding the often significant costs of drug therapies related to other medical and psychological conditions, and the costs of any lost time from work experienced by their families due to responsibilities related to the care of a PWS patient.

Currently there is no approved treatment for PWS, and most research to date has targeted the treatment of specific symptoms. For many individuals affected by the disorder, the elimination of some of the most difficult aspects of the syndrome, such as hyperphagia and obesity, would represent a significant improvement in quality of life and provide the potential opportunity for patients to live independently.

POMC Deficiency Obesity

POMC deficiency obesity is an ultra-rare genetic disorder, with severe, early onset obesity and profound hyperphagia as hallmark clinical features. Patients with POMC deficiency obesity are extremely rare, with approximately 50 POMC deficient patients reported to date. 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 disorder is approximately 100 to 500 patients worldwide, 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 discussion 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 results from two different homozygous genetic defects that result either in loss of POMC neuropeptide synthesis or disruption of the required processing of the POMC neuropeptide product to MSH. The first is a loss of function defect in the POMC gene itself, where the lack of the POMC gene expression and absence of POMC-derived neuropeptides ultimately results in lack of stimulation of downstream MC4 neurons. This form of POMC deficiency may also be associated with hormonal deficiencies, such as hypoadrenalism, and red hair and fair skin are also common in this disorder. The second genetic defect results from the need for the POMC protein product to be processed by the PCSK processing enzyme. The end result of these two defects is the lack of MSH that binds and activates MC4R, leading to severe, early onset obesity and profound hyperphagia.

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. Currently there are no approved or effective therapies for POMC deficiency obesity.

Other Upstream Genetic Defects in the MC4 Pathway

In addition to PWS and POMC deficiency obesity, 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 deficiencies farther upstream from POMC and MC4R, such as LepR deficiency obesity.

POMC Heterozygous Deficiency Obesity

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. 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. 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. Based on epidemiology studies in small cohorts of patients with severe early onset obesity and adult obesity, we estimate that the addressable patient population for POMC heterozygous deficiency obesity is approximately 4,000 patients in the United States.

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 will be initiating another Phase 2 proof of concept trial in the first half of 2016 to confirm our hypothesis that the subset of patients with very severe POMC heterozygous deficiency obesity may be highly responsive to setmelanotide therapy. There is currently no approved therapy for POMC heterozygous deficiency obesity.

Leptin Receptor Deficiency Obesity

LepR deficiency causes hyperphagia and severe, early onset obesity and accounts for an estimated prevalence of 1% of subjects with severe, early onset obesity, defined here as a body mass index, or BMI, of greater than 40 kg/m^2. Additional clinical symptoms include mild alterations in immune function and delayed puberty. Based on epidemiology studies in small cohorts of patients with severe, early onset obesity, we estimate the prevalence of LepR deficiency obesity is between 500 and 2,000 patients worldwide. 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. Therefore, patients with this indication also manifest intense hyperphagia and severe obesity from early childhood. Currently there is no approved therapy for LepR deficiency obesity.

Obesity Caused by Downstream Genetic Deficiencies Affecting the MC4 Pathway

MC4 Heterozygous Deficiency Obesity

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 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 has demonstrated 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.

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 either PWS or POMC deficiency obesity. Bariatric surgery is contraindicated in patients with PWS, and is also not an option in patients with other upstream defects in the MC4 pathway who have severe obesity and hyperphagia.

Setmelanotide: A First-in-Class Phase 2 MC4R Agonist

Setmelanotide is a potent, first-in-class, MC4R agonist peptide administered by daily SC injection. Setmelanotide is in Phase 2 clinical trials for the treatment of rare genetic disorders of obesity caused by MC4 pathway deficiencies. 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 early onset and severe obesity. The first generation MC4R agonists were small molecules that failed 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. Previous setmelanotide clinical trials have enrolled over 200 general obese patients and demonstrated significant weight loss with good tolerability.

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

We have initiated two Phase 2 clinical trials of setmelanotide for the treatment of rare genetic disorders of obesity, one for POMC deficiency obesity and one for PWS. Based on FDA consultations to date, we believe we can seek indications for obesity caused by 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 2 clinical trials of setmelanotide in these indications as the foundation for proceeding directly to pivotal clinical trials. We also plan to initiate Phase 2 proof of concept trials in the first half of 2016 in POMC heterozygous deficiency obesity patients and in patients with LepR deficiency obesity, additional populations with genetically-defined deficiencies upstream in the MC4 pathway.

We believe our initial data in POMC deficiency obesity provides 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.

To date, most of our completed setmelanotide clinical trials have been in the general obese population. These trials have provided additional safety data as we focus on rare, genetic segments 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 studies in rare genetic disorders of obesity.

Setmelanotide: Phase 2 Clinical Programs in Genetically Defined Obesity

	POMC Deficiency	PWS	POMC Heterozygous Deficiency	LepR Deficiency
Clinical trial phase	Phase 2	Phase 2	Phase 2	Phase 2
Status	Initiated 1Q2015	Initiated 4Q2014	Initiating 1H2016	Initiating 1H2016
Treatment groups[(1)]	Setmelanotide	Setmelanotide, Placebo	Setmelanotide, Placebo	Setmelanotide
Number of patients[(2)]	4 - 6	36	4 - 6	2 - 6[(3)]
Patient demographics	Adult, POMC deficient[(4)]	PWS Adults/Adolescents	POMC heterozygous deficiency with morbid obesity	LepR deficient
Duration of treatment	12 weeks + Extensions	8 - 10 weeks	12 weeks	12 weeks + Extensions
Location	Germany, United States	United States	United States, Germany, France, UK	United States, Germany, France, UK

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

(2) Approximate number of patients anticipated to be enrolled.

(3) Either a separate trial or additional patients included in the ongoing POMC deficiency trial in some locations.

(4) POMC deficiency includes homozygous deficiency in either the POMC or PCSK genes.

Setmelanotide: Clinical Development Program in Genetically Defined Obesity

Phase 2 Clinical Development in POMC Deficiency Obesity

We have initiated a Phase 2 proof of concept, open label clinical trial in patients with POMC deficiency obesity. With two patients in this trial, we believe that we have provided proof of concept for the compelling efficacy of setmelanotide in this disorder.

The first setmelanotide-treated patient was a 20-year old woman, who at three months of age experienced the onset of obesity and severe hyperphagia. In spite of enormous efforts, the patient was never able to stabilize her body weight, except for brief periods, and she has remained severely hyperphagic. Ahead of our trial, the patient's self-reported trial hunger score was eight or nine out of ten 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 her significant risk of comorbidities and a reduced life expectancy.

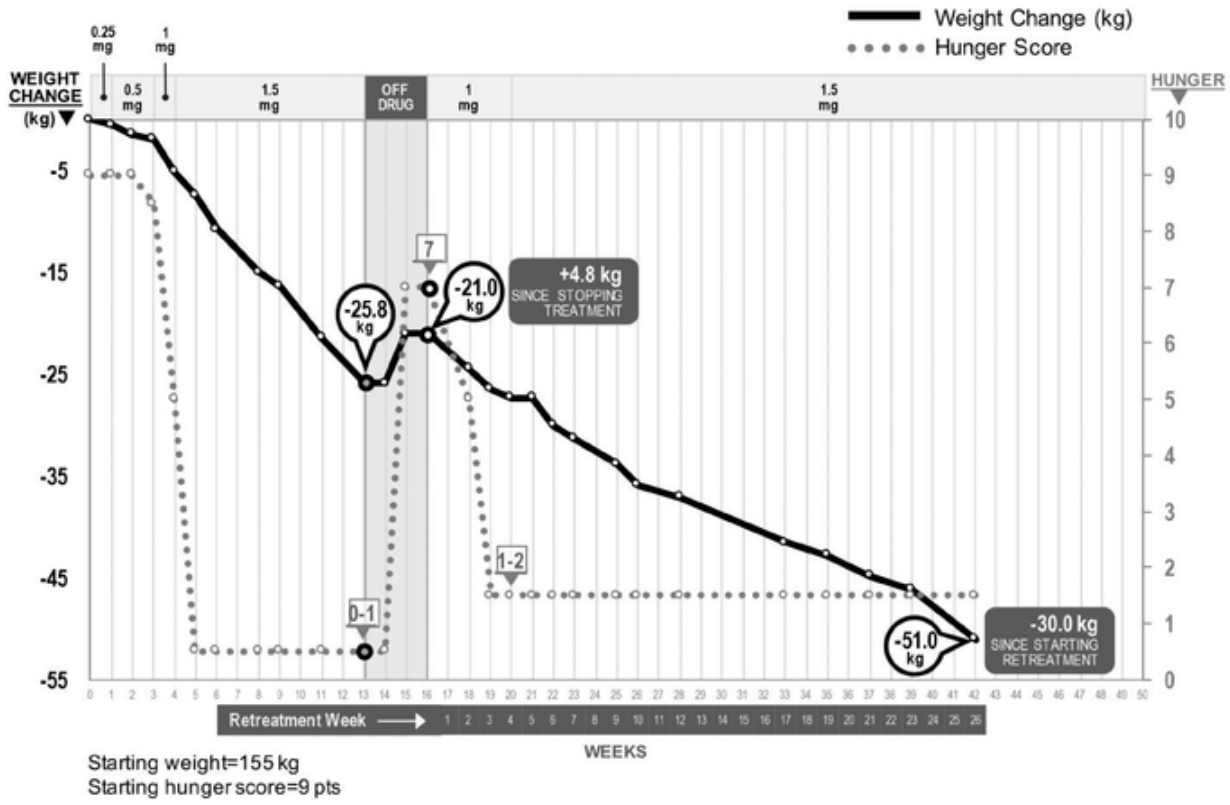
The trial, a 13-week, open label, ascending dose Phase 2 trial, was approved by the German Federal Institute for Drugs and Medical Devices, with open-label one year extensions, and will include approximately four to six patients with genetically confirmed POMC deficiency obesity. After efficacy-gated dose escalation, aiming for weekly weight loss of approximately two kg, or 4.4 lbs., per week, the primary endpoint is 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. A similar companion protocol, without long-term extensions, will also be initiated in the United States under the United States investigational new drug application, or IND.

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 on a scale of 0, representing no hunger, to 10, or extreme hunger, mirrored the rate of weight loss, moving from scores of eight to nine prior to our trial, or close to extreme hunger, to zero to one, representing close to no hunger, 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, taking total weight loss in the trial to 51.0 kg, or 112.4 lbs., representing 32.9% of her initial body weight. There was no apparent difference in the rate of weight loss during the extension phase versus the main trial.

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

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



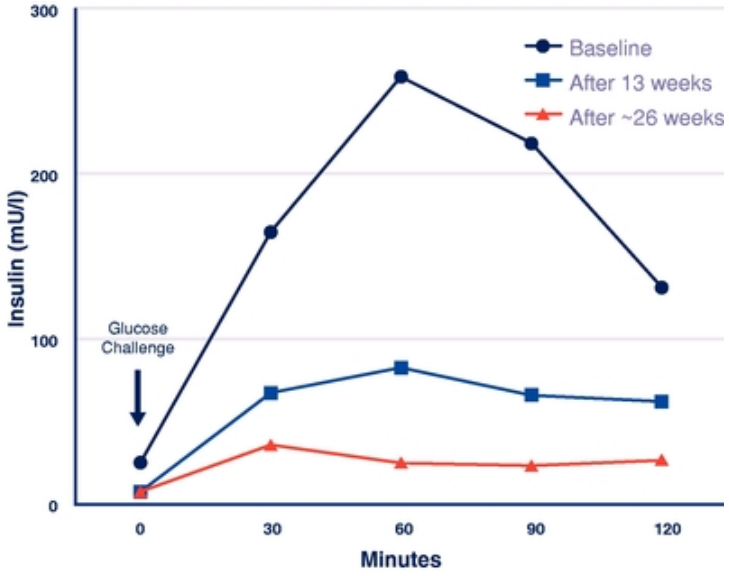
(1) Thirteen weeks of initial treatment, three weeks withdrawal from drug, then re-treatment in a long-term extension. Daily setmelanotide dose adjustments over time are indicated at the top of the panel.

