UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-Q

☒ **QUARTERLY REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the quarterly period ended March 31, 2018
OR

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the transition period from to
Commission file number 001-38223

RHYTHM PHARMACEUTICALS, INC.

(Exact name of registrant as specified in its charter)

Delaware	**46-2159271**
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)

500 Boylston Street
11th Floor
Boston, MA 02116
(Address of principal executive offices)
(Zip Code)

(857) 264-4280
(Registrant's telephone number, including area code)

Unchanged
(Former name, former address and former fiscal year, if changed since last report)

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15 (d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ☒ No ☐
Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes ☒ No ☐
Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

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

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☒
Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes ☐ No ☒.

The number of shares outstanding of the registrant's Common Stock as of May 11, 2018 was 27,530,184.

RHYTHM PHARMACEUTICALS, INC.

FORM 10-Q

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PART I – FINANCIAL INFORMATION

Item 1. Financial Statements.

Rhythm Pharmaceuticals, Inc.

Condensed Consolidated Balance Sheets

(in thousands, except share and per share data)

	(Unaudited) March 31, 2018	December 31, 2017
Assets		
Current assets:		
Cash and cash equivalents	$ 43,167	$ 34,236
Short-term investments	93,286	113,846
Prepaid expenses and other current assets	1,961	2,589
Total current assets	138,414	150,671
Property, plant and equipment, net	779	840
Restricted cash	250	225
Total assets	$ 139,443	$ 151,736
Liabilities, convertible preferred stock and stockholders' equity		
Current liabilities:		
Accounts payable	$ 2,456	$ 2,427
Deferred rent	85	83
Accrued expenses and other current liabilities	3,038	4,210
Total current liabilities	5,579	6,720
Long-term liabilities:		
Deferred rent	206	228
Total liabilities	5,785	6,948
Commitments and contingencies		
Preferred stock:		
Convertible Preferred Stock, $0.001 par value: 10,000,000 shares authorized; no shares issued and outstanding at March 31, 2018 and December 31, 2017, respectively	—	—
Stockholders' equity:		
Common stock, $0.001 par value: 120,000,000 shares authorized; 27,284,140 shares issued and outstanding March 31, 2018 and December 31, 2017, respectively	27	27
Additional paid-in capital	260,342	255,013
Accumulated deficit	(126,711)	(110,252)
Total stockholders' equity	133,658	144,788
Total liabilities, convertible preferred stock and stockholders' equity	$ 139,443	$ 151,736

The accompanying notes are an integral part of these financial statements

Rhythm Pharmaceuticals, Inc.

Condensed Consolidated Statements of Operations and Comprehensive Loss

(in thousands, except share and per share data)

(Unaudited)

	Three months ended March 31,	
	2018	2017
Operating expenses:		
Research and development	$ 12,286	$ 4,873
Selling, general, and administrative	4,715	1,516
Total operating expenses	17,001	6,389
Loss from operations	(17,001)	(6,389)
Other income (expense):		
Interest income, net	542	29
Total other income (expense):	542	29
Net loss and comprehensive loss	$ (16,459)	$ (6,360)
Net loss attributable to common stockholders	$ (16,459)	$ (7,526)
Net loss attributable to common stockholders per common share, basic and diluted	$ (0.60)	$ (0.74)
Weighted average common shares outstanding, basic and diluted	27,284,140	10,196,292

The accompanying notes are an integral part of these financial statements

Rhythm Pharmaceuticals, Inc.

Condensed Consolidated Statements of Cash Flows

(in thousands, except share and per share data)

(Unaudited)

	Three months ended March 31,	
	2018	2017
Operating activities		
Net loss	$ (16,459)	$ (6,360)
Adjustments to reconcile net loss to cash used in operating activities:		
Non-cash research and development license expense	4,448	—
Stock-based compensation expense	958	264
Depreciation and amortization	61	54
Non-cash rent expense	(20)	(18)
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	581	(305)
Deferred issuance costs	—	(82)
Accounts payable, accrued expenses and other current liabilities	(1,220)	(464)
Due to related parties	—	(105)
Net cash used in operating activities	(11,651)	(7,016)
Investing activities		
Purchases of short-term investments	(2,023)	(12,009)
Maturities of short-term investments	22,630	3,990
Purchases of property, plant and equipment	—	—
Net cash provided by (used in) investing activities	20,607	(8,019)
Financing activities		
Net proceeds from issuance of Series A Convertible Preferred Stock	—	20,377
Net cash provided by financing activities	—	20,377
Net increase (decrease) in cash, cash equivalents and restricted cash	8,956	5,342
Cash, cash equivalents and restricted cash at beginning of year	34,461	6,765
Cash, cash equivalents and restricted cash at end of year	$ 43,417	$ 12,107

The accompanying notes are an integral part of these financial statements

Rhythm Pharmaceuticals, Inc.

Notes to Unaudited Condensed Consolidated Financial Statements

(In thousands, except share and per share information)

1. Nature of Business

Rhythm Pharmaceuticals, Inc. (the "Company"), is a biopharmaceutical company focused on the development and commercialization of peptide therapeutics for the treatment of genetic deficiencies that result in life-threatening metabolic disorders. The Company's lead product candidate is setmelanotide ("RM-493"), which is a potent, first-in-class, melanocortin-4, or MC4, receptor, agonist for the treatment of rare genetic disorders of obesity caused by MC4 pathway deficiencies. The Company is currently evaluating setmelanotide for the treatment of six genetic disorders of obesity: pro-opiomelanocortin, or POMC, leptin receptor, or LepR, Bardet-Biedl syndrome, Alström syndrome, POMC heterozygous, and POMC epigenetic disorders.

In March 2018 the Company acquired exclusive, worldwide rights from Takeda Pharmaceutical Company Limited ("Takeda") to develop and commercialize T-3525770 (now "RM-853"). RM-853 is a potent, orally available ghrelin o-acyltransferase ("GOAT") inhibitor currently in preclinical development for Prader-Willi Syndrome ("PWS"). PWS is a rare genetic disorder that results in hyperphagia and early-onset, life-threatening obesity, for which there are no approved therapeutic options.

Corporate Reorganization

The Company is a Delaware corporation organized in February 2013 under the name Rhythm Metabolic, Inc. Prior to the Company's organization and the Corporate Reorganization referred to below, the Company was part of Rhythm Pharmaceuticals, Inc. (the "Predecessor Company"), a Delaware corporation which was organized in November 2008 and which commenced active operations in 2010.

In March 2013, the Predecessor Company underwent a corporate reorganization, (the "Corporate Reorganization"), pursuant to which all of the outstanding equity securities of the Predecessor Company were exchanged for units of Rhythm Holding Company, LLC, a newly-organized limited liability company (the "LLC entity"). After the consummation of this exchange and as part of the Corporate Reorganization, the Predecessor Company contributed setmelanotide and the MC4R agonist program to the Company and distributed to the LLC entity all of the then issued and outstanding shares of the Company's stock. The result of the Corporate Reorganization was that the Company and the Predecessor Company became wholly-owned subsidiaries of the LLC entity and the two product candidates and related programs that were originally held by the Predecessor Company were separated, with relamorelin and the ghrelin agonist program being retained by the Predecessor Company and setmelanotide and the MC4R agonist program being held by the Company. The Predecessor Company, after consummation of the Corporate Reorganization, is referred to within these Notes to Financial Statements as the Relamorelin Company and/or Motus.

On October 13, 2015, the Relamorelin Company changed its name to Motus Therapeutics, Inc. ("Motus") and the Company changed its name to Rhythm Pharmaceuticals, Inc. On December 15, 2016, Motus was sold to a large pharmaceutical company. On August 21, 2017, the LLC entity distributed to its members all of its shares of the Company (see Note 5 for further discussion).

Liquidity

The Company has incurred operating losses and negative cash flows from operations since inception. As of March 31, 2018, the Company had an accumulated deficit of $126,711. The Company has primarily funded these losses through capital contributions received from the LLC entity and the sale of preferred and common stock to outside investors. To date, the Company has no product revenue and management expects operating losses to continue for the foreseeable future. The Company has devoted substantially all of its resources to its drug development efforts, comprising research and development, manufacturing, conducting clinical trials for its product candidates, protecting its intellectual property

and general and administrative functions relating to these operations. The future success of the Company is dependent on its ability to develop its product candidates and ultimately upon its ability to attain profitable operations. At March 31, 2018, the Company had $136,453 of cash and cash equivalents and short-term investments on hand. 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 when needed, the Company would be forced to scale back, terminate its operations or seek to merge with or be acquired by another company. Management believes that the Company's existing cash resources will be sufficient to fund the Company's operating plan into the second half of 2019.

2. Summary of Significant Accounting Policies

Basis of Presentation

The Company's unaudited condensed consolidated financial statements have been prepared in conformity with accounting principles generally accepted in the United States (“GAAP”) and the applicable rules and regulations of the Securities and Exchange Commission (“SEC”) regarding interim financial reporting. 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”). As permitted under these rules, certain footnotes or other financial information that are normally required by GAAP have been condensed or omitted.

The accompanying interim balance sheet as of March 31, 2018, the statements of operations and comprehensive loss for the three months ended March 31, 2018 and 2017, the statement of cash flows for the three months ended March 31, 2018 and 2017 and the related footnote disclosures are unaudited. 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 all normal recurring adjustments necessary for the fair presentation of the interim financial statements. The results for the three months ended March 31, 2018 are not necessarily indicative of the results expected for the full fiscal year.

The Company has historically existed and functioned as part of the consolidated businesses of the Predecessor Company. As noted above, the Predecessor Company's setmelanotide and the MC4R agonist program were transferred to the Company as part of the Corporate Reorganization on March 21, 2013. These financial statements include the results of operations of setmelanotide and the MC4R agonist program from its inception.

On September 22, 2017, the Company's board of directors approved a 1-for-9.17 reverse 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 reverse stock split.

On October 5, 2017, 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 120,000,000 shares of common stock, $0.001 par value per share and 10,000,000 shares of preferred stock, $0.001 par value per share.

On October 10, 2017 the Company completed its initial public offering (“IPO”) of 8,107,500 shares of common stock at an offering price of $17.00 per share, which included the exercise in full by the underwriters of their option to purchase up to 1,057,500 additional shares of common stock. The Company received gross proceeds of approximately $137,828 or net proceeds of $125,658 after deducting underwriting discounts, commissions and estimated offering expenses. In connection with the IPO, the Company’s outstanding shares of convertible preferred stock were automatically converted into 17,406,338 shares of common stock.

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 accrued expenses, stock-based compensation expense, the valuation allowance on the Company's deferred tax assets, and the fair value of the Series A Investor Instrument (see Note 4).

Principles of Consolidation

The consolidated financial statements include the accounts of Rhythm Pharmaceuticals, Inc. and its subsidiaries. All significant intercompany balances and transactions have been eliminated in consolidation.

Off-Balance Sheet Risk and Concentrations of Credit Risk

Financial instruments, which potentially subject the Company to significant concentration of credit risk, consist primarily of cash and cash equivalents and short-term investments, which are maintained at two federally insured financial institutions. The deposits held at these two institutions are in excess of federally insured limits. The Company has not experienced any losses in such accounts and management believes that the Company is not exposed to significant credit risk due to the financial position of the depository institutions in which those deposits are held. The Company has no off-balance sheet risk, such as foreign exchange contracts, option contracts, or other foreign hedging arrangements.

Segment Information

Operating segments are defined as components of an entity about which separate discrete information is available for evaluation by the chief operating decision maker, or decision-making group, in deciding how to allocate resources and in assessing performance. The Company views its operations and manages its business in one operating segment operating exclusively in the United States.

2017 Series A Investor Instrument

The Company has classified its 2017 Series A Investor Instrument (See Note 4) as a liability as it is a free-standing financial instrument. The 2017 Series A Investor Instrument was recorded at fair value upon the issuance of the Company’s series A preferred stock in January 2017, and subsequently remeasured to fair value at each reporting period. Changes in fair value of the financial instrument is recognized as a component of other income (expense), net in the statement of operations and comprehensive loss. The Company estimated the fair value of the 2017 Series A Investor Right/Obligation as the probability-weighted present value of the expected benefit of the investment.

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

Net Loss Per Share Attributable to Common Shareholders

Basic net loss per share attributable to common stockholders is calculated by dividing net loss attributable to common stockholders by the weighted average shares outstanding during the period, without consideration for Common Stock equivalents. Net loss attributable to common stockholders is calculated by adjusting the net loss of the Company for cumulative preferred stock dividends. During periods of income, the Company allocates participating securities a proportional share of income determined by dividing total weighted average participating securities by the sum of the total weighted average common shares and participating securities (the “two class method”). The Company's convertible preferred stock participates in any dividends declared by the Company and are therefore considered to be participating securities. Participating securities have the effect of diluting both basic and diluted earnings per share during periods of income. During periods of loss, the Company allocates no loss to participating 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.

The following table includes the potential common shares, presented based on amounts outstanding at each period end, that were excluded from the computation of diluted net loss per share attributable to common stockholders for the periods indicated:

	Three Months Ended March 31,	
	2018	2017
Stock options	2,427,629	1,037,131
Series A convertible preferred shares	—	6,594,870
Total	2,427,629	7,632,001

Basic and diluted earnings per share is calculated as follows:

	Three Months Ended March 31,	
	2018	2017
Numerator:		
Net loss	$ (16,459)	$ (6,360)
Cumulative dividends on convertible preferred shares	—	(1,166)
Loss attributable to common shares—basic and diluted	$ (16,459)	$ (7,526)
Denominator:		
Weighted-average number of common shares—basic and diluted	27,284,140	10,196,292
Loss per common share—basic and diluted	$ (0.60)	$ (0.74)

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.

Application of New or Revised Accounting Standards

From time to time, new accounting pronouncements are issued by the FASB and adopted by the Company as of the specified effective date. Unless otherwise discussed, the Company believes that the impact of recently issued standards that are not yet effective will not have a material impact on its financial position or results of operations upon adoption.

In April 2012, the Jump-Start Our Business Startups Act (the "JOBS Act") was signed into law. The JOBS Act contains provisions that, among other things, reduce certain reporting requirements for an "emerging growth company." As an emerging growth company, the Company elected to not take advantage of the extended transition period afforded by the JOBS Act for the implementation of new or revised accounting standards, and as a result, will comply with new or revised accounting standards on the relevant dates on which adoption of such standards is required for non-emerging growth companies.

In February 2016, the FASB issued ASU 2016-02, Leases (Topic 842). ASU 2016-02 requires lessees to recognize lease assets and lease liabilities for those leases classified as operating leases under previous GAAP. A lessee should recognize in the statement of financial position a liability to make lease payments (the lease liability) and a right-of-use asset representing its right to use the underlying asset for the lease term. For leases with a term of 12 months or less, a lessee is permitted to make an accounting policy election by class of underlying asset not to recognize lease assets and lease liabilities. The recognition, measurement, and presentation of expenses and cash flows arising from a lease by a lessee have not significantly changed from previous GAAP. There continues to be a differentiation between finance leases and operating leases. ASU 2016-02 is effective for fiscal years beginning after December 15, 2018, and interim periods within those fiscal years, and early adoption is permitted. The Company is currently in the process of evaluating the impact of adoption of ASU No. 2016-02 on its financial position and results of operations.

In November 2016, the FASB issued ASU No. 2016-18, Statement of Cash Flows (Topic 230): Restricted Cash ("ASU 2016-18") that changes the presentation of restricted cash and cash equivalents on the statement of cash flows. Restricted cash and restricted cash equivalents will be included with cash and cash equivalents when reconciling the beginning-of-period and end-of-period total amounts shown on the statement of cash flows. This amendment is effective for fiscal years beginning after December 15, 2017, including interim periods within those fiscal years. Early adoption is permitted, including adoption in an interim period. The adoption of this ASU did not have a material impact on the Company's statements of cash flows.

In May 2017, the FASB issued ASU 2017-09, Compensation-Stock Compensation (Topic 718): Scope of Modification Accounting, ("ASU 2017-09"). ASU 2017-09 provides clarity and reduces both (1) diversity in practice and (2) cost and complexity when applying the guidance in Topic 718, to a change to the terms or conditions of a share-based payment award. The amendments in ASU 2017-09 should be applied prospectively to an award modified on or after the adoption date. This ASU is effective for fiscal years, and interim periods within those years, beginning after December 15, 2017. The adoption of this ASU did not have a material impact on the Company's financial position or results of operations.

3. Accrued Expenses

Accrued expenses consisted of the following:

	March 31, 2018	December 31, 2017
Research and development costs	$ 1,426	$ 2,771
Professional fees	1,137	327
Payroll related	462	1,094
Other	13	18
Accrued expenses	$ 3,038	$ 4,210

4. Fair Value of Financial Assets and Liability

As of March 31, 2018 and December 31, 2017, the carrying amount of cash and cash equivalents and short-term investments was $136,453 and $148,082, respectively, which approximates fair value. Cash and cash equivalents and short-term investments includes investments in money market funds that invest in U.S. government securities that are valued using quoted market prices. Accordingly, money market funds and government funds are categorized as Level 1 and had a total balance of $51,742 and $34,698 as of March 31, 2018 and December 31, 2017, respectively. The financial

assets valued based on level 2 inputs consist of corporate debt securities and commercial paper, which consist of investments in highly-rated investment-grade corporations.

A financial liability was recognized by the Company during the three months ended March 31, 2017 related to the 2017 Series A Investor Instrument. The liability was valued based on significant inputs not observable in the market, which represents a Level 3 measurement within the fair value hierarchy. Upon the closing of the second tranche of the 2017 Series A preferred financing in August 2017, this liability was settled.