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 of 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.

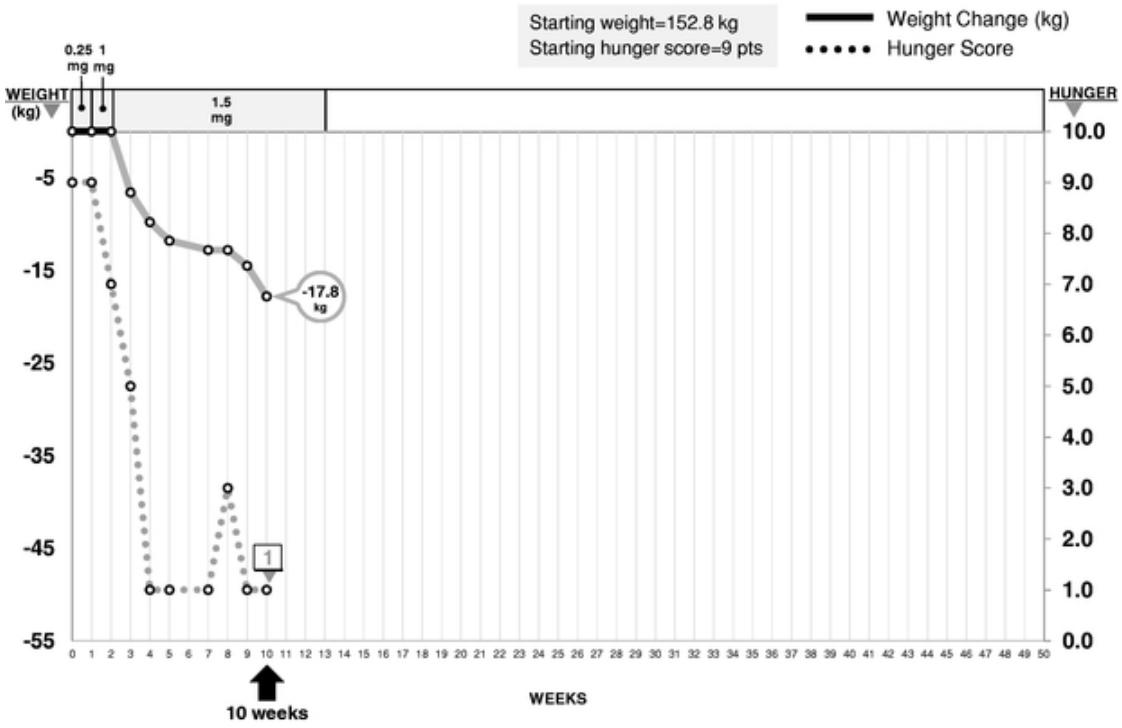
Setmelanotide Treatment Effects on Insulin Resistance (Insulin Response in Oral Glucose Tolerance Test) at Baseline, After 13 Weeks of Treatment (Phase 1), and at Approximately 26 Weeks (Phase 2) During the Long-term Extension for our Initial Patient



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

After 10 weeks of therapy, with approximately the first two weeks at sub-therapeutic doses, our second patient demonstrated weight loss of 17.8 kg, or 39.2 lbs., representing 11.6% 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 mirrored the rate of weight loss, moving from scores of nine prior to our trial, or close to extreme hunger, to one on most weeks, representing close to no hunger, as the patient was treated with increasing doses of setmelanotide. Once this patient completes the initial 13 weeks of this trial, it is planned that she will also enter long-term extensions.

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



(1) Ten weeks of initial treatment; 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 experiences, 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 results from the initial patients in our POMC deficiency 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 severe 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. Lastly, 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 approximately nine months of treatment of our first patient also supports the ability of setmelanotide to be effective for longer treatment periods.

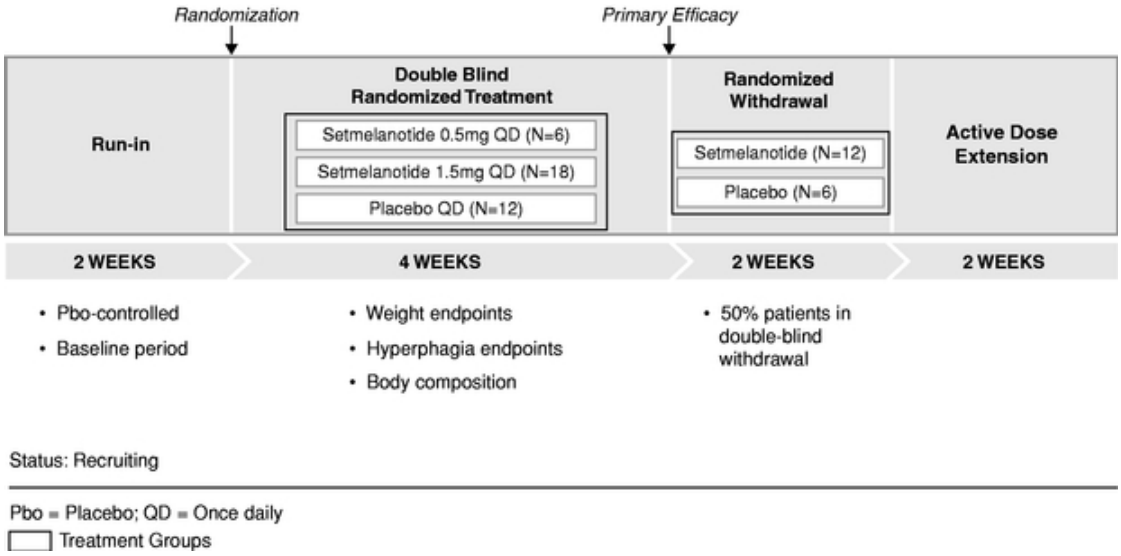
This initial proof of concept data provide support for the belief that setmelanotide will restore activity in patients with upstream defects in the MC4 pathway, will help patients lose weight, and will reduce hyperphagia. Since POMC deficiency obesity patients are considered to be a population of patients closely related to PWS patients, as each share a defect in the POMC neurons, we can hypothesize a productive therapeutic response of PWS patients to treatment with setmelanotide. Similarly, we would expect efficacy in other upstream MC4 pathway genetic disorders, such as POMC heterozygous deficiency obesity and LepR deficiency obesity.

Phase 2 Clinical Development in PWS Patients

We have initiated a Phase 2 proof of concept, double-blind, placebo-controlled, randomized clinical trial in PWS which is expected to enroll approximately 36 patients for up to eight weeks of active setmelanotide treatment, administered once daily by SC injection. This trial is intended to assess the effects of setmelanotide on weight reduction, and PWS-specific hyperphagia-related behaviors, as well as determine its safety profile. Based on the data from this Phase 2 clinical trial, we believe we may be positioned to proceed into a Phase 3 clinical trial that could lead to an indication for the treatment of PWS patients.

The trial includes 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 will be 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 will be three treatment arms in the trial: placebo; 0.5 mg of setmelanotide SC injection daily, which we expect to be a subtherapeutic dose; and 1.5 mg of setmelanotide SC injection daily. Patients recruited are 16 to 65 years of age, with a BMI of greater than 27 kg/m^2, and with a genetically confirmed diagnosis of PWS. Patients recruited will live in a family setting, rather than in a group home. Primary endpoints for the trial include safety and tolerability, weight loss and hyperphagia, with hyperphagia to be measured by a PWS hyperphagia observer reported outcome, or ORO, questionnaire. Secondary endpoints include 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. Evaluations will be assessed at the end of the four-week double blind parallel group stage, as well as after the withdrawal stage and open label extension.

10-week Double Blind, Placebo-controlled Parallel Group Study with a Randomized Placebo-controlled Withdrawal Phase and Open Label Active Treatment Extension



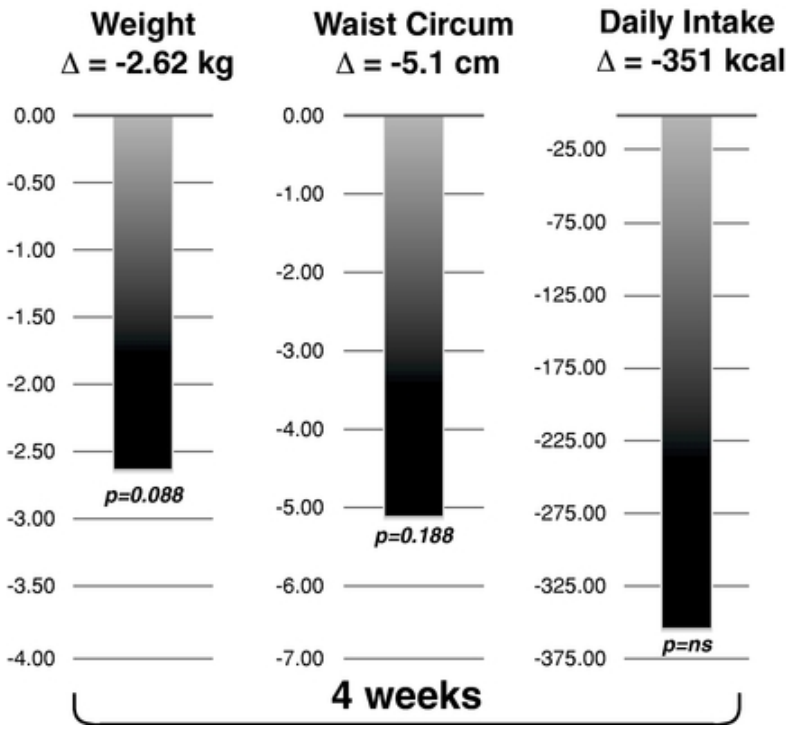
Phase 1b Clinical Development in Patients with Heterozygous MC4R Gene Mutations

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.

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.

Planned Phase 2 Clinical Development in POMC Heterozygous Deficiency Obesity

We plan to initiate a Phase 2 clinical trial in patients who are severely obese, or whose BMI is equal to or greater than 40kg/m^2, and who are POMC heterozygous deficient. These patients have a heterozygous genetic mutation of the POMC or PCSK gene resulting in full or partial loss of POMC signaling to the downstream MC4R. The purpose of this trial is to provide proof of concept that severely impaired POMC 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. We plan to initiate this clinical trial in the first half of 2016 and to conduct this clinical trial at sites in the United States and Europe.

Planned 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. We plan to study these patients with homozygous loss-of-function LepR mutations starting in the first half of 2016. We may amend our ongoing Phase 2 clinical trial in POMC deficiency obesity to include this related genetically-defined population of severely obese patients, or we may initiate a separate Phase 2 clinical trial. The purpose of this trial is to provide proof of concept that severely impaired LepR deficient patients will also demonstrate significant weight loss similar to that seen in patients with POMC deficiency obesity. We anticipate that in this trial, approximately two to six patients, identified by genetic diagnostic screening, will receive setmelanotide by once daily SC injection for approximately twelve weeks of treatment.

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.

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.

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 Volunteers	Obesity	Continuous infusion	36 healthy obese subjects	Completed
RM-493-002 Multiple Ascending Dose Trial in Healthy Obese Volunteers	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, data analysis still ongoing
RM-493-005 Pre-screening Genetic Testing of Healthy Obese Volunteers	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	99 healthy obese subjects	Completed, data analysis still ongoing

SC=subcutaneous. Completed=completed the in-life portion of the trial.

Phase 2 Clinical Development in the General Obese Population

Phase 2 Clinical Trial Results with Continuous Infusion

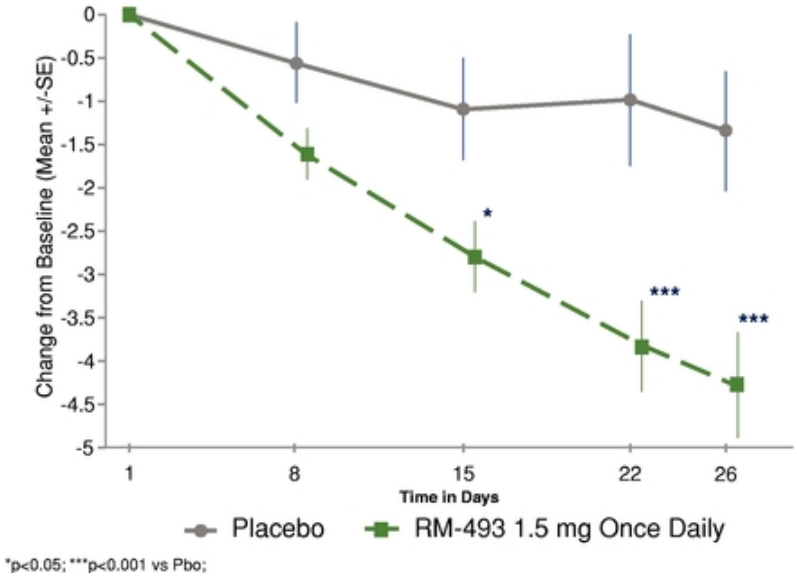
We conducted our first Phase 2 clinical trial of setmelanotide using continuous SC infusion. This was a 12-week, Phase 2 proof of concept clinical trial in general obese patients using the SC continuous infusion formulation of setmelanotide delivered by an insulin pump. We treated approximately 74 obese 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.

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



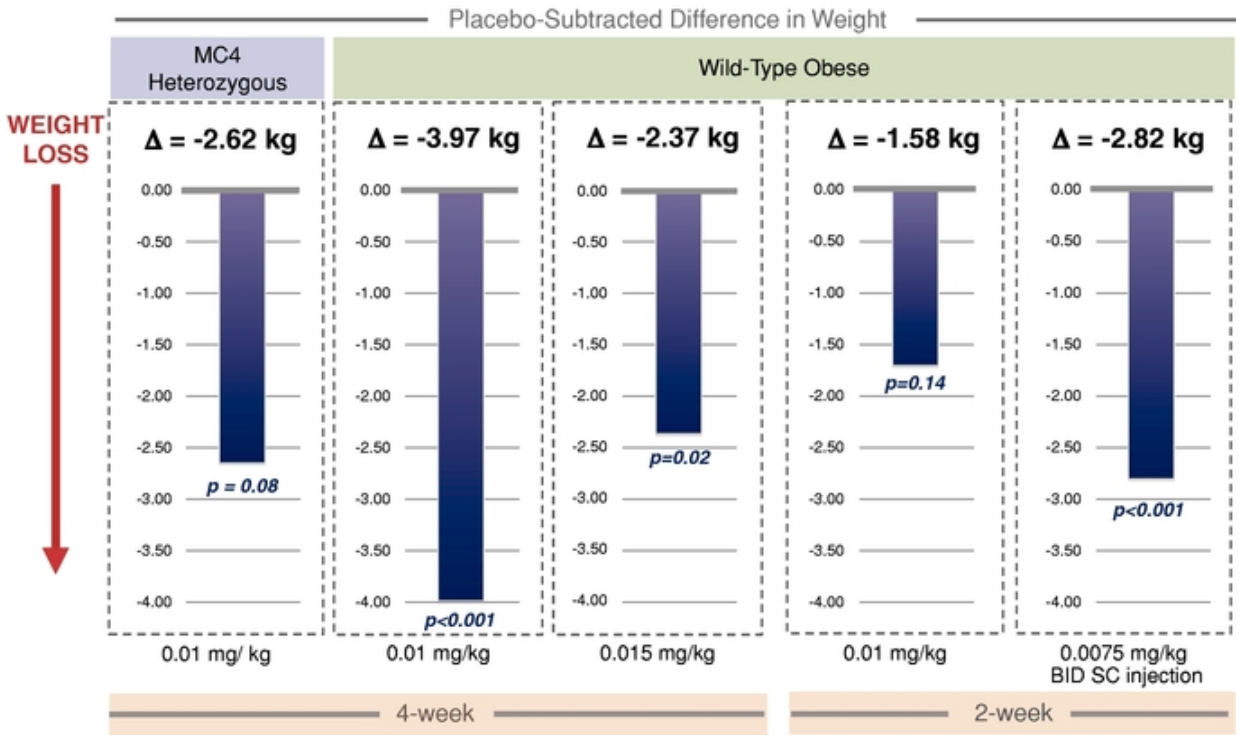
Phase 1 Clinical Development in the General Obese Population

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 volunteers, 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.

Safety and Tolerability

Historically, clinical data with other MC4R therapies suggested that MC4R-mediated 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 appeared different among each of the other MC4R therapies, underscoring the

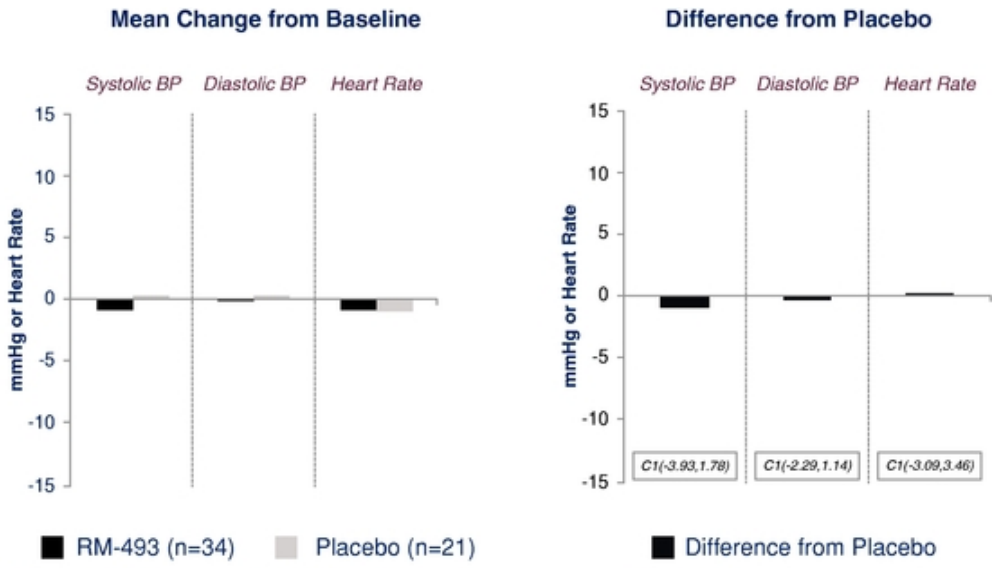
complex physiology of MC4R. With setmelanotide, there has been little, if any, evidence of blood pressure or heart rate changes, preliminarily supporting an important differentiation of setmelanotide from previous MC4R therapies. Careful monitoring for blood pressure and heart rate changes, as well as 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.

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. 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 were 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 of 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 considers 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, 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.

We completed one and three month toxicology studies, 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. We are currently initiating chronic toxicity studies and a juvenile toxicology study that are designed to rapidly 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 in length, but the FDA may allow NDA filing without one or both of the carcinogenicity studies for these rare disease populations.

In addition to developing the once daily SC injectable formulation of setmelanotide that we will use in all planned future clinical trials, we have developed compelling preclinical data with a once weekly slow release formulation, and we are rapidly moving this latter formulation forward. We will likely proceed to pharmacokinetic trials of this formulation in the next one to two years.

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 PWS, POMC deficiency obesity, POMC heterozygous deficiency obesity or LepR deficiency obesity. Bariatric surgery is contraindicated in patients with PWS, and the severe obesity and hyperphagia associated with these other genetic disorders of obesity are also considered to be risk factors for bariatric surgery. We are also aware that Zafgen, Inc. is conducting a clinical trial in PWS with belorinab, a MetAP2 inhibitor thought to affect the metabolism of fat. We are aware of a clinical trial that was recently completed by Ferring Pharmaceuticals, Inc. to evaluate the use of carbetocin, an analogue of a brain peptide hormone oxytocin, hypothesized to increase trust, reduce anxiety and improve behavior in patients with PWS. We also are aware of a clinical trial being conducted by Essentialis, Inc. to evaluate the safety and tolerability of controlled-release diazoxide in patients with PWS and to explore the effects of diazoxide on hyperphagia-related behaviors and energy expenditure. In August 2015, Novo Nordisk announced it will initiate a Phase 3 trial of Saxenda (liraglutide injection) for weight management in pediatric PWS patients. Also, Alize Pharma recently started a Phase 2 clinical trial in PWS of AZP-531, its unacylated ghrelin analog.

Licensing Agreements

In February 2010, the Predecessor Company entered into a license agreement with 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 Restructuring 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.

Commercial Operations

We intend to establish our own commercial sales and marketing organization in the United States and core strategic markets. We intend to establish a specialty sales force that will target physicians treating PWS and other rare genetic disorders of obesity, including pediatric and adult endocrinologists, as well as pharmacists. The sales force will be supported by sales management, internal sales support, an internal marketing group and distribution support. Additionally, the sales and marketing teams will manage relationships with key accounts including managed care organizations, group-purchasing organizations, hospital systems, and government accounts. We will also 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 three families which are exclusively owned and maintained by us that relate to the melanocortin program.

Our MC4 portfolio, which includes setmelanotide, consists of nine 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 September 28, 2015, the portfolio licensed for the MC-4 program consists of two issued United States patents and 29 issued non-United States patents across four of the nine families. We are actively pursuing 10 United States patent applications and 67 non-United States applications in 14 jurisdictions.

In the patent family directed to the composition of matter for setmelanotide, we have one issued United States patent and 16 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.

Intellectual Property Protection Strategy

We currently seek, and intend to continue seeking, patent protection whenever commercially reasonable for any patentable aspects of our existing product candidate 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 Peptisyntha SA, 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 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 regulatory 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 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, 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;
- 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 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.

Human Clinical Trials 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 cGCP 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. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. An IND automatically becomes effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions related to a proposed clinical trial and places the trial on clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. The FDA can place an IND on clinical hold at any point in development, and depending upon the scope of the hold, clinical trials may not restart until resolution of the outstanding concerns to the FDA's satisfaction.

In addition, 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 a 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. Information about certain clinical trials must be submitted within specific timeframes to the National Institutes of Health for public dissemination on their ClinicalTrials.gov website.

Human clinical trials are typically conducted in three 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.

Post-approval studies, or Phase 4 clinical trials, may be conducted after initial marketing approval. These studies are used to gain additional experience from the 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. The FDA or the sponsor or its data monitoring committee 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 cGCPs 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.

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. 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 and Priority Review 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 fast track designation, breakthrough therapy designation and priority review 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 drugs, for the treatment of a serious or life-threatening disease or condition where non-clinical or clinical data 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 NDA 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 complete NDA 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, in 2012, Congress enacted the Food and Drug Administration Safety and Innovation Act, or FDASIA. This law established a new "breakthrough therapy" designation. A product may be designated as a breakthrough therapy if it is intended, either 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 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 designation includes all of the features of Fast Track designation, as well as more intensive FDA interaction and guidance. 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 efficient clinical trials.

Third, the FDA may designate a product for priority review if it is a drug 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 drug represents a significant improvement in safety and effectiveness 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 drug 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.

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 marketing, labeling, advertising and promotion of products that are placed on the market. Drugs may be promoted only for the approved indications and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability.

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.

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.

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 in its orphan product application, it may not be entitled to exclusivity. Orphan exclusivity will not bar approval of another product 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.

Patent Term 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.

Pharmaceutical Coverage, Pricing 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 our products 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 our product candidate is approved, sales of our products 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, product candidates may not be considered medically necessary or cost effective. A decision by a third-party payor not to cover our product candidate 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 our product candidate 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 our product candidate 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. European Union 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 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. Recently, many countries in the European Union have increased the amount of discounts required on pharmaceuticals and these efforts could continue as countries attempt to manage healthcare expenditures, especially in light of the severe fiscal and debt crises experienced by many countries in the European Union. The downward pressure on health care costs in general, particularly prescription drugs, has become intense. As a result, increasingly high barriers are being erected to the entry of new products. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various European Union member states, and parallel trade, i.e., arbitrage between low-priced and high-priced member states, can further reduce prices. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our products, if approved in those countries.