The following tables present information about the Company's financial assets 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 March 31, 2018 using:			
	Level 1	Level 2	Level 3	Total
Assets:				
Cash Equivalents:				
Corporate Debt Securities and Commercial Paper	$ —	$ 6,989	$ —	$ 6,989
Money Market Funds	36,779	—	—	36,779
Marketable Securities:				
Corporate Debt Securities and Commercial Paper	—	78,323	—	78,323
U.S. Treasury Securities	14,963	—	—	14,963
Total	$ 51,742	$ 85,312	$ —	$ 137,054

	Fair value Measurements as of December 31, 2017 using:			
	Level 1	Level 2	Level 3	Total
Assets:				
Cash Equivalents:				
Corporate Debt Securities	$ —	$ 15,104	$ —	$ 15,104
Money Market Funds	17,753	—	—	17,753
Marketable Securities:				
Corporate Debt Securities	—	96,901	—	96,901
U.S. Treasury Securities	16,945	—	—	16,945
Total	$ 34,698	$ 112,005	$ —	$ 146,703

Marketable Securities

The following tables summarize the Company's marketable securities:

	March 31, 2018			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Assets				
Corporate Debt Securities and Commercial Paper (due within 1 year)	$ 78,528	$ —	$ (205)	$ 78,323
U.S. Treasury Securities (due within 1 year)	14,979	—	(16)	14,963
	$ 93,507	$ —	$ (221)	$ 93,286

	December 31, 2017			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Assets				
Corporate Debt Securities (due within 1 year)	$ 97,029	$ —	$ (128)	$ 96,901
U.S. Treasury Securities (due within 1 year)	16,958	—	(13)	16,945
	$ 113,987	$ —	$ (141)	$ 113,846

Below is a roll forward of the fair value of the 2017 Series A Investor Instrument for the three months ended March 31, 2017:

	2017 Series A Investor Instrument
Fair value at December 31, 2016	$ —
Fair value upon the January 2017 Initial Closing, net	328
Change in fair value	—
Fair value at March 31, 2017	$ 328

The fair value of the Series A Investor Instrument is the sum of the probability-weighted fair value of the 2017 Investor Right/Obligation and the 2017 Series A Call Option.

The following assumptions and inputs were used in determining the fair value of the 2017 Series A Investor Call Option valued using the Black- Scholes option pricing model:

	March 31, 2017
Series A Convertible Preferred Stock Exercise Price	$ 1.00
Series A Convertible Preferred Stock Fair Value	$ 1.39
Expected term	3.5 months
Expected volatility	82.0 %
Expected interest rate	0.76 %
Expected dividend yield	—

In August 2017, upon the closing of the second tranche of the series A preferred stock financing, the 2017 Series A Investor Call Option expired unexercised.

The Company estimated the fair value of the 2017 Series A Investor Right/Obligation as the probability-weighted present value of the expected benefit of the investment. The expected benefit is the difference between the expected future value of shares issued upon the second tranche closing and the investment price for the second tranche closing. The expected future value is estimated as a weighted average of IPO and remain private scenarios, and the future value is converted to a present value assuming a closing date of October 15, 2017 and a nominal, risk-free discount rate.

5. Preferred and Common Stock

Preferred Stock

Upon the closing of the IPO, the series A convertible preferred stock automatically converted into shares of common stock on a 9.17-for-1 basis.

Common Stock

In March 2013, the Company issued 10,196,292 shares of common stock at a purchase price of $0.001 per share. Prior to August, 2017, the LLC entity owned all of these shares.

On August 21, 2017, the LLC entity exchanged 8,578,646 of its shares of the Company's common stock for 78,666,209 shares of the Company's series A-1 junior preferred stock and the LLC entity distributed all of its shares of the Company's series A-1 junior preferred stock to the holders of its preferred units and the remaining 1,617,646 shares of its common stock to the holders of its common units. Following this distribution, the LLC entity no longer owns any of the Company's shares. The series A-1 junior preferred stock is not redeemable and does not have a stated dividend or liquidation preference. These shares converted to common stock on a 9.17-to-1 basis upon the closing of the IPO in October 2017.

In September 2017, the Company's board of directors approved a 1-for-9.17 reverse 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 reverse stock split.

On October 10, 2017 the Company completed its IPO of 8,107,500 shares of common stock at an offering price of $17.00 per share, which included the exercise in full by the underwriters of their option to purchase up to 1,057,500 additional shares of common stock. The Company received gross proceeds of approximately $137,828 or net proceeds of $125,658 after deducting underwriting discounts, commissions and estimated offering expenses. In connection with the IPO, the Company’s outstanding shares of convertible preferred stock were automatically converted into 17,406,338 shares of common stock.

On April 3, 2018, in association with the Takeda license agreement, the Company issued 223,544 shares of common stock. See Note 6 for further discussion.

6. 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 3 clinical trials, and relamorelin. As a result of the Corporate Reorganization described in Note 1, the Ipsen license was converted to separate license agreements for the setmelanotide program held by the Company and the relamorelin program held by the Relamorelin Company, respectively. Under the terms of the setmelanotide Ipsen license agreement, assuming that setmelanotide is successfully developed, receives regulatory approval and is commercialized, Ipsen may receive aggregate payments of up to $40,000 upon the achievement of certain development and commercial milestones and royalties on future product sales in the mid-single digits. Substantially all of such aggregate payments of up to $40,000 are for milestones that may be achieved no earlier than first commercial sale of setmelanotide. In the event that the Company executes a sublicense agreement, it shall make payments to Ipsen, depending on the date of such sublicense agreement, ranging from 10% to 20% of all revenues actually received under such sublicense agreement.

In July 2017, the Company made a prepayment on the first milestone event associated with this license agreement. The first milestone relates to the initiation of a Phase 3 study for setmelanotide in a pivotal multi-center human clinical trial in a large number of patients. The prepayment associated with this milestone was $1,000 and was recorded as research and development expenses during the three months ended March 31, 2018 when the milestone criteria was met in full.

In January 2016, the Company entered into a license agreement with Camurus AB, or Camurus, for the use of Camurus’ drug delivery technology. The contract includes a non-refundable and non-creditable signing fee of $500, which was paid during January 2016. The Camurus agreement also includes up to $7,750 in one-time, non-refundable development milestones achievable upon certain regulatory successes. The Company is also required to pay to Camurus, mid to mid-high single digit royalties, on a product-by-product and country-by-country basis of annual net sales, until the later of (i) 10 years after the date of first commercial sale of such product in such country; or (ii) the expiration of the last to expire valid claim of all licensed patent rights in such country covering such product. The Company is also required to pay one-time, non-refundable, non-creditable sales milestones upon the achievement of certain sales levels for such product that cannot be in excess of $57,000.

In March 2017, the Company achieved the first milestone event associated with this license agreement. The Company completed the first manufactured batch using the Camurus drug delivery technology and filed an investigational new drug application with the FDA. The fee associated with this milestone was $250.

In December 2017, the Company achieved the second milestone event associated with this license agreement. The Company completed the Phase I proof of concept study using the Camurus drug delivery technology. The fee associated with this second milestone was $1,000 and was recorded as research and development expense.

In March 2018, the Company entered into a license agreement with Takeda, for the rights of a program that includes the clinical candidate RM-853, which is a GOAT inhibitor, which is currently in preclinical development for PWS. Pursuant to the license agreement the Company was required to pay a non-refundable and non-creditable signing fee, which the Company settled by issuing on April 3, 2018, 223,544 shares of common stock valued at $4,448. Under the terms of the license agreement, assuming that RM-853 is successfully developed, receives regulatory approval and is commercialized, the Company is also required to pay up to $70,000 in one-time, non-refundable development milestone payments upon the achievement of certain clinical and regulatory milestones. The Company is also required to pay up to $70,000 in one-time, non-refundable, non-creditable sales milestone payments upon the achievement of certain sales levels. The Company is also required to pay to Takeda, mid to mid-high single digit royalties (subject to certain potential reductions over time), on a product-by-product and country-by-country basis of annual net sales, of each product in such country, beginning on the first commercial sale of a product in such country, and continuing until the latest of (i) 10 years after the date of first commercial sale of such product in such country; or (ii) the expiration of the last to expire valid claim of a Takeda patents covering the composition or use of such product in such country; or (iii) the expiration of all regulatory exclusivity for such product in such country. The Company recorded the fair value of the common stock to be issued to the licensors as research and development expense, as the license does not have a future alternative use, in accordance with ASC Topic 730, *Research and Development.* As the shares were not issued prior to the end of the period, the Company evaluated the forward contract and concluded that it met the criteria for equity classification and such amounts have been recorded within additional paid-in capital as of March 31, 2018.

7. Related-Party Transactions

Expenses paid directly to consultants considered to be related parties amounted to $472 and $229 for the three months ended March 31, 2018 and 2017, respectively. Outstanding payments due to these related parties as of March 31, 2018 and December 31, 2017 were $102 and $112, respectively, and were included within accounts payable on the balance sheet.