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 with providers, consultants, third-party payors and customers are subject to broadly applicable fraud and abuse, anti-kickback, false claims laws, reporting of payments to physicians and teaching physicians and patient privacy laws and regulations and other healthcare laws and regulations that may constrain our business

and/or financial arrangements. Restrictions under applicable federal and state healthcare laws and regulations, include the following:

- the United States federal Anti-Kickback Statute, which prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, paying, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made, in whole or in part, under a federal healthcare program such as Medicare and Medicaid;

- the federal civil and criminal false claims laws, including the civil False Claims Act, and civil monetary penalties laws, which prohibit individuals or entities from, among other things, knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false, fictitious or fraudulent or knowingly making, using or causing to made or used a false record or statement to avoid, decrease or conceal an obligation to pay money to the federal government.

- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created additional federal criminal laws that prohibit, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, and their respective implementing regulations, including the Final Omnibus Rule published in January 2013, which impose obligations, including mandatory contractual terms, 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, under the Patient Protection and Affordable Care Act, as amended by the Health Care Education Reconciliation Act, or the Affordable Care Act, which requires certain manufacturers of drugs, devices, biologics and medical supplies to report annually to the Centers for Medicare & Medicaid Services, or CMS, within the United States Department of Health and Human Services, information related to payments and other transfers of value made by that entity to physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members; and

- analogous state and foreign 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.

Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring drug manufacturers to report information related to payments to physicians and other health care providers or marketing expenditures. State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

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, the United States Congress enacted the

Affordable Care Act, which, among other things, includes changes to the coverage and payment for products under government health care programs. Among the provisions of the Affordable Care Act 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 would 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;

- expanded 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;

- addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected;

- expanded the types of entities eligible for the 340B drug discount 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. PPACA provided that under certain circumstances, IPAB recommendations 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. Funding has been allocated to support the mission of the Center for Medicare and Medicaid Innovation from 2011 to 2019.

Other legislative changes have been proposed and adopted in the United States since the Affordable Care Act was enacted. For example, in August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2012 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions of Medicare payments to providers of up to 2% per fiscal year, which went into effect in April 2013 and will remain in effect through 2024 unless additional Congressional action is taken. In January 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, further reduced Medicare payments to several providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

There have been, and likely will continue to be, legislative and regulatory proposals at the foreign, federal and state levels directed at broadening the availability of healthcare and containing or lowering the cost of healthcare. Such reforms could have an adverse effect on anticipated revenues from product candidates that we may successfully develop and for which we may obtain marketing approval and may affect our overall financial condition and ability to develop product candidates.

Other Federal and State Regulatory 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. Compliance with these laws is difficult and time consuming, and companies that do not comply with these state laws face civil penalties.

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 our product candidate to the extent we choose to sell any products outside of the United States. Whether or not we obtain FDA approval for a product, we must obtain approval of a product by the comparable regulatory authorities of foreign countries 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

Pursuant to the currently applicable Clinical Trials Directive 2001/20/EC and the Directive 2005/28/EC on cGCP, an applicant must obtain the approval from the competent national authority of the European Union Member State in which the clinical trial is to be conducted. If the clinical trial is conducted in different European Union Member States, the competent authorities in each of these European Union Member States must provide their approval for the conduct of the clinical trial. Furthermore, the applicant may only start a clinical trial at a specific study site after the competent ethics committee has issued a favorable opinion.

In April 2014, the European Union adopted a new Clinical Trials Regulation (EU) No 536/2014, which is set to replace the current Clinical Trials Directive 2001/20/EC. The new Clinical Trials Regulation will be directly applicable in and binding in all 28 European Union Member States without the need for any national implementing legislation. The new Clinical Trials Regulation (EU) No 536/2014 will become applicable no earlier than 28 May 2016. It will overhaul the current system of approvals for clinical trials in the European Union. Specifically, the new legislation aims at simplifying and streamlining the approval of clinical trials in the European Union. Under the new coordinated procedure for the approval of clinical

trials, the sponsor of a clinical trial will be required to submit a single application for approval of a clinical trial to a reporting European Union Member State, or RMS, through a European Union portal. The submission procedure will be the same irrespective of whether the clinical trial is to be conducted in a single European Union Member State or in more than one European Union Member State. The Clinical Trials Regulation also aims to streamline and simplify the rules on safety reporting for clinical trials. As an example, suspected unexpected serious adverse reactions can be reported by the sponsor directly to EudraVigilance instead of being submitted to each European Union Member State.

Marketing Authorization

In the European Union, marketing authorizations for medicinal products can be obtained through several different procedures founded on the same basic regulatory process.

The centralized procedure provides for the grant of a single marketing authorization that is valid for all European Union Member States. The centralized procedure is compulsory for medicinal products produced by certain biotechnological processes, products designated as orphan medicinal products, and products with a new active substance indicated for the treatment of certain diseases. It is optional for those products that are highly innovative or for which a centralized process is in the interest of patients. Under the centralized procedure in the European Union, the maximum timeframe for the evaluation of a marketing authorization application is 210 days (excluding clock stops, when additional written or oral information is to be provided by the applicant in response to questions asked by the Committee for Medicinal Products for Human Use, or CHMP). Accelerated evaluation may be granted by the CHMP in exceptional cases. These are defined as circumstances in which a medicinal product is expected to be of a "major public health interest." Three cumulative criteria must be fulfilled in such circumstances: the seriousness of the disease, such as heavy disabling or life-threatening diseases, to be treated; the absence or insufficiency of an appropriate alternative therapeutic approach; and anticipation of high therapeutic benefit. In these circumstances, the European Medicines Agency, or EMA, ensures that the opinion of the CHMP is given within 150 days.

The decentralized procedure provides for approval by one or more other "concerned" European Union Member States of an assessment of an application for marketing authorization conducted by one European Union Member State, known as the reference European Union Member State. In accordance with this procedure, an applicant submits an application for marketing authorization to the reference European Union Member State and the concerned European Union Member States. This application is identical to the application that would be submitted to the EMA for authorization through the centralized procedure. The reference European Union 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 European Union Member States who, within 90 days of receipt must decide whether to approve the assessment report and related materials. If a concerned European Union 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 European Union Member States. In accordance with the mutual recognition procedure, the sponsor applies for national marketing authorization in one European Union Member State. Upon receipt of this authorization the sponsor can then seek the recognition of this authorization by other European Union Member States. Authorization in accordance with either of these procedures will result in authorization of the medicinal product only in the reference European Union Member State and in the other concerned European Union Member States.

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, an applicant must demonstrate compliance with all measures included in a Pediatric Investigation Plan, or PIP, approved by the Pediatric Committee of the EMA, covering all subsets of the pediatric

population, unless the EMA has granted a product-specific waiver, class waiver, or a deferral for one or more of the measures included in the PIP.

Regulatory Data Exclusivity in the European Union

In the European Union, innovative medicinal products authorized in the European Union on the basis of a full marketing authorization application (as opposed to an application for marketing authorization that relies on data available in the marketing authorization dossier for another, previously approved, medicinal product) are entitled to eight years of data exclusivity. During this period, applicants for authorization of generics of these innovative products cannot rely on data contained in the marketing authorization dossier submitted for the innovative medicinal product. Innovative medicinal products are also entitled to 10 years' market exclusivity. During this 10 year period no generic of this medicinal product can be placed on the European Union market. The overall 10 year period will be extended to a maximum of 11 years if, during the first eight years of those 10 years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to authorization, is 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 may 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 is valid for five years, in principle, and it may be renewed after five years on the basis of a reevaluation of the risk benefit balance by the EMA or by the competent authority of the relevant European Union Member State. To that end, the marketing authorization holder must provide the EMA or the relevant competent authority of the European Union Member State 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. Once renewed, the marketing authorization is valid for an unlimited period, unless the European Commission or the relevant competent authority of the European Union Member State decides, on justified grounds relating to pharmacovigilance, to proceed with one additional five year renewal period. Any marketing authorization that is not followed by the marketing of the medicinal product on the European Union market (in the case of the centralized procedure) or on the market of the European Union Member State which delivered the marketing authorization within three years after authorization ceases to be valid.

Regulatory Requirements after Marketing Authorization

Similarly to the U.S., 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 European Union Member States both before and after grant of the manufacturing and marketing authorizations.

The holder of a European Union marketing authorization for a medicinal product must also comply with European Union pharmacovigilance legislation and its related regulations and guidelines which entail many requirements for conducting pharmacovigilance, or the assessment and monitoring of the safety of medicinal products. These rules can impose on central marketing authorization holders for medicinal products the obligation to conduct a labor intensive collection of data regarding the risks and benefits of marketed products and to engage in ongoing assessments of those risks and benefits, including the possible requirement to conduct additional clinical studies.

The manufacturing process for medicinal products in the European Union is highly regulated and regulators may shut down manufacturing facilities that they believe do not comply with regulations. Manufacturing requires a manufacturing authorization, and the manufacturing authorization holder must comply with various requirements set out in 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. Similarly, the distribution of medicinal products into and within the European Union is subject to compliance with the applicable European Union laws, regulations and guidelines, including the requirement to hold appropriate authorizations for distribution granted by the competent authorities of the European Union Member States.

In the European Union, the advertising and promotion of our products are subject to European Union Member States' laws governing promotion of medicinal products, interactions with physicians, misleading and comparative advertising and unfair commercial practices. In addition, other legislation adopted by individual European Union 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. 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 the European Union level and in the individual European Union Member States also prohibit the direct-to-consumer advertising of prescription-only medicinal products. 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.

Orphan Drug Designation and Exclusivity

Regulation (EC) No 141/2000 and Regulation (EC) No. 847/2000 provide that a product can be designated as an orphan medicinal product 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 10,000 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 the medicinal product is unlikely to be developed. 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 medicinal product 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 European Union 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.

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 five employees providing services to us under our Payroll Services Agreement, three of whom hold Ph.D. or M.D. degrees. Of these employees, three are engaged in development activities and two 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 2,930 square foot facility in Boston, Massachusetts used primarily for corporate functions. The lease for this space expires in December 2016 and we have rights to this space pursuant to our Payroll Services Agreement with the Relamorelin Company. We plan to move to a larger facility as the number of our personnel increases.

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 as of September 30, 2015 and positions of our directors and executive officers. Each executive officer provides services to us pursuant to the Payroll Services Agreement and will become an employee of ours prior to consummation of this offering. Drs. Gottesdiener, Van der Ploeg and Fiedorek and Mr. Henderson will not be contractually obligated to spend a specified number of hours per week providing consulting services to the Relamorelin Company, but their employment letters with us will permit them to render consulting services to the Relamorelin Company, provided that such consulting services do not prevent them from carrying out their duties and responsibilities to us. Each executive officer will be elected annually and will serve until his re-election, or earlier resignation or removal. The executive officers 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.	61	Chief Executive Officer and Director
Bart Henderson	57	President & Founder
Lex H.T. Van der Ploeg, Ph.D.	60	Chief Scientific Officer
Fred T. Fiedorek, M.D.	61	Chief Medical Officer
Todd Foley	44	Director
Ed Mathers	55	Director
Neil Exter	57	Director
Christophe R. Jean	59	Director
Jonathan T. Silverstein, J.D.	48	Director
David Meeker	61	Director
David McGirr	61	Director

Keith M. Gottesdiener, M.D. | *Chief Executive Officer*

Dr. Gottesdiener has been Chief Executive Officer and a member of the board of directors since October 2011. He joined Rhythm 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 is also a director and the chief executive officer of the Relamorelin Company and the LLC entity. 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.