8. Income Taxes

For the year ended December 31, 2017, 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.

Item 2. 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 unaudited condensed consolidated financial statements and related notes appearing elsewhere in this Quarterly Report on Form 10-Q. In addition to historical information, this discussion and analysis contains forward-looking statements that involve risks, uncertainties and assumptions, including statements regarding our financial performance, including our expectations regarding our existing cash, operating losses, expenses and sources of future financing; statements regarding our ability to hire and retain necessary personnel; statements regarding patient enrollments and the timing thereof; statements regarding the timing of announcements regarding results of clinical trials; statements regarding our ability to protect our intellectual property; statements regarding our ability to negotiate our collaboration agreements, if needed; statements regarding our marketing, commercial sales, and revenue generation; and other statements identified by words such as "anticipates," "believes," "could," "estimates," "expects," "intends," "may," "might," "likely," "plans," "potential," "predicts," "projects," "seeks," "should," "target," "will," "would," or similar expressions and the negatives of those terms include forward looking statements that involve risks and uncertainties. Forward-looking statements are not promises or guarantees of future performance, and are subject to a variety of risks and uncertainties, many of which are beyond our control, and which could cause actual results to differ materially from those contemplated in such forward-looking statements. These factors include those set forth in Part II, Item 1A under the heading "Risk Factors" of this Quarterly Report on Form 10-Q. Our actual results may differ materially from those anticipated in these forward-looking statements as a result of certain factors. We discuss factors that we believe could cause or contribute to these differences below and elsewhere in this report, including those set forth in Part II, Item 1A under the heading "Risk Factors" of this Quarterly Report on Form 10-Q.

Overview

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

We have demonstrated proof of concept in Phase 2 clinical trials in POMC deficiency obesity, LepR deficiency obesity and Bardet-Biedl syndrome, three genetic disorders of extreme and unrelenting appetite and obesity, in which setmelanotide dramatically reduced both weight and hunger. The U.S. Food and Drug Administration, or the FDA, has acknowledged the importance of these results by giving setmelanotide Breakthrough Therapy designation for the treatment of obesity associated with genetic defects upstream of the MC4 receptor in the leptin-melanocortin pathway, which includes both POMC deficiency obesity and LepR deficiency obesity. In May 2018, the FDA has also agreed that Bardet-Biedl syndrome and Alstrom Syndrome have been included under the existing Breakthrough Therapy designation for setmelanotide. Setmelanotide is currently in Phase 3 development for POMC deficiency obesity and LepR deficiency obesity. We continue to enroll patients in our POMC deficiency obesity Phase 3 clinical trial and expect to complete enrollment of the ten required patients in the first half of 2018 and to report Phase 3 data in the first half of 2019. We are currently in an ongoing pivotal Phase 3 clinical trial for setmelanotide in LepR deficiency obesity. We continue to enroll patients in our LepR deficiency obesity Phase 3 clinical trial, and expect to complete enrollment in 2018. We have demonstrated proof of concept in our Phase 2 clinical trial in Bardet-Biedl syndrome, and expect to meet with regulatory authorities in early 2018 to plan a pivotal Phase 3 clinical trial in Bardet-Biedl syndrome that we anticipate we can initiate in 2018. We have also initiated Phase 2 clinical trials in Alström syndrome, POMC heterozygous deficiency obesity and POMC epigenetic disorders. We anticipate reporting preliminary results in these additional Phase 2 indications in the first

half of 2018. Approximately 300 obese subjects and patients have been treated with setmelanotide in previous and ongoing clinical trials in which setmelanotide demonstrated statistically significant weight loss with good tolerability.

We have leveraged skilled experts, consultants, contract research organizations, or CROs, and contractors to manage our clinical operations under the leadership and direction of our management. We expect to expand our infrastructure to manage our clinical, finance and commercial operations with a higher proportion of full-time employees. We have twenty-five employees. Of these employees, thirteen are engaged in development activities, four are engaged in commercialization activities and eight are engaged in support administration, including business development and finance. In the near-term, we expect to significantly expand our clinical, commercial and finance personnel, in particular, and will incur increased expenses as a result.

In March 2018 we acquired exclusive, worldwide rights from Takeda Pharmaceutical Company Limited ("Takeda") to develop and commercialize T-3525770 (now "RM-853"). RM-853 is a potent, orally available ghrelin o-acyltransferase ("GOAT") inhibitor currently in preclinical development for Prader-Willi Syndrome ("PWS"). PWS is a rare genetic disorder that results in hyperphagia and early-onset, life-threatening obesity, for which there are no approved therapeutic options. We will assume sole responsibility for the global product development and commercialization of RM-853. Takeda received an upfront fee of $4.4 million which we settled in April 2018 with shares of our common stock, and will receive back-end development milestones, and single-digit royalties on future RM-853 sales.

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 the private placement of equity securities to outside investors. On October 10, 2017 we completed our initial public offering, or IPO, of 8,107,500 shares of common stock at an offering price of $17.00 per share, which included the exercise in full by the underwriters of their option to purchase up to 1,057,500 additional shares of common stock. We received gross proceeds of approximately $137.8 million, before deducting underwriting discounts, commissions and offering related transaction costs. In connection with the IPO, our outstanding shares of convertible preferred stock were automatically converted into 17,406,338 shares of common stock. We will not generate revenue from product sales until we successfully complete development and obtain regulatory approval for setmelanotide, which we expect will take a number of years and is subject to significant uncertainty. We expect to continue to fund our operations through the sale of equity, debt financings or other sources. We intend to build our own marketing and commercial sales infrastructure and we may enter into collaborations with other parties for certain markets outside the United States. However, we may be unable to raise additional funds or enter into such other arrangements when needed on favorable terms, or at all. If we fail to raise capital or enter into such other arrangements as, and when, needed, we may have to significantly delay, scale back or discontinue the development or commercialization of setmelanotide.

As of March 31, 2018, we had an accumulated deficit of $126.7 million. Our net losses were $16.5 million and $6.4 million for the three months ended March 31, 2018 and 2017, 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 contract manufacturing organizations, or 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 March 31, 2018, our existing cash and cash equivalents and short-term investments were approximately $136.5 million. We expect that our existing cash and cash equivalents and short-term investments will enable us to fund our operating expenses into the second half of 2019.

Corporate Background and Distribution

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

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

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

In January 2017 and August 2017, we sold 20,475,001 shares and 20,474,998 shares, respectively, of our series A convertible preferred stock to certain investors. Following the closing of our series A convertible preferred stock financings, the LLC entity remained our largest stockholder, with the balance of our stock being owned by our series A investors. In August 2017, the LLC entity exchanged 8,578,646 of its shares of our common stock for 78,666,209 newly-issued shares of our series A-1 junior preferred stock and the LLC entity distributed all of its shares of our series A-1 junior preferred stock to the holders of its preferred units and the remaining 1,617,646 shares of our common stock to the holders of its common units. We refer to the exchange and distribution as the Distribution. The series A-1 junior preferred stock converted into shares of our common stock on a 9.17-for-1 basis upon the closing of our IPO. Following the Distribution, the LLC entity did not own any of our common stock.

In connection with our IPO, we effected a 1-for-9.17 reverse stock split of our outstanding common stock on September 29, 2017. All share and per share amounts in the financial statements have been retrospectively adjusted for all periods presented to give effect of the reverse stock split.

Financial Operations Overview

Revenue

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

Research and development expenses

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

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

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

The following table summarizes our current research and development expenses.

	Three Months Ended March 31,	
Research and Development Summary	**2018**	**2017**
Research and Development Expense	$ 12,286	$ 4,873

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

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

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

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

Selling, general and administrative expenses

Selling expenses consist of professional fees related to preparation for the eventual commercialization of setmelanotide, if approved, as well as salaries and related benefits for commercial employees, including stock-based compensation. As we accelerate our preparation for commercialization and, if it is approved, start to market setmelanotide and as we explore new collaborations to develop and commercialize setmelanotide, we anticipate that these expenses will materially increase.

General and administrative expenses consist primarily of salaries and other related costs, including stock-based compensation, relating to our full-time employees. Other significant costs include rent, legal fees relating to patent and corporate matters and fees for accounting and consulting services.

The following table summarizes our current selling, general and administrative expenses.

	Three Months Ended March 31,	
Selling, general and administrative Summary	**2018**	**2017**
Selling, general and administrative expense	$ 4,715	$ 1,516

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

Critical Accounting Policies and Estimates

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

While our significant accounting policies are described in more detail in the notes to our financial statements included elsewhere in this Quarterly Report on Form 10-Q, 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.

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.

2017 Series A Investor Instrument

Pursuant to the 2017 series A preferred stock purchase agreement, by and among us and certain purchasers, and as part of an initial tranche closing, we issued 20,475,001 shares of series A preferred stock at a purchase price of $1.00 per share in January 2017. The series A preferred stock purchase agreement provided for the delayed issuance by us of up to an additional 20,474,998 shares of series A preferred stock as part of a second tranche closing at a purchase price of $1.00 per share. The series A investors had the obligation, upon notification by us, or the 2017 Series A Investor Right/Obligation, to purchase 20,474,998 additional shares of series A preferred stock as part of a second tranche of financing at such time as: (1) our cash, cash equivalents and short-term investments balance, net of accounts payable and accrued liabilities, falling below $5.0 million and (2) our satisfaction of contractual and customary representations and warranties, or the 2017 Second Tranche Milestone. On August 18, 2017, the series A investors waived the $5.0 million cash balance requirement of the 2017 second tranche milestone and such second tranche financing was consummated. As a result of these two tranches, we issued 40.95 million shares of our series A preferred stock, resulting in aggregate gross proceeds of $40.95 million.

We have classified our 2017 Series A Investor Instrument (See Note 4 to our financial statements included elsewhere in this Quarterly Report on Form 10-Q) as a liability as it is a free-standing financial instrument. The 2017 Series A Investor Instrument was recorded at fair value upon the issuance of our series A preferred stock in January 2017, and subsequently remeasured to fair value at each reporting period. Changes in fair value of this financial instrument is recognized as a component of other income (expense), net in the statement of operations and comprehensive loss. We estimated the fair value of the 2017 Series A Investor Right/Obligations as the probability-weighted present value of the expected benefit of the investment.

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

Stock-based compensation

In August 2015, our Board of Directors and our stockholders approved and we adopted the 2015 equity incentive plan, as amended and in effect prior to the closing of our IPO, or the 2015 Plan, which we terminated upon consummation of our IPO and replaced with the 2017 equity incentive plan, or the 2017 Plan. The 2017 Plan provides for the grant of incentive and non-qualified stock options and restricted stock and stock grants to employees, consultants, advisors and directors, as determined by the Board of Directors. We have reserved 5,109,904 shares of common stock under the 2017 Plan. The first option grants issued by us under the 2015 Plan were issued in the fourth quarter of 2015. Shares of common stock issued upon exercise of stock options are generally issued from authorized but unissued shares. The 2017 Plan provides that the exercise price of incentive stock options cannot be less than 100% of the fair market value of the common stock on the date of the award for participants who own less than 10% of the total combined voting power of stock, and not less than 110% for participants who own more than 10% of the voting power. Options and restricted stock granted under the 2017 Plan will vest over periods as determined by our Compensation Committee and approved by our Board of Directors.

We estimate the fair value of our stock-based awards to employees and non-employees using the Black-Scholes option-pricing model, which requires the input of highly subjective assumptions, including (a) the expected volatility of our stock, (b) the expected term of the award, (c) the risk-free interest rate, and (d) expected dividends. Previously due to the lack of a public market for the trading of our common stock and a lack of company-specific historical and implied volatility data, we have based our estimate of expected volatility on the historical volatility of a group of companies in the pharmaceutical and biotechnology industries in a similar stage of development as us and that are publicly traded. For these analyses, we have selected companies with comparable characteristics to ours including enterprise value, risk profiles and with historical share price information sufficient to meet the expected life of the stock-based awards. We compute the historical volatility data using the daily closing prices for the selected companies' shares during the equivalent period of the calculated expected term of our stock-based awards. We will continue to apply this process until a sufficient amount of historical information regarding the volatility of our own stock price becomes available. We have estimated the expected life of our employee stock options using the "simplified" method, whereby, the expected life equals the average of the vesting term and the original contractual term of the option. The risk-free interest rates for periods within the expected life of the option are based on the U.S. Treasury yield curve in effect during the period the options were granted. Upon adopting ASU 2016-09, *Improvements to Employee Share-Based Payment Accounting (Topic 718)* on January 1, 2017, we have elected to account for forfeitures as they occur.

Income taxes

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

We account for uncertain tax positions in accordance with the provisions of Accounting Standards Codification, or ASC, Topic 740, *Accounting for Income Taxes*, or ASC 740. When uncertain tax positions exist, we recognize the tax benefit of tax positions to the extent that the benefit will more likely than not be realized. The determination as to whether the tax benefit will more likely than not be realized is based upon the technical merits of the tax position as well as consideration of the available facts and circumstances. As of December 31, 2017, 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.

As of December 31, 2017, we had net operating loss carryforwards to reduce federal and state incomes taxes of approximately $73.1 million and $3.8 million, respectively. If not utilized, these carryforwards begin to expire in 2033. At December 31, 2017, we also had available research and development tax credits for federal and state income tax purposes of approximately $1.9 million and $0.5 million, respectively. The federal and state credits begin to expire in 2033 and 2028, respectively. Additionally, as of December 31, 2017, we had a federal orphan drug credits related to qualifying research of $2.3 million. These tax credit carryforwards begin to expire in 2033 for federal purposes and 2028 for state purposes.

Utilization of the net operating loss and tax credit carryforwards may be subject to a substantial annual limitation due to ownership change limitations that have occurred previously or that could occur in the future, as provided by Section 382 of the Internal Revenue Code of 1986, as amended, or the Code, or Section 382, as well as similar state provisions and other provisions of the Code. Ownership changes may limit the amount of net operating losses and tax credit carryforwards that can be utilized annually to offset future taxable income and tax, respectively. In general, an ownership change, as defined by Section 382, results from transactions that increase the ownership of 5.0% stockholders in the stock of a corporation by more than 50% in the aggregate over a three-year period.

Results of Operations

Comparison of three months ended March 31, 2018 and 2017

The following table summarizes our results of operations for the three months ended March 31, 2018 and 2017, together with the changes in those items in dollars and as a percentage:

	Three Months Ended March 31,		Change	
	2018	2017	$	%
	(in thousands)			
Statement of Operations Data:				
Operating Expenses:				
Research and development	$ 12,286	$ 4,873	$ 7,413	152 %
Selling, general, and administrative	4,715	1,516	3,199	211 %
Total operating expenses	17,001	6,389	10,612	166 %
Loss from operations	(17,001)	(6,389)	(10,612)	166 %
Other (expense) income, net	542	29	513	NM %
Net loss and comprehensive loss	$ (16,459)	$ (6,360)	$ (10,099)	159 %

Research and development expense. Research and development expense increased by $7.4 million to $12.3 million in 2018 from $4.9 million in 2017, an increase of 152%. The increase was primarily due to the non-cash expense related to the license acquired from Takeda for RM-853, a $1.0 million milestone expense associated with the license agreement with Ipsen and the hiring of additional clinical and development personnel during the second half of 2017.

Selling, general and administrative expense. Selling, general and administrative expense increased by $3.2 million to $4.7 million in 2018 from $1.5 million in 2017, an increase of 211%. The increase was primarily due to increased headcount, the development and building of our commercial organization to drive patient identification, as well as increased professional and consultings fees associated with being a public company.

Liquidity and Capital Resources

As of March 31, 2018, our existing cash and cash equivalents and short-term investments were approximately $136.5 million.

Cash flows

The following table provides information regarding our cash flows for the three months ended March 31, 2018 and 2017:

	Three Months Ended March 31,	
	2018	2017
	(in thousands)	
Net cash provided by (used in):		
Operating activities	$ (11,651)	$ (7,016)
Investing activities	20,607	(8,019)
Financing activities	—	20,377
Net increase (decrease) in cash, cash equivalents and restricted cash	$ 8,956	5,342

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 $11.7 million for the three months ended March 31, 2018 and consisted primarily of a net loss of $11.0 million adjusted for non-cash items, which consisted of the non-cash research and development license expense for RM-853, stock-based compensation, depreciation and amortization and deferred rent expense. The change in operating assets and liabilities reflected a total use of cash of approximately $0.7 million mainly for a decrease in accrued expenses and prepaid expenses.

Net cash used in operating activities was $7.0 million for the three months ended March 31, 2017, and consisted primarily of a net loss of $6.1 million adjusted for non-cash items, which consisted of stock-based compensation, depreciation and amortization and deferred rent expense. The significant items in the change in operating assets and liabilities include a decrease in accounts payable of $0.5 million and an increase in prepaid clinical trial expenses of approximately $0.3 million.

Net cash provided by (used in) investing activities

Net cash provided by investing activities for the three months ended March 31, 2018 relates to the net maturities of short-term investments of $20.6 million.

Net cash used in investing activities for the three months ended March 31, 2017 relates to the net purchases of short-term investments of $8.0 million.

Net cash provided by financing activities

Net cash provided by financing activities was $20.4 million for the three months ended March 31, 2017, which represents the net proceeds from the first tranche of our issuance of series A preferred stock in January 2017.

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 also expect to incur additional costs associated with operating as a public company.

We expect that our existing cash and cash equivalents will enable us to fund our operating expenses into the second half of 2019. We may need to obtain substantial additional funding in connection with our research and

development activities and any continuing operations thereafter. If we are unable to raise capital when needed or on favorable terms, we would be forced to delay, reduce or eliminate our research and development programs or future commercialization efforts.