Bart Henderson, MBA | *President & Founder*

Mr. Henderson has been President since February 2010 and is a founder of Rhythm. Previously, he was Entrepreneur-in-Residence at MPM Capital and Chief Business Officer of Radius, where he was a founding employee and led the acquisition of four pipeline programs. Mr. Henderson founded sales and marketing at Vertex when the company launched its first product, broadened its product pipeline, signed corporate partnerships valued at $1.2 billion, and raised $715 million in financing. He founded business development at Microbia (now Ironwood Pharmaceuticals Inc.), which signed its first corporate partnerships and significantly expanded its pipeline during his tenure. Mr. Henderson is also the President and Treasurer of the Relamorelin Company and the LLC entity. In addition, Mr. Henderson held marketing management positions at Amgen and Merck. He holds an MBA from Dartmouth's Tuck School of Business and a B.A. from Amherst College.

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 Rhythm, 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 is also the Chief Scientific Officer of the Relamorelin Company and the LLC entity. 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 is also the Chief Medical Officer of the Relamorelin Company and the LLC entity. 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., Selexys Pharmaceuticals Corp. and Valeritas, 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 Envisia Therapeutics Inc., Intarcia Therapeutics, Inc., Liquidia Technologies, Inc., Lumos Pharma, Inc., Lumena Pharmaceuticals, Inc., Mirna Therapeutics, Inc., Ra Pharmaceuticals, Inc., and Satori Pharmaceuticals Incorporated, 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. 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, 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 2015, *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.

David Meeker

Dr. Meeker has served as a member of our board of directors since November 2015. 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. 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 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 OrbiMed Private Investments V, LP, who is currently Jonathan Silverstein, and who will be continuing as a director following the offering, (v) one director designated by Sutrepa SAS, who is currently Christophe Jean, and who will be continuing as a director following the offering, and (vi) 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 and , and their terms will expire at the annual meeting of stockholders to be held in ;

- our Class II directors will be , and , and their terms will expire at the annual meeting of stockholders to be held in ; and
- our Class III directors will be and , and their terms will expire at the annual meeting of stockholders to be held in .

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

Our board of directors is currently led by our chief executive officer. Our board of directors believes that this leadership structure is the most effective for us at this time. Because our chief executive officer is closest to the many facets of our business, our board of directors believes that the chief executive officer is in the best position to lead our board of directors most effectively. In addition, as the chief executive officer is directly involved in managing the company, and this leadership structure facilitates timely communication with the board on critical business matters. Furthermore, we believe that this leadership structure is appropriate for our company because (i) our chief executive officer conveys a singular, cohesive message to our stockholders, employees, industry partners and the investment community and (ii) this structure eliminates any ambiguity as to who is accountable for the company's performance. Our directors and management team engage frequently and directly in the flow of information and ideas and we believe our leadership structure facilitates the quality, quantity and timeliness of the information flow and communication. Our board of directors believes that there is a well-functioning and effective balance between strong company leadership and oversight by active, independent directors. Our board will consider in the future whether to designate a chair.

Lead Independent Director

Our board of directors has appointed to serve as our lead independent director. As lead independent director, presides over periodic meetings of our independent directors, serves as a liaison between our chief executive officer and the independent directors and performs such additional duties as our board of directors may otherwise determine and delegate.

Board Committees

Prior to the consummation of this offering, our board of directors will establish 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 initial members of our audit committee will be , who will be the chair of the committee, and . 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 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 initial members of our compensation committee will be , who will be the chair of the committee, and . 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 initial members of our governance and nominating committee will be , who will be the chair of the committee, and . 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 has served in various roles at Merck, most recently as Senior Vice President of Global Clinical Development Operations.

Code of Business Conduct and Ethics

We will adopt 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 and Lex H.T. Van der Ploeg, Ph.D. Each of our named executive officers has a letter agreement with the Relamorelin Company, is currently an employee of the Relamorelin Company and provides services to us pursuant to a Payroll Services Agreement with the Relamorelin Company. Each of our our named executive officers will become our full-time employee and will enter into a letter agreement with us prior to consummation of this offering. The compensation discussed below was paid to our executive officers by the Relamorelin Company and the compensation decisions discussed below were made by the compensation committee of the LLC entity's board of managers, 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 2014 to our named executive officers or accrued for those executive officers for services rendered during 2014.

Name & Principal Position	Year	Salary ($)	Non-Equity Incentive Plan Compensation ($)(2)	Total ($)(1)
Keith M. Gottesdiener, M.D. *Chief Executive Officer*	2014	$ 450,882	$ 225,442	$ 676,324
Bart Henderson *President*	2014	$ 320,789	$ 128,316	$ 449,110
Lex H.T. Van der Ploeg, Ph.D.[3] *Chief Scientific Officer*	2014	$ 172,396	$ 34,479	$ 206,875

(1) Reflects compensation for services by the named executive officers. Pursuant to the Payroll Services Agreement, these costs are shared with the Relamorelin Company on a proportional use basis. Costs have been allocated consistent with Staff Accounting Bulletin Topic 1B.

(2) Amounts represent incentive payments earned in 2014 and paid during 2015 based on achievement of performance goals and other factors.

(3) Reflects Dr. Van der Ploeg's part-time employment during 2014.

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

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	2014 Base Salary ($)
Keith M. Gottesdiener, M.D.	450,882
Bart Henderson	320,789
Lex H.T. Van der Ploeg, Ph.D.	172,396

The 2014 base salary for each named executive officer became effective on January 1, 2014.

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 2014 was generally based on the extent to which the officer achieved the corporate goals that the committee established at the beginning of 2014. After the end of 2014, 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 is eligible to receive a target bonus of up to 50% of his base salary, and Dr. Van der Ploeg is eligible to receive a target bonus of up to 20% 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 January 2015, the committee reviewed the 2014 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 2014. For 2014, Dr. Gottesdiener received 100% of his target bonus percentage, for a net bonus of 50% of his base salary, Mr. Henderson received 80% of his target bonus percentage, for a net bonus of 40% of his base salary, and Dr. Van der Ploeg received 100% of his target bonus percentage, for a net bonus of 20% of his base salary.

Pension Benefits

Our named executive officers did not participate in, or otherwise receive any benefits under, any pension or retirement plan during 2014, 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 2014.

Agreements with our Named Executive Officers

Each of our named executive officers is subject to a letter agreement with the Relamorelin Company and we have a Payroll Services Agreement with the Relamorelin Company pursuant to which they provide services to us. Prior to consummation of this offering, each named executive officer will enter into a new letter agreement with us which we anticipate will be on similar terms as the letter agreements described below.

Agreement with Dr. Gottesdiener. Under Dr. Gottesdiener's letter agreement, he is entitled to an annual base salary of at least $450,882, 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 at least $320,789, 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 Dr. Van der Ploeg. Under Dr. Van der Ploeg's letter agreement, he is entitled to an annual base salary of at least $172,396, is eligible to receive an annual target performance bonus of up to 20% of his base salary, as determined by the committee, and will be 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 exceptions, 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, and reimbursement of his medical benefit premiums for up to 12 months. In addition, upon termination Dr. Gottesdiener may exercise each option then outstanding and exercisable, but only until the earlier to occur of (i) the expiration of the term of such option, or (ii) the expiration of the limited period of time set forth in the applicable plan and/or stock option agreement following the termination date.

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, a payment equal to 100% of his annual target bonus for the year in which the termination occurs and reimbursement of his medical benefit premiums for up to 12 months. In addition, each unvested equity award held by Dr. Gottesdiener will immediately become fully vested. Any award with an exercise provision will remain

exercisable until the earlier to occur of (i) the expiration of the term of such option, or (ii) the expiration of the limited period of time set forth in the applicable plan and/or stock option agreement following the termination date.

Mr. Henderson and Dr. Van der Ploeg. Under the terms of each of Mr. Henderson's and Dr. Van der Ploeg's letter agreements, 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, each 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. In addition, upon termination he may exercise each option then outstanding and exercisable, but only until the earlier to occur of (i) the expiration of the term of such option, or (ii) the expiration of the limited period of time set forth in the applicable plan and/or stock option agreement following the termination date.

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 and Dr. Van der Ploeg, in lieu of the above benefits, will each 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, a payment equal to 100% of his annual target bonus for the year in which the termination occurs and reimbursement of his medical benefit premiums for up to 12 months. In addition, each unvested equity award held by the executive will immediately become fully vested. Any award with an exercise provision will remain exercisable until the earlier to occur of (i) the expiration of the term of such option, or (ii) the expiration of the limited period of time set forth in the applicable plan and/or stock option agreement following the termination date.

For purposes of these letter agreements and those we intend to enter into, "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.

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 with the target or its successor.

Employee Benefit and Stock Plans

Amended and Restated 2015 Equity Incentive Plan

We currently have a 2015 equity incentive 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 amended and restated 2015 equity incentive plan, which we refer to herein as the 2015 equity incentive plan, does not purport to be complete and is qualified by reference to the full text of the 2015 equity incentive plan, which we will file as an exhibit to our registration statement of which this prospectus is a part.

The 2015 equity incentive 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 2015 equity incentive plan. Our directors, officers and other employees, as well as others performing consulting or advisory services for us, are eligible for grants under the 2015 equity incentive plan. The purpose of the 2015 equity incentive 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 2015 equity incentive 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 2015 equity incentive plan. The compensation committee may delegate to an executive officer or officers the authority to grant awards under the 2015 equity incentive plan subject to applicable law and to guidelines specified by the compensation committee. Subject to the terms of the 2015 equity incentive 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 2015 equity incentive 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 2015 equity incentive 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 2015 equity incentive 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 2015 equity incentive 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 % 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 2015 equity incentive plan for such year or that the increase in the number of shares of stock authorized under the 2015 equity incentive 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 2015 equity incentive plan exceed

shares of stock. In general, if awards under the 2015 equity incentive 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 2015 equity incentive 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 2015 equity incentive 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 2015 equity incentive 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 each of our CEO and our three most highly compensated employees other than the CEO and CFO to $1.0 million dollars, but excludes from that limit "performance-based compensation." Any form of award permitted under the 2015 equity incentive 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 2015 equity incentive 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 2015 equity incentive 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 2015 equity incentive 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 2015 equity incentive plan, or suspend or terminate it entirely, retroactively or otherwise. However, except as set forth in the 2015 equity incentive plan, we must obtain stockholder approval to increase the number of shares available under the 2015 equity incentive 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 2015 equity incentive 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 2015 equity incentive plan is earlier terminated by our board of directors, the 2015 equity incentive plan terminates immediately prior to the tenth anniversary of the earlier of the adoption of the 2015 equity incentive plan by our board of directors and approval of the 2015 equity incentive 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 2015 equity incentive plan in the future, or the individuals who may be selected to receive such awards because awards under the 2015 equity incentive plan are granted at the discretion of the compensation committee.

2016 Employee Stock Purchase Plan

We expect our board of directors to adopt and our stockholders to approve the 2016 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 the Company. 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, 2026, by an amount equal to the lesser of (i) % of outstanding shares as of the end of the immediately preceding fiscal year and (ii) . 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 % 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

No compensation was paid to or earned by our non-employee directors during our 2014 fiscal year. In , our board of directors adopted a nonemployee 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 fee of $ 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
Chairman of the audit committee	$
Member of the audit committee (other than chairman)	$
Chairman of the compensation committee	$
Member of the compensation committee (other than chairman)	$
Chairman of the governance and nominating committee	$
Member of the governance and nominating committee (other than chairman)	$

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 shares of our common stock under our 2015 equity incentive plan on the date he or she first becomes a nonemployee director. These option grants will vest annually over a four-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 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.

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
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

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 the Relamorelin Company, and we currently have a Payroll Services Agreement with the Relamorelin Company for their services. For information about the employment letters with our named executive officers, refer to "Executive and Director Compensation—Agreements with our Named Executive Officers." Our board members are also members of the boards of the LLC entity and/or the Relamorelin Company. See "Management."