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

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

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

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances and licensing arrangements. In August 2015, December 2015, January 2017 and August 2017, respectively, we issued 25,000,000, 15,000,000, 20,475,001 and 20,474,998, shares of series A preferred stock, respectively, at a price of $1.00 per share, resulting in gross proceeds of $81.0 million. In October 2017 we completed our IPO in which we received net proceeds of $125.7 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 agreements with Ipsen, Camurus and Takeda, have not been included as contractual obligations as we cannot reasonably estimate if or when they will occur. Under the terms of the Ipsen license agreement, assuming that setmelanotide is successfully developed, receives regulatory approval and is commercialized, Ipsen may receive aggregate payments of up to $40.0 million upon the achievement of certain development and commercial milestones under the license agreement and royalties on future product sales. The majority of the aggregate payments under the Ipsen license agreement are for milestones that may be achieved no earlier than first commercial sale of setmelanotide. In the event that we enter into a sublicense agreement, we will make payments to Ipsen, depending on the date of the sublicense agreement, ranging from 10% to 20% of all revenues actually received under the sublicense agreement. Under the terms of the Camurus license agreement, assuming that setmelanotide is successfully developed, receives regulatory approval and is commercialized, Camurus may receive aggregate payments of up to $64.75 million upon the achievement of certain development and commercial milestones under the license agreement and royalties on future product sales. The majority of the aggregate payments under the Camurus license agreement are for milestones that may be achieved no earlier than first commercial sale of this formulation of setmelanotide. Under the terms of the Takeda license agreement, assuming that RM-853, is successfully developed, receives regulatory approval and is commercialized, Takeda may receive aggregate payments of up to $140.0 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 Takeda license agreement are for milestones that may be achieved no earlier than first commercial sale of the RM-853.

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

Future minimum payments under the Lease Agreement as of March 31 2018, are as follows:

	Operating Lease
2018	$ 224
2019	305
2020	311
2021	131
Total	$ 971

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.

Item 3. Quantitative and Qualitative Disclosures About Market Risk.

We are exposed to market risk related to changes in interest rates. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates, particularly because our investments, including cash equivalents, are in the form, or may be in the form of, money market funds or marketable securities and are or may be invested in U.S. Treasury and U.S. government agency obligations. Due to the short-term maturities and low risk profiles of our investments, an immediate 100 basis point change in interest rates would not have a material effect on the fair market value of our investments.

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

JOBS Act

In April 2012, the Jumpstart our Business Startups Act of 2012, or 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 of 1933, as amended, or 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 our IPO, (b) in which we have total annual gross revenue of at least $1.07 billion, or (c) in which we are deemed to be a large accelerated filer, which means the market value of our common stock that is held by non-affiliates exceeds $700 million as of the prior December 31st, and (2) the date on which we have issued more than $1.0 billion in non-convertible debt securities during the prior three-year period.

Item 4. Controls and Procedures.

Evaluation of Disclosure Controls and Procedures

Disclosure controls and procedures, as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended, or the Exchange Act, are controls and other procedures designed to ensure that information required to be disclosed in reports filed or submitted under the Exchange Act is recorded, processed, summarized, and reported within the time periods specified by the rules and forms promulgated by the SEC. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that such information is accumulated and communicated to management, including the chief executive officer and the chief financial officer, as appropriate, to allow timely decisions regarding required disclosure.

In connection with the preparation of this Quarterly Report on Form 10-Q, we completed an evaluation, as of March 31, 2018, under the supervision and with the participation of our management, including our Chief Executive Officer and Chief Financial Officer, as to the effectiveness of our disclosure controls and procedures (as such term is defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act).

It should be noted that any system of controls, however well designed and operated, can provide only reasonable, and not absolute, assurance that the objectives of the system will be met. In addition, the design of any control system is based in part upon certain assumptions about the likelihood of future events. Based upon the evaluation, our Chief Executive Officer and Chief Financial Officer have concluded that, as of March 31, 2018, our disclosure controls and procedures were effective at a reasonable assurance level.

Changes in Internal Control Over Financial Reporting

There were no changes in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) that occurred during the period covered by this report that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

PART II - OTHER INFORMATION

Item 1. Legal Proceedings.

We are not currently a party to any material legal proceedings.

Item 1A. Risk Factors

Our operations and financial results are subject to various risks and uncertainties, including those described below, which could adversely affect our business, financial condition, results of operations, cash flows, and the trading price of our common stock. Additional risks and uncertainties not presently known to us or that we currently deem immaterial also may impair our business operations. You should carefully consider the risks described below and the other information in this Quarterly Report on Form 10-Q, including our unaudited consolidated financial statements and the related notes thereto and "Management's Discussion and Analysis of Financial Condition and Results of Operations."

Risks Related to Our Financial Position and Need for Capital

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

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

Since our inception, we have focused substantially all of our efforts and financial resources on the research and development of setmelanotide, which is currently in Phase 3 clinical development for two indications, POMC deficiency obesity and LepR deficiency obesity, and in various phases of development for other indications. We have funded our operations to date primarily through capital contributions from the Predecessor Company, the Relamorelin Company and the LLC entity and proceeds from sales of preferred stock and have incurred losses in each year since our inception. See "*Part I, Item 2. Management's Discussion and Analysis of Financial Condition and Results of Operations—Corporate Background and Distribution.*"

Our net loss and comprehensive losses were $16.5 million and $6.4 million for the three months ended March 31, 2018 and 2017, respectively. As of March 31, 2018, we had an accumulated deficit of $126.7 million. Substantially all of our operating losses have resulted from costs incurred in connection with our development program and from general and administrative costs associated with our operations. Our prior losses, combined with expected future losses, have had and will continue to have an adverse effect on our stockholders' deficit and working capital. We expect our research and development expenses to significantly increase in connection with our additional clinical trials of setmelanotide and development of any other product candidates we may choose to pursue. In addition, if we obtain marketing approval for setmelanotide, we will incur significant sales, marketing and outsourced manufacturing expenses. We also will incur additional costs associated with operating as a public company. As a result, we expect to continue to incur significant and increasing operating losses for the foreseeable future. Because of the numerous risks and uncertainties associated with developing pharmaceutical products, we are unable to predict the extent of any future losses or when we will become profitable, if at all. Even if we do become profitable, we may not be able to sustain or increase our profitability on a quarterly or annual basis.

Our ability to become profitable depends upon our ability to generate revenue. To date, we have not generated any revenue from setmelanotide, and we do not know when, or if, we will generate any revenue. We do not expect to generate significant revenue unless and until we obtain marketing approval for, and begin to sell, setmelanotide. Our ability to generate revenue depends on a number of factors, including, but not limited to, our ability to:

- initiate and successfully complete later-stage clinical trials that meet their clinical endpoints;

- initiate and successfully complete all safety studies required to obtain U.S. and foreign marketing approval for setmelanotide as a treatment for obesity caused by genetic deficiencies affecting the MC4 pathway;

- successfully manufacture or contract with others to manufacture setmelanotide;

- commercialize setmelanotide, if approved, by building an internal sales force or entering into collaborations with third parties; and

- achieve market acceptance of setmelanotide in the medical community and with third-party payors.

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

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

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

Through August 2015, we received capital contributions from the Predecessor Company, the Relamorelin Company and the LLC entity. In August 2015, December 2015, January 2017 and August 2017, we raised aggregate gross proceeds of $25.0 million, $15.0 million, $20.5 million and $20.5 million, respectively, through our issuance of series A preferred stock. In October 2017 we completed our initial public offering, or IPO of 8,107,500 shares of common stock at an offering price of $17.00 per share, which included the exercise in full by the underwriters of their option to purchase up to 1,057,500 additional shares of common stock. We received gross proceeds of approximately $137.8 million, before deducting underwriting discounts, commissions and offering related transaction costs. As of March 31, 2018, our cash and cash equivalents and short-term investments were approximately $136.5 million. We expect our existing cash and cash equivalents will enable us to fund our operating expenses into the second half of 2019. However, our operating plan may change as a result of many factors currently unknown to us, and we may need to seek additional funds sooner than planned, through public or private equity or debt financings, government or other third-party funding, marketing and distribution arrangements and other collaborations, strategic alliances and licensing arrangements, or a combination of these approaches. We will also require additional capital to obtain regulatory approval for, and to commercialize, setmelanotide. Raising funds in the current economic environment may present additional challenges. Even if we believe we have sufficient funds for our current or future operating plans, we may seek additional capital if market conditions are favorable or if we have specific strategic considerations.

Any additional fundraising efforts may divert our management from their day-to-day activities, which may adversely affect our ability to develop and commercialize setmelanotide. In addition, we cannot guarantee that future financing will be available in sufficient amounts or on terms acceptable to us, if at all. Moreover, the terms of any financing may adversely affect the holdings or the rights of our stockholders and the issuance of additional securities, whether equity or debt, by us, or the possibility of such issuance, may cause the market price of our shares to decline. The sale of additional equity or convertible securities would dilute all of our stockholders. The incurrence of indebtedness would result in increased fixed payment obligations and we may be required to agree to certain restrictive covenants, such as limitations

on our ability to incur additional debt, limitations on our ability to acquire, sell or license intellectual property rights, and other operating restrictions that could adversely impact our ability to conduct our business. We could also be required to seek funds through arrangements with collaborative partners or other third parties at an earlier stage than otherwise would be desirable and we may be required to relinquish rights to setmelanotide or technologies or otherwise agree to terms unfavorable to us, any of which may have a material adverse effect on our business, operating results and prospects.

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

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

The historical financial information we have included in this Quarterly Report on Form 10-Q may not reflect what our results of operations, financial position and cash flows would have been had we been an independent company during the periods presented. This is primarily because:

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

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

Risks Related to the Development of Setmelanotide

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

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

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

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

Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in later stage clinical trials after achieving positive results in early stage development, and we cannot be certain that we will not face similar setbacks. These setbacks have been caused by, among other things, pre-clinical findings made while clinical trials were underway. However, we have completed the key toxicology studies that the U.S. Food and Drug Administration, or the FDA, will require for our first approval, and which we believe the European Medicines Agency, or EMA, will require for approval, which include, among others, chronic toxicity studies, reproductive and developmental toxicity studies, and juvenile toxicology studies. Based on the totality of animal testing results to date, including the lack of any observed genotoxicity or tissue proliferative activity of setmelanotide in chronic toxicity studies, the FDA has agreed to permit us to defer carcinogenicity studies until after approval of a new drug application, or NDA, for setmelanotide. Accordingly, we believe that we will be able to defer all carcinogenicity studies until after we receive regulatory approval to market setmelanotide in the U.S. While we believe this also to be true for the EMA, the EMA has not yet provided firm guidance on the need for carcinogenicity studies and accordingly, there can be no guarantee that we will be able to achieve this deferral which could impact the timing of any potential EU approval.

In addition to the foregoing issue, the FDA has requested that in our chronic rat and monkey studies we re-assess certain cells in brain, renal and liver tissues for the presence of vacuoles, which are common membrane-bound compartments. The recommendation was based on the FDA’s review of a summary of a monkey study that noted the presence of macrophage aggregates, which are groupings of specific white blood cells, in the choroid plexus, a network of blood vessels and epithelial tissue in the membrane lining outside the brain and spinal cord. The FDA noted that the

existence of macrophage aggregates appears to be related to the polyethylene glycol, or PEG, vehicle in the product, rather than setmelanotide itself. A similar question was raised by the competent authorities in France, in connection with the use of PEG in products for younger pediatric indications in discussion of our Pediatric Investigational Plan, or PIP. Based on this, we performed this re-assessment, which confirmed that no additional findings were present in any monkey tissues, but which did find a very small number of rats with vacuolated epithelial cells, or brain surface lining cells, in the choroid plexus of minimal severity that also appeared to be related to the PEG vehicle. We do not believe these findings raise any important safety concerns, in part because of the minimal severity, the localization of these aggregates, the lack of any adverse histopathological changes, and the lack of findings in other tissues. However, neither the FDA nor European regulatory agencies, has indicated that they agree with our position. It is possible the FDA may require us to reflect these findings in the toxicological portion of the product labeling, and this may delay study in the youngest pediatric patients in some European countries, such as France.

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

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

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

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

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

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

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

    - U.S. Census Bureau figures for adults and children, and Centers for Disease Control and Prevention, or CDC, prevalence numbers for severe adult obese patients (body mass index, or BMI, greater than

40 kg/ m^2) and for severe early onset obese children (99th percentile at ages two to 17 years old); and

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

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

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

  - Published prevalence estimates of one in 100,000 in North America, which projects to approximately 3,250 people in the United States. We believe the majority of these patients are addressable patients; and

  - We believe that with wider availability of genetic testing expected for Bardet-Biedl syndrome and increased awareness of new treatments, the number of patients diagnosed with this disorder will increase.

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

  - Published prevalence estimates of one in 1,000,000 in North America, which projects to approximately 325 people in the United States. We believe the majority of these patients are addressable patients; and

  - We believe that with wider availability of genetic testing expected for Alström syndrome and increased awareness of new treatments, the number of patients diagnosed with this disorder will increase.

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

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

We are conducting additional clinical epidemiology studies to strengthen these prevalence projections. In parallel, we have developed a patient registry for diagnosed patients with POMC deficiency and LepR deficiency (and other genetic disorders of obesity) which will further inform prevalence projections for these rare genetic orders.

Another method to estimate the size of these ultra-rare populations by genetic epidemiology is using newly available large genomic databases, containing full genome sequencing or exome sequencing. Ultra-rare orphan diseases are generally categorized as those that affect fewer than 20 patients per million. We have begun some substantial efforts with a series of such databases and/or collaborators. Much of our preliminary work has been with a database of approximately 140,000 genomes, which is representative of the U.S. population. These efforts generally are based on the prevalence of heterozygous mutations, as true null mutations are ultra-rare, and then standard scientific methods such as the Hardy-Weinberg equilibrium calculations, are applied to estimate the prevalence in the U.S. population. These methods

make assumptions that may not be sufficiently robust for ultra-rare genetic disorders, and have the inherent variability of estimates for rare events. In addition, the databases currently available only provide limited clinical data, such as, age, weight and BMI, that would be needed to associate genetic defects with severe obesity. Our continued investigations support that the genetic epidemiological estimates are larger than the clinical epidemiological estimates, but we will likely need to reconcile the scientific definition of mutations with the regulatory definition. However, until these data are confirmed, we must continue to base our patient population estimates on clinical epidemiological information.

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

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

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

The pediatric population is an important patient population for setmelanotide and our addressable patient population estimates include pediatric populations. However, it may be more challenging to conduct studies in this population, and to locate and enroll pediatric patients. Additionally, it may be challenging to ensure that pediatric or adolescent patients adhere to clinical trial protocols.

We currently are treating patients 12 years of age and older in our trials, but we aim to gain regulatory approval and labeling for patients six years of age and older. We have received permission from the FDA and other equivalent competent authorities in the EU member states to enroll these younger patients, aged six to 11, in our pivotal trials. However, there may be issues that preclude the ultimate approval and labeling including, but not limited to, potential disagreement on dose titration, or delivery methods for small doses, or the suitability of patient reported outcomes in younger patients, as well as avoiding over-suppression of normal appetite in adolescents. In addition, the competent authorities in the EU member states may consider the polyethylene glycol vehicle in the product to carry additional risks in pediatric patients, and may look to new formulations, such as our once-weekly formulation, as being more suitable to younger pediatric patients. We also may not have one-year clinical data in six to 11 year old patients at the time of the POMC NDA filing, if we begin recruiting six to 11 year old patients into our pivotal trials, though we can provide one-year clinical data when it becomes available. We cannot predict if the FDA or other equivalent competent authorities in the EU member states will approve setmelanotide in younger pediatric patients, nor provide an estimate for the timing for approval, if any, for the use of setmelanotide for such patients. Furthermore, if the FDA or other equivalent competent authorities in the EU member states do not approve the use of setmelanotide in this population, the product candidate will not be labeled for promotion for these patients, even if they approve an NDA for setmelanotide for patients 12 and older.

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

Patient enrollment is also affected by other factors including:

- the severity of the disease under investigation;
- the eligibility criteria for the clinical trial in question;

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

Our inability to enroll a sufficient number of patients for our clinical trials would result in significant delays, could require us to abandon one or more clinical trials altogether and could delay or prevent our receipt of necessary regulatory approvals. Enrollment delays in our clinical trials may result in increased development costs for setmelanotide, which would cause the value of our company to decline and limit our ability to obtain additional financing.

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

We completed Phase 2 clinical trials for setmelanotide in 2016 for POMC deficiency obesity and are currently advancing an ongoing pivotal Phase 3 clinical trial for setmelanotide for POMC deficiency obesity. We completed Phase 2 clinical trials for setmelanotide for LepR deficiency obesity, and are currently advancing an ongoing pivotal Phase 3 clinical trial for setmelanotide in LepR deficiency obesity. These trials are overlapping in timing and duration and it is possible that a combined NDA may be discussed with the FDA and other regulatory agencies, which would have an impact on NDA timing and complexity.

We have demonstrated proof of concept in Bardet-Biedl syndrome and expect to meet with the FDA in early 2018 to plan a pivotal Phase 3 clinical trial in Bardet-Biedl syndrome that we anticipate we can initiate in 2018. We believe that the Bardet-Biedl syndrome Phase 3 pivotal trial may be somewhat different in design that those for POMC and LepR deficiency obesity, respectively, most likely due to the larger available patient population for inclusion in a clinical study.