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 December , 2015, 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 December , 2015. 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 December , 2015, assuming the conversion of our outstanding preferred stock into common stock, as if the conversion had occurred as of December , 2015. 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., 855 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:				
Rhythm Holding Company, LLC	93,500,000	70.0%		%
OrbiMed Private Investments V, LP[1] 601 Lexington Avenue, 54th Floor New York, NY 10022-4629	17,500,000	13.1%		%
667, L.P. and Baker Brothers Life Sciences, L.P.[2] 667 Madison Avenue, 21st Floor New York, NY 10065	8,000,000	6.0%		%
Directors and Named Executive Officers:				
Keith M. Gottesdiener, M.D.	—	—		%
Bart Henderson	—	—		%
Lex H.T. Van der Ploeg, Ph.D.	—	—		%
Todd Foley	—	—		%
Ed Mathers	—	—		%
Neil Exter	—	—		%
Christophe R. Jean	—	—		%
Jonathan T. Silverstein, J.D.	—	—		%
David Meeker	—	—		%
David McGirr	—	—		%
All executive officers and directors as a group (10 persons)	—	—		%

* Represents beneficial ownership of less than 1%.

(1) The 17,500,000 shares of series A preferred stock listed above are 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 is a Member of Advisors.

(2) The 8,000,000 shares of series A preferred stock listed above are 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.

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.

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 our 2015 equity incentive 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 the Company's 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 the Company's 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 the Company's stockholders following the closing of this offering.

- Our Class I directors will be and ;
- Our Class II directors will be , and ; and
- Our Class III directors will be , and .

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 of the Company 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 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 intend to apply 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 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 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 consequences, any tax consequences arising under any state, local, or non-U.S. tax laws, the impact of any applicable income 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 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 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 U.S.), 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 U.S.) 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 held 5% or less 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 10% 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 our 2015 equity incentive 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 substantially 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 our 2015 equity incentive 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 and Merrill Lynch, Pierce, Fenner & Smith Incorporated 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	
Piper Jaffray & Co.	
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 and Merrill Lynch, Pierce, Fenner & Smith Incorporated 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 and Merrill Lynch, Pierce, Fenner & Smith Incorporated 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 the Company 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 and Merrill Lynch, Pierce, Fenner & Smith Incorporated, 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.

Directed Share Program

At our request, the underwriters have reserved percent of the shares of common stock to be issued by the Company and offered by this prospectus for sale, at the initial public offering price, to our directors, officers, employees, business associates and related persons. If purchased by these persons, these shares will be subject to a 180-day lock-up restriction. The number of shares of common stock available for sale to the general public will be reduced to the extent these individuals purchase such reserved shares. Any reserved shares that are not so purchased will be offered by the underwriters to the general public on the same basis as the other shares offered by this prospectus.

Selling Restrictions

European Economic Area

In relation to each Member State of the European Economic Area which has implemented the Prospectus Directive, each, a Relevant Member State, an offer to the public of any shares of our common stock may not be made in that Relevant Member State, except that an offer to the public in that Relevant Member State 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 Member State:

(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 Member State 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 Member State 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 Member State by any measure implementing the Prospectus Directive in that Member State, 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 Member State), and includes any relevant implementing measure in the Relevant Member State, 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, 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, 2013 and 2014, 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 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.
INDEX TO FINANCIAL STATEMENTS

	Page
Report of Independent Registered Public Accounting Firm	F-2
Balance Sheets as of December 31, 2013 and 2014 and September 30, 2015 (unaudited)	F-3
Statements of Operations and Comprehensive Loss for the Years Ended December 31, 2013 and 2014 and the Nine Months Ended September 30, 2014 and 2015 (unaudited)	F-4
Statements of Convertible Preferred Stock and Stockholders' Equity (Deficit) for the Years Ended December 31, 2014 and 2015 and the Nine Months Ended September 30, 2015 (unaudited)	F-5
Statements of Cash Flows for the Years Ended December 31, 2013 and 2014 and the Nine Months Ended September 30, 2014 and 2015 (unaudited)	F-6
Notes to Financial Statements	F-7

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

The Board of Directors and Management of
Rhythm Pharmaceuticals, Inc.

We have audited the accompanying balance sheets of Rhythm Pharmaceuticals, Inc. (the "Company") as of December 31, 2013 and 2014, and the related statements of operations and comprehensive loss, convertible preferred stock and stockholders' equity (deficit), and cash flows for each of the two years in the period ended December 31, 2014. 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, 2013 and 2014, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2014, in conformity with U.S. generally accepted accounting principles.

/s/ Ernst & Young LLP

Boston, Massachusetts
October 13, 2015

RHYTHM PHARMACEUTICALS, INC.

BALANCE SHEETS

(in thousands, except share and per share data)

	December 31, 2013	December 31, 2014	September 30, 2015 (unaudited)	Pro Forma September 30, 2015 (unaudited)
Assets				
Current assets:				
Cash and cash equivalents	$ 241	$ 152	$ 23,906	$ 38,906
Prepaid expenses and other current assets	264	42	51	51
Total current assets	505	194	23,957	38,957
Deferred issuance costs	—	—	733	733
Total assets	$ 505	$ 194	$ 24,690	$ 39,690
Liabilities and stockholders' equity (deficit)				
Current liabilities:				
Accounts payable	$ 815	$ 535	$ 949	$ 949
Due to Motus Therapeutics, Inc.	—	—	303	303
Accrued expenses and other current liabilities	1040	17	668	668
Total current liabilities	1,855	552	1,920	1,920
Non-current liabilities				
Series A Investor Right/Obligation and Series A Investor Call Option	—	—	500	—
Total liabilities	1,855	552	2,420	1,920
Stockholders' equity (deficit):				
Series A Convertible Preferred Stock, $1.00 par value: 40,000,000 shares authorized; 25,000,000 shares issued and outstanding at September 30, 2015, no shares issued and outstanding at December 31, 2013, December 31 2014 or September 30, 2015 (pro forma) (aggregate liquidation preferences of $25,318 at September 30, 2015)	—	—	24,476	—
Common stock, $0.001 par value: 150,000,000 shares authorized; 93,500,000 shares issued and outstanding at December 31, 2013, December 31, 2014 and September 30, 2015; 133,500,000 shares issued and outstanding at September 30, 2015 (pro forma)	93	93	93	133
Additional paid-in capital	31,662	39,147	42,229	82,165
Accumulated deficit	(33,105)	(39,598)	(44,528)	(44,528)
Total stockholders' equity (deficit)	(1,350)	(358)	(2,206)	37,770
Total liabilities and stockholders' equity	$ 505	$ 194	$ 24,690	$ 39,690

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, 2013	Year Ended December 31 2014	Nine Months Ended September 30, 2014	Nine Months Ended September 30, 2015
			(unaudited)	
Operating expenses:				
Research and development	$ 10,498	$ 5,280	$ 4,661	$ 3,530
General and administrative	1,701	1,213	1,070	1,400
Total operating expenses	12,199	6,493	5,731	4,930
Loss from operations	12,199	6,493	5,731	4,930
Net Loss and Comprehensive loss	$ (12,199)	$ (6,493)	$ (5,731)	$ (4,930)
Net loss attributable to common stockholders	$ (12,199)	$ (6,493)	$ (5,731)	$ (5,248)
Net loss attributable to common stockholders per common share, basic and diluted	$ (0.13)	$ (0.07)	$ (0.06)	$ (0.06)
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)		$ (0.07)		$ (0.05)
Pro forma weighted average common shares outstanding, basic and diluted (unaudited)		93,500,000		98,830,882

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		Additional Paid-In Capital	Accumulated Deficit	Total Stockholders' and Members' Equity (Deficit)
	Shares	Amounts	Shares	Amount			
Balance at December 31, 2012	—	$ —	—	$ —	$ 20,744	$ (20,906)	$ (162)
Initial issuance of common stock	—	—	93,500,000	93	(93)	—	—
Equity contribution	—	—	—	—	10,884	—	10,884
Stock compensation expense	—	—	—	—	127	—	127
Net loss	—	—	—	—	—	(12,199)	(12,199)
Balance at December 31, 2013	—	—	93,500,000	93	31,662	(33,105)	(1,350)
Equity contribution	—	—	—	—	7,419	—	7,419
Stock compensation expense	—	—	—	—	66	—	66
Net loss	—	—	—	—	—	(6,493)	(6,493)
Balance at December 31, 2014	—	—	93,500,000	93	39,147	(39,598)	(358)
Equity contribution	—	—	—	—	2,094	—	2,094
Stock compensation expense	—	—	—	—	65	—	65
Modification of warrant in connection with a license agreement	—	—	—	—	923	—	923
Issuance of Series A Convertible Preferred Stock	25,000,000	24,476	—	—	—	—	—
Net loss	—	—	—	—	—	(4,930)	(4,930)
Balance at September 30, 2015 (*unaudited*)	25,000,000	$ 24,476	93,500,000	$ 93	$ 42,229	$ (44,528)	$ (2,206)
Settlement of Series A Investor Right/Obligation	—	500	—	—	—	—	—
Issuance of Series A Convertible Preferred Stock	15,000,000	15,000	—	—	—	—	—
Conversion of Series A Convertible Preferred Stock into common stock on a one-to-one basis	(40,000,000)	(39,976)	40,000,000	40	39,936	—	39,976
Pro-forma balance at September 30, 2015 (*unaudited*)	—	$ —	133,500,000	$ 133	$ 82,165	$ (44,528)	$ 37,770

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, 2013	Year Ended December 31, 2014	Nine Months Ended September 30, 2014	Nine Months Ended September 30, 2015
			(unaudited)	
Operating activities				
Net loss	$ (12,199)	$ (6,493)	$ (5,731)	$ (4,930)
Adjustments to reconcile net loss to cash used in operating activities:				
Stock-based compensation expense	127	66	59	65
Modification of warrant in connection with license agreement	—	—	—	923
Changes in operating assets and liabilities:				
Prepaid expenses and other assets	1,227	222	220	(742)
Accounts payable	(700)	(280)	(588)	414
Due to Motus Therapeutics, Inc.	—	—	—	303
Accrued expenses and other current liabilities	902	(1,023)	(702)	651
Net cash used in operating activities	(10,643)	(7,508)	(6,742)	(3,316)
Financing activities				
Net proceeds from issuance of Series A Convertible Preferred Stock	—	—	—	24,976
Equity contribution	10,884	7,419	6,785	2,094
Net cash provided by financing activities	10,884	7,419	6,785	27,070
Net increase (decrease) in cash and cash equivalents	241	(89)	43	23,754
Cash and cash equivalents at beginning of period	—	241	241	152
Cash and cash equivalents at end of period	$ 241	$ 152	$ 284	$ 23,906

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 September 30, 2015 and for the nine months ended September 30, 2014 and 2015 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 metabolic disorders. The Company's lead product candidate is setmelanotide (RM-493), which is a potent, first-in-class, Phase 2 melanocortin-4, or MC4, receptor agonist for the treatment of rare genetic disorders of obesity caused by MC4 pathway deficiencies.

The Company initiated two Phase 2 clinical trials in patients with genetic deficiencies affecting the MC4 pathway during 2015, one for the treatment of obesity in patients with Prader-Willi Syndrome ("PWS"), and one for the treatment of pro-opiomelanocortin ("POMC") deficiency obesity.

Corporate Restructuring

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 Restructuring 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 restructuring, (the "Corporate Restructuring"), 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 Restructuring, 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 Restructuring 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. We refer to the Predecessor Company after consummation of the Corporate Restructuring as the Relamorelin Company.

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

Liquidity

The Company has incurred losses since inception and negative cash flows from operating activities. As of December 31, 2014 and September 30, 2015, the Company entity had an accumulated deficit of $39,598 and $44,528, respectively. The Company anticipates that it will continue to incur significant operating losses for the next several years as it continues to develop setmelanotide. In the future, the Company will be dependent on obtaining funding from third parties, such as proceeds from the issuance of debt, sale of equity, and funded research and development programs, to maintain the Company's operations and meet the Company's obligations. There is no guarantee that additional equity or other financings will be available to the Company on acceptable terms, or at all. If the Company fails to obtain additional funding

Rhythm Pharmaceuticals, Inc.

Notes to Financial Statements (Continued)

(including data applicable to unaudited periods)

(Information as of September 30, 2015 and for the nine months ended September 30, 2014 and 2015 is unaudited)

(In thousands, except share and per share information)

1. Nature of Business (Continued)

when needed, the Company would be forced to scale back, or terminate its operations or seek to merge with or be acquired by another company. Management believes that the Company's existing cash resources, including amounts raised through the issuance of $25,000 of preferred stock in August 2015 (see Note 4), will be sufficient to fund the Company's operating plan through at least the first half of 2017.

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 Restructuring 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 Restructuring, the Company also entered a formal payroll services intercompany agreement with the Relamorelin Company. The Company has no employees. All employees are contracted with the Relamorelin Company, but resources are shared with the Company. 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. 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.

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 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.

Rhythm Pharmaceuticals, Inc.

Notes to Financial Statements (Continued)

(including data applicable to unaudited periods)

(Information as of September 30, 2015 and for the nine months ended September 30, 2014 and 2015 is unaudited)

(In thousands, except share and per share information)

2. Summary of Significant Accounting Policies (Continued)

As described above, Relamorelin Company employee costs are allocated to the Company. For those employees who are anticipated to become employees of the Company in the future, their full employment cost was $2,175, $2,255 and $1,716 for the years ended December 31, 2013 and December 31, 2014 and the nine months ended September 30, 2015, respectively.

The Company is not a party to the lease for the facility it shares with the Relamorelin Company. As a result, it has not presented a lease obligation footnote within the notes to these financial statements.

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 and the valuation allowance on the Company's deferred tax assets.

Unaudited Interim Presentation

The accompanying interim balance sheet as of September 30, 2015, the statements of operations and comprehensive loss and cash flows for the periods ended September 30, 2014 and 2015 and the statement of convertible preferred stock and stockholders' equity (deficit) for the nine months ended September 30, 2015 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 nine months ended September 30, 2014 and 2015 are not necessarily indicative of the results expected for the full fiscal year.

During the three months ended September 30, 2015, the Company identified a $630 overstatement of its research and development expense previously reported for the six months ended June 30, 2014. The correction of the error decreased net loss and research and development expense by $630 for the six months ended June 30, 2014 and decreased basic and diluted net loss per common share by $0.01 per share

Rhythm Pharmaceuticals, Inc.

Notes to Financial Statements (Continued)

(including data applicable to unaudited periods)

(Information as of September 30, 2015 and for the nine months ended September 30, 2014 and 2015 is unaudited)

(In thousands, except share and per share information)

2. Summary of Significant Accounting Policies (Continued)

for the same period. The error had no impact on the audited financial statements for the year ended December 31, 2014.

Unaudited Pro Forma Financial Information

The unaudited pro forma balance sheet and statement of convertible preferred stock and stockholders' equity (deficit) as of September 30, 2015 reflect the closing of the issuance of Series A Convertible Preferred Stock (see Note 11) and the related conversion of the Series A Investor Right/Obligation and termination of the Series A Investor Call Option and, subsequently, the conversion of all the outstanding shares of Series A Convertible Preferred Stock into shares of Common Stock. For the purposes of presenting the unaudited proforma balance sheet and the statement of convertible preferred stock and stockholders' equity (deficit), management has assumed that there was no change in the fair value of the Series A Investor Right/Obligation and Series A Investor Call Option subsequent to September 30, 2015. Any change in the actual fair value as of the closing of the Second Tranche will be recognized in other income/(expense) for the three month period ended December 31, 2015.

Unaudited pro forma net loss per share attributable to common stockholders 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

The Company has no off-balance sheet risk, such as foreign exchange contracts, option contracts, or other foreign hedging arrangements. The Company does not carry an investment portfolio.

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 only include bank demand deposits.

Rhythm Pharmaceuticals, Inc.

Notes to Financial Statements (Continued)

(including data applicable to unaudited periods)

(Information as of September 30, 2015 and for the nine months ended September 30, 2014 and 2015 is unaudited)

(In thousands, except share and per share information)

2. Summary of Significant Accounting Policies (Continued)

Deferred Issuance Costs

Deferred issuance costs, which primarily consist of direct incremental legal and accounting fees relating to the potential IPO, are capitalized. The deferred issuance costs will be offset against initial public offering ("IPO") proceeds upon the consummation of the offering. In the event the offering is terminated, deferred issuance costs will be expensed. No amounts were capitalized as of December 31, 2013 and 2014 and $733 was capitalized at September 30, 2015, and is included in non-current assets.

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.

Series A Investor Right/Obligation and Series A Investor Call Option

The Company classifies its Series A Investor Right/Obligation and its Series A Investor Call Option (see Note 4) as liabilities on its balance sheets as they are free-standing financial instruments. The Series A Investor Right/Obligation and the Series A Investor Call Option were initially recorded at fair value upon the issuance of Series A Convertible Preferred Stock in August 2015, and they are subsequently remeasured to fair value at each balance sheet date. Changes in fair value of the Series A Investor Right/Obligation and the Series A Investor Call Option are recognized as a component of other income (expense), net in the statement of operations and comprehensive loss. The Company will continue to adjust the liabilities for changes in fair value until the earlier of the exercise of the Series A Investor Right/Obligation and Series A Investor Call Option or their expiration. For the period ending September 30, 2015, there was no change in the fair value of the Series A Investor Right/Obligation liability or the Series A Investor Call Option liability.

The Company uses the Black-Scholes option-pricing model, which incorporates assumptions and estimates, to value the Series A Investor Call Option. The Company has assessed these assumptions and estimates on a quarterly basis as additional information impacting the assumptions is 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 Option, risk-free interest rate, expected dividend yield and expected volatility of the price of the underlying preferred stock. The Company determines 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 historically has been a private company and 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 Option. 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 Option. A dividend yield of zero is assumed.

Rhythm Pharmaceuticals, Inc.

Notes to Financial Statements (Continued)

(including data applicable to unaudited periods)

(Information as of September 30, 2015 and for the nine months ended September 30, 2014 and 2015 is unaudited)

(In thousands, except share and per share information)

2. Summary of Significant Accounting Policies (Continued)

The Company has estimated the fair value of the Series A Investor Right/Obligation as the probability-weighted present value of the expected benefit of the investment (see Note 5).

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 cost, 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 Restructuring, 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 Restructuring. 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

Rhythm Pharmaceuticals, Inc.

Notes to Financial Statements (Continued)

(including data applicable to unaudited periods)

(Information as of September 30, 2015 and for the nine months ended September 30, 2014 and 2015 is unaudited)

(In thousands, except share and per share information)

2. Summary of Significant Accounting Policies (Continued)

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 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 nine months ended September 30, 2014 and 2015 (unaudited) 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. The unaudited pro forma information reflects the automatic conversion, at the closing of a qualified public offering, of the Company's Preferred Stock into shares of Common Stock.

Basic and diluted earnings per share is calculated as follows:

	Year Ended December 31,		Nine Months Ended September 30,	
	2013	2014	2014 (unaudited)	2015 (unaudited)
Numerator:				
Net loss	$ (12,199)	$ (6,493)	$ (5,731)	$ (4,930)
Cumulative dividends on convertible preferred shares	—	—	—	(318)
Loss attributable to common shares—basic and diluted	$ (12,199)	$ (6,493)	$ (5,731)	$ (5,248)
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)	$ (0.07)	$ (0.06)	$ (0.06)

Rhythm Pharmaceuticals, Inc.

Notes to Financial Statements (Continued)

(including data applicable to unaudited periods)

(Information as of September 30, 2015 and for the nine months ended September 30, 2014 and 2015 is unaudited)

(In thousands, except share and per share information)

2. Summary of Significant Accounting Policies (Continued)

Pro forma earnings per share is computed as follows:

	Year Ended December 31, 2014	Nine Months Ended September 30, 2015
	(unaudited)	
Numerator:		
Net loss attributable to common shares—basic and diluted	$ (6,493)	$ (4,930)
Add: Cumulative dividends on convertible preferred shares	—	—
Net loss attributable to common stockholders—basic and diluted	$ (6,493)	$ (4,930)
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	—	5,330,882
Pro forma weighted-average shares outstanding	93,500,000	98,830,882
Pro forma net loss per share—basic and diluted	$ (0.07)	$ (0.05)

Patent Costs

Costs to secure and defend patents are expensed as incurred and are classified as general and administrative expenses. Patent costs were $121 and $142 for the years ended December 31, 2013 and 2014, and $127 and $77 for the nine months ended September 30, 2014 and 2015, 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.

On April 5, 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 has 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.

During the quarter ended September 30, 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

Rhythm Pharmaceuticals, Inc.

Notes to Financial Statements (Continued)

(including data applicable to unaudited periods)

(Information as of September 30, 2015 and for the nine months ended September 30, 2014 and 2015 is unaudited)

(In thousands, except share and per share information)

2. Summary of Significant Accounting Policies (Continued)

are issued. The standard will be effective for the first interim period within annual reporting periods beginning after December 15, 2016. Early adoption is permitted. The Company is currently evaluating the potential impact that ASU No. 2014-15 may have on its financial position and results of operations.

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 matters that require additional disclosure. Subsequent events have been evaluated as required. See Note 11.

3. Accrued Expenses

Accrued expenses consisted of the following:

	Year ended December 31,		Nine months ended September 30,
	2013	2014	2015
Research and development costs	$ 1,040	$ 17	$ 22
Other	—	—	646
Accrued expenses	$ 1,040	$ 17	$ 668

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 Series A Preferred Stock Purchase Agreement provides 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 will automatically be settled upon the achievement of a specific milestone, resulting in the issuance of shares of Series A Convertible Preferred Stock (the "Series A Investor Right/Obligation") (see Note 11). The Series A Investor Call Option becomes exercisable in the event that a Second Tranche Closing has not been consummated. Both the Series A Investor Right/Obligation and the Series A Investor Call Option have been evaluated and determined to be free standing instruments and are being accounted as liabilities (see Note 2). Upon the closing of an initial public offering with a minimum price per share and gross proceeds of at least $1.00 and $50 million, respectively, the Series A Convertible Preferred Stock will automatically convert into shares of common stock on a 1-for-1 basis.

Rhythm Pharmaceuticals, Inc.

Notes to Financial Statements (Continued)

(including data applicable to unaudited periods)

(Information as of September 30, 2015 and for the nine months ended September 30, 2014 and 2015 is unaudited)

(In thousands, except share and per share information)

4. Preferred Stock (Continued)

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 daily and compound 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 September 30, 2015, 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 September 30, 2015, cumulative preference dividends amounted to $318, or $0.01 per share.

Liquidation

In the event of any liquidation, dissolution or winding-up of the Company, 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

Rhythm Pharmaceuticals, Inc.

Notes to Financial Statements (Continued)

(including data applicable to unaudited periods)

(Information as of September 30, 2015 and for the nine months ended September 30, 2014 and 2015 is unaudited)

(In thousands, except share and per share information)

4. Preferred Stock (Continued)

shall be deemed to be a liquidation event. A sale, exclusive license, transfer or other disposition of all or substantially all of the assets of the Company shall also be deemed a 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 September 30, 2015, the liquidation preference of the outstanding shares of Series A Convertible Preferred Stock was approximately $25,318.

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 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 in the event of any stock dividend, stock split, combination or recapitalization affecting the Series A Convertible Preferred Stock. As of September 30, 2015, the outstanding shares of Series A Convertible Preferred Stock were convertible into 25,000,000 shares of common stock.

5. Fair Value of Financial Liability

For the years ended December 31, 2014 and 2013, the Company had no financial assets or liabilities. The first financial liability was recognized during the nine months ending September 30, 2015. The following tables present information about the Company's financial liability 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 September 30, 2015 Using:			
	Level 1	Level 2	Level 3	Total
Series A Investor Right/Obligation and Series A Investor Call Option	$ —	$ —	$ 500	$ 500
Total	$ —	$ —	$ 500	$ 500

Rhythm Pharmaceuticals, Inc.

Notes to Financial Statements (Continued)

(including data applicable to unaudited periods)

(Information as of September 30, 2015 and for the nine months ended September 30, 2014 and 2015 is unaudited)

(In thousands, except share and per share information)

5. Fair Value of Financial Liability (Continued)

The liability in the table above is based on significant inputs not observable in the market, which represents a Level 3 measurement within the fair value hierarchy (see Note 4).

	Series A Investor Right/Obligation And Series A Investor Call Option	Total
Fair value at December 31, 2014	$ —	$ —
Initial fair value	$ 500	$ 500
Change in fair value	—	—
Fair value at September 30, 2015	$ 500	$ 500

The following assumptions and inputs were used in determining the fair value of the Series A Investor Call Option valued using the Black-Scholes option pricing model:

	September 30, 2015
Series A Convertible Preferred Stock Exercise Price	$1.00
Series A Convertible Preferred Stock Fair Value	$0.81
Expected term	2 months
Expected volatility	22.0%
Risk-free interest rate	0.01%
Expected dividend rate	0%

The Company has estimated the fair value of the 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 through a backsolve calculation which assumes a 70 percent probability of closing, a discount rate of 17.1% and a second tranche closing date of November 30, 2015. The discount rate is estimated using the capital asset pricing model.

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, 2014 and September 30, 2015, 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

Rhythm Pharmaceuticals, Inc.

Notes to Financial Statements (Continued)

(including data applicable to unaudited periods)

(Information as of September 30, 2015 and for the nine months ended September 30, 2014 and 2015 is unaudited)

(In thousands, except share and per share information)

6. Common Stock (Continued)

and outstanding as of September 30, 2015. The Company has reserved 16,500,000 shares of common stock for issuance to officers, directors, employees and consultants of the Company pursuant to 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, no shares have been issued pursuant to restricted stock purchase agreements, no options to purchase shares of common stock have been granted, and 16,500,000 shares of common stock remain available for issuance to officers, directors, employees and consultants pursuant to the 2015 Stock Incentive Plan (the "Plan").

7. Stock-based Compensation

2015 Stock Incentive Plan

The Plan was approved by the Company's Board of Directors in August 2015. 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. The Company has reserved 16,500,000 shares of common stock. There have been no grants under the Plan through September 30, 2015 (see Note 11). 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.

The LLC entity's stock compensation expense has been allocated to the Company using the same proportional use basis as outlined in Note 2 for other shared costs. Prior to August 2015, the Company did not have its own stock-based compensation plan. The following table summarizes the classification of the Company's stock-based compensation expenses recognized in the Company's statements of operations and comprehensive loss.

	Year Ended December 31,		Nine Months Ended September 30,	
	2013	2014	2014	2015
			(unaudited)	
Research and development	$ 37	$ 23	$ 21	$ 45
General and administrative	90	43	38	20
Total	$ 127	$ 66	$ 59	$ 65

The remainder of this Note discloses the stock-based compensation activity of the Predecessor Company and the LLC entity.

Rhythm Pharmaceuticals, Inc.

Notes to Financial Statements (Continued)

(including data applicable to unaudited periods)

(Information as of September 30, 2015 and for the nine months ended September 30, 2014 and 2015 is unaudited)

(In thousands, except share and per share information)

7. Stock-based Compensation (Continued)

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 Restructuring, 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 vesting terms as originally granted in the particular option agreement. Any unvested portion of the stock option at the Corporate Restructuring 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 Restructuring 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 Restructuring, 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-to-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 Restructuring 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 Restructuring 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 Restructuring.

All restricted common units granted subsequent to the Corporate Restructuring 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 September 30, 2015 and for the nine months ended September 30, 2014 and 2015 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, 2014 is as follows:

	Number of Units	Weighted-Average Grant Date Fair Value Per Unit
Outstanding unvested as of December 31, 2013	298,783	$ 1.21
Granted	—	—
Vested	(119,758)	1.21
Cancelled	(13,964)	1.21
Outstanding unvested as of December 31, 2014	165,061	1.21

The LLC entity recorded total stock-based compensation expense for stock options and restricted common units granted to employees, directors and non-employees of $254, $161, $125 and $254 during the years ended December 31, 2013 and 2014 and the nine months ended September 30, 2014 and 2015, respectively. As of December 31, 2014 and September 30, 2015, unrecognized compensation cost of $199 and $556, respectively, related to non-vested employee stock-based compensation arrangements is expected to be recognized over weighted-average periods of 0.6 and 1.6 years, respectively.

Restricted Common Unit Grants to Non-Employees

During the year ended December 31, 2013, and the nine months ended September 30, 2015 subsequent to the Corporate Restructuring, 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. Stock-based compensation expense of $2, $17, $17 and $24 was recorded for the years ended December 31, 2013 and 2014 and the nine months ended September 30, 2014 and 2015, respectively, relating to non-employee and option awards.

Rhythm Pharmaceuticals, Inc.

Notes to Financial Statements (Continued)

(including data applicable to unaudited periods)

(Information as of September 30, 2015 and for the nine months ended

September 30, 2014 and 2015 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 is in Phase 2 clinical trials. As a result of the Corporate Restructuring 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.

9. Related-Party Transactions

The Company shares 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 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. These costs totaled $20,744, $5,059, $1,765, $1,424 and $564 prior to December 31, 2012 and for the years ended December 31, 2013 and 2014 and for the nine months ended September 30, 2014 and 2015, respectively. From August 1, 2015, Company expenses paid by the Relamorelin Company on behalf of the Company amounted to $303 and were recorded as liability. 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 Motus 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

Rhythm Pharmaceuticals, Inc.

Notes to Financial Statements (Continued)

(including data applicable to unaudited periods)

(Information as of September 30, 2015 and for the nine months ended

September 30, 2014 and 2015 is unaudited)

(In thousands, except share and per share information)

9. Related-Party Transactions (Continued)

entity totaled $0, $5,952, $5,720, $5,420 and $1,595 prior to December 31, 2012 and for the years ended December 31, 2013 and 2014 and for the nine months ended September 30, 2014 and 2015, respectively. There were no cash transfers in the period from August 1, 2015 to September 30, 2015. 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, 2012, 2013 and 2014 and September 30, 2015, these capital contributions totaled $20,744, $31,662, $39,147 and $42,229, 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 $241, $178, $108 and $144 for the years ended December 31, 2013 and 2014 and for the nine months ended September 30, 2014 and 2015, respectively.

The LLC entity also engaged Ipsen to perform development services. The LLC entity paid $26, $0, $0 and $0 for the years ended December 31, 2013 and 2014, and for the nine months ended September 30, 2014 and 2015, respectively, for services performed. Ispen is also a shareholder of the LLC entity.

10. 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 Restructuring, 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 Restructuring.

For the years ended December 31, 2013 and 2014, and nine months ending September 30, 2014 and 2015, 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.

A reconciliation of the income tax expense at the federal statutory tax rate to the Company's effective income tax rate follows:

	Year Ended December 31,	
	2013	2014
Statutory tax rate	34.00%	34.00%
State tax, net of federal benefit	5.24%	5.21%
Research and development credit	4.88%	3.19%
Other	(0.28)%	(0.36)%
Change in valuation allowance	(43.84)%	(42.04)%
Effective tax rate	0.00%	0.00%

Rhythm Pharmaceuticals, Inc.

Notes to Financial Statements (Continued)

(including data applicable to unaudited periods)

(Information as of September 30, 2015 and for the nine months ended

September 30, 2014 and 2015 is unaudited)

(In thousands, except share and per share information)

10. Income Tax (Continued)

The principal components of the Company's deferred tax assets are as follows:

	As of December 31,	
	2013	2014
Deferred tax assets:		
Net operating loss carryforwards	$ 3,772	$ 5,979
Research and development credits	595	802
Capitalized license fee	244	278
Total gross deferred tax assets	4,611	7,059
Deferred tax liability	—	—
Valuation allowance	(4,611)	(7,059)
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, 2013 and 2014 and for the nine months ending September 30, 2014 and 2015, 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 $4,611 in 2013 and $2,448 in 2014 primarily relates to the net loss incurred by the Company during each period.

As of December 31, 2013, the Company had federal and state net operating loss carryforwards of approximately $11,000 and $2,000, respectively which are available to reduce future taxable income. As of December 31, 2014, the Company had federal and state net operating loss carryforwards of approximately $17,000 and $3,000, 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.

As of December 31, 2013, the Company had federal and state tax credits of approximately $403 and $292, respectively, which may be used to offset future tax liabilities. As of December 31, 2014, the Company had federal and state tax credits of approximately $596 and $313, respectively, which may be used to offset future tax liabilities. 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

Rhythm Pharmaceuticals, Inc.

Notes to Financial Statements (Continued)

(including data applicable to unaudited periods)

(Information as of September 30, 2015 and for the nine months ended

September 30, 2014 and 2015 is unaudited)

(In thousands, except share and per share information)

10. Income Tax (Continued)

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, 2013 and 2014 and for September 30, 2015. 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, 2013, and December 31, 2014 and September 30, 2015, 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.

11a. Subsequent Events

The Company has completed an evaluation of all subsequent events after the audited balance sheet date of December 31, 2014 through October 13, 2015, 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, 2014, and events which occurred subsequently but were not recognized in the financial statements.

11b. Subsequent Events (unaudited)

The Company has completed an evaluation of all subsequent events after the unaudited balance sheet date of September 30, 2015 through December 9, 2015, 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 September 30, 2015, and events which occurred subsequently but were not recognized in the financial statements.

In November 2015, the Company executed an office lease agreement for which occupancy begins in April 2016 and extends through a five year term. Total payments due pursuant to the lease are approximately $1.5 million.

In November 2015, the Company granted 7,000,519 common stock options to certain of it's employees and non-employees. These options had an exercise price of $0.50 per share and vest over three to four years.

In December 2015, pursuant to the Series A Convertible Preferred Stock Purchase Agreement, by and among the Company and certain Purchasers (as defined therein), and upon the achievement of the Second Tranche Milestone, the Company issued 15,000,000 shares of Series A Convertible Preferred Stock, par value $0.001 per share, at a purchase price of $1.00 per share, resulting in gross proceeds of $15,000 to the Company.

* * * * * *

Table of Contents

Shares

Common Stock

PRELIMINARY PROSPECTUS

MORGAN STANLEY *BofA MERRILL LYNCH* *PIPER JAFFRAY*

NEEDHAM

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.

, 2015

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	$ *
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, and December 1, 2015 we issued 25,000,000 shares and 15,000,000 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.

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.

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 the dates indicated.

RHYTHM PHARMACEUTICALS, INC.

By: _____

Keith M. Gottesdiener
Chief Executive Officer

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Keith M. Gottesdiener and Bart Henderson 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
_____ Keith M. Gottesdiener	Chief Executive Officer and Director (Principal Executive Officer)	, 2015
_____ Bart Henderson	President (Principal Financial and Accounting Officer)	, 2015
_____ Neil Exter	Director	, 2015
_____ Todd Foley	Director	, 2015
_____ Christophe R. Jean	Director	, 2015

Name	Title	Date
Ed Mathers	Director	, 2015
Jonathan T. Silverstein	Director	, 2015
David P. Meeker	Director	, 2015
David W. J. McGirr	Director	, 2015

EXHIBIT INDEX

Number	Description
1.1*	Form of Underwriting Agreement.
3.1*	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*	Investors' Rights Agreement, dated August 3, 2015, 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 , 2015, by and between the Registrant and Bart Henderson.
10.4†*	Offer Letter, dated , 2015, by and between the Registrant and Keith M. Gottesdiener.
10.5†*	Offer Letter, dated , 2015, by and between the Registrant and Lex Van der Ploeg.
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 Peptisyntha SA).
10.8*	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.
10.9†*	Rhythm Pharmaceuticals, Inc. 2016 Employee Stock Purchase Plan.
10.10*	Lease, dated November 25, 2015, by and between 500 Boylston & 222 Berkeley Owner (DE) LLC and the Registrant.
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.

** Previously submitted.

† 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.