We have also initiated Phase 2 clinical trials for Alström syndrome, POMC heterozygous deficiency obesity, and POMC epigenetic disorders. Successful completion of such Phase 3 clinical trials is a prerequisite to submitting an NDA to the FDA, a marketing authorization application to the EMA, and other applications for marketing authorization to equivalent competent authorities in foreign jurisdictions, and consequently, the ultimate approval and commercial marketing of setmelanotide. While we believe that a transition from proof of concept to pivotal trials may be more straight-forward for Alström syndrome, it is likely that Phase 2 clinical trials will be longer and more complex for POMC heterozygous deficiency obesity and POMC epigenetic disorders, due to the greater variety of clinical presentation in those conditions.

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 successful completion of clinical trials can be delayed or prevented for a number of reasons, including but not limited to:

- the FDA or other equivalent competent authorities in foreign jurisdictions may deny permission to proceed with our planned Phase 3 clinical trials or any other clinical trials we may initiate, or may place a clinical trial on hold;
- delays in filing or receiving approvals or additional IND that may be required;
- negative results from our ongoing and planned preclinical studies, or the FDA or other equivalent competent authorities in foreign jurisdictions requiring additional preclinical studies;

- delays in commencing additional necessary preclinical studies, including carcinogenicity and juvenile toxicology studies;
- delays in reaching or failing to reach agreement on acceptable terms with prospective contract research organizations, or CROs, and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- since many already diagnosed patients are at academic sites, delays in conducting clinical trials at academic sites due to the particular challenges and delays typically associated with those sites, as well as the lack of alternatives to these sites which have already-diagnosed patients;
- inadequate quantity or quality of setmelanotide or other materials necessary to conduct clinical trials, including delays in the manufacturing of sufficient supply of finished drug product;
- difficulties in obtaining Institutional Review Board, or IRB, and/or ethics committee approval to conduct a clinical trial at a prospective site or sites;
- challenges in recruiting and enrolling patients to participate in clinical trials, including the size and nature of the patient population, the proximity of patients to clinical trial sites, eligibility criteria for the clinical trial, the nature of the clinical trial protocol, the availability of approved effective treatments for the relevant disease and competition from other clinical trial programs for similar indications;
- severe or unexpected drug-related side effects experienced by patients in a clinical trial, including side effects previously identified in our completed clinical trials;
- delays in identifying and recruiting patients with any of the genetic causes of obesity in indications that we are targeting;
- disagreement by the FDA, other regulatory agencies or the equivalent competent authorities in foreign jurisdictions with our clinical trial designs, which may in turn cause delays in initiating our clinical trials, or may lead to rejection of our interpretation of data from clinical trials or to changes in the requirements for approval even after it has reviewed and commented on the design for our clinical trials;
- the requirement to have a placebo controlled study even though the FDA and EMA did not impose one for POMC deficiency obesity, as we cannot be certain that this will be true for other indications or that the FDA or EMA, an advisory committee or the equivalent competent authorities in foreign jurisdictions will not change its guidance, as it has done so in the past for other open control trials;
- uncertainty related to the length of placebo-controlled intervals in clinical trials;
- the need to perform non-inferiority trials, which can be larger, longer and more costly, if treatment is approved for similar indications;
- potential delays in the enrollment for our clinical trials of LepR deficiency obesity due to the fact that we have not yet had discussions with the FDA regarding clinical trials for LepR deficiency obesity and, accordingly, do not know if the FDA will disagree with our clinical trial design;
- POMC heterozygous deficiency may have additional challenges, including that the FDA the EMA, or the equivalent competent authorities in foreign jurisdictions may require that we show that setmelanotide works better in these patients than in the genetically normal population; other challenges associated with these patients may include additional delays in initiating clinical trials for this indication due to uncertainty about the subset of these patients who will respond effectively to setmelanotide and the lack of discussion for this indication with the FDA;

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

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

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

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

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

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

- changes in government regulations or administrative actions;

- problems with clinical trial supply materials; and

- lack of adequate funding to continue the clinical trial.

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

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

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

In addition, as part of commencing our Phase 3 clinical trial for setmelanotide in POMC deficiency obesity, we sought FDA concurrence with, and received substantial input on, the use of Patient Reported Outcome, or PRO, and Observer Reported Outcome, or ORO questionnaires for measuring subjective endpoints for changes in hunger and/or food-seeking behavior and compulsions. We believe we can apply the same guidance to our future pivotal trials in other

indications. 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 trials for setmelanotide, based on the FDA feedback, we plan to measure the ability of setmelanotide to mitigate hunger and/or hyperphagia, the overriding physiological drive to eat, through PRO and ORO questionnaires. The questionnaires are designed to elicit feedback from patients on how well setmelanotide decreases their hunger, and from their family members or caregivers on the effect of setmelanotide on the patients' food seeking behavior.

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

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

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

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

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

Injection site reactions have been seen in subcutaneous, or SC injections with setmelanotide. In addition, setmelanotide has likely off-target effects on the closely-related MC1 receptor, which mediates tanning in response to sun exposure. Other MC1 mediated effects include darkening of skin blemishes, such as freckles and moles, and hair color change in one subject. These effects have generally been reversible in clinical trials, but it is still unknown if they will be reversible with long-term exposure. The MC1 mediated effects may also carry risks. The long-term impact of MC1

activation has not been tested in clinical trials, and could potentially include increases in skin cancer, excess biopsy procedures and cosmetic blemishes. These skin changes may also result in unblinding, which could make interpretation of clinical trial results more complex and possibly subject to bias.

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

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

In addition, our interpretation of the safety data from our clinical trials is contingent upon the review and ultimate approval of the FDA, other regulatory authorities or other equivalent competent authorities in foreign jurisdictions. The FDA or other equivalent competent authorities in foreign jurisdictions may not agree with our methods of analysis or our interpretation of the results. In addition, the long-term effects of setmelanotide have only been tested in a limited number of patients.

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

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

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

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

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

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

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

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

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

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

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

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

Designation as Breakthrough Therapy is within the discretion of the FDA. Accordingly, even if we believe setmelanotide meets the criteria for designation as Breakthrough Therapy for other uses, the FDA may disagree. In any event, the receipt of Breakthrough Therapy designation for a product candidate, or acceptance for one or more of the FDA's other expedited programs, may not result in a faster development process, review or approval compared to products considered for approval under conventional FDA procedures and does not guarantee ultimate approval by the FDA. Additionally, the FDA may later decide that the product candidate no longer meets the conditions for designation and may withdraw designation at any time or decide that the time period for FDA review or approval will not be shortened.

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

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

We have entered into a license agreement with Camurus AB, or Camurus, for the use of Camurus' drug delivery technology, FluidCrystal, to formulate setmelanotide. This formulation, if successfully developed for setmelanotide, will be delivered subcutaneously, similar to our current formulation, except that we anticipate it will be injected once weekly. The initial Phase 1 pharmacokinetic data from healthy obese volunteers supports once-weekly dosing, but has only been administered for short durations. It is possible that the tolerability profile and/or pharmacokinetics in patients will not be similar to that of healthy obese volunteers, making development of this product more complex. In addition, we have not consulted with regulatory agencies about the path for approval of the once-weekly formulation, and, accordingly, we cannot estimate the time, cost, and probability of success for approval. The Camurus formulations have also not been approved for any product at this time, which further complicates our understanding for the path to approval.

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

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

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

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

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

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

We also are discussing with the FDA the specific mutations, or variants, that will define each indication for which we intend to seek approval. Our efforts have focused on loss-of-function variants that effectively inactivate the genes in the MC4 pathway, and we have proposed rules to define these variants for approval, and which can be used to categorize

new variants as they are identified. It is still uncertain if the FDA will agree to our proposed definitions or use alternative approaches for categorizing and validating these variants.

In addition, we intend to apply genetic tests to address goals beyond seeking FDA approval of setmelanotide, including to support efforts to explore and expand the diagnosis of patients with genetic causes of obesity, and to assist in building awareness of these illnesses. As such, we may develop or work with partners to develop additional genetic tests in the area of genetic obesity, including panels that may study a larger number of genes. There are many factors that might influence the success of these efforts, which could be impactful on our commercial efforts, including the cost, analytical methods, and the ability to provide clinical and diagnostic information to patients and doctors.

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

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

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

Prader-Willi syndrome, or PWS, is a complex disease, and companies have had difficulties in developing new therapies for PWS.

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

In addition, we have begun a program for a new mechanism that may have therapeutic effects in PWS, but this program is in preclinical development, and our candidate, RM-853, may not succeed in completing the pre-IND studies needed to proceed to clinical trials, or may fail in early Phase 1 studies due to unfavorable safety, pharmacokinetics or for other reasons. The hypothesis supporting the therapeutic effects of this mechanism is also based on limited clinical and preclinical information, and even if RM-853 were to progress to a Phase 2 proof of concept study, it is unclear if there will be safety and efficacy to support proceeding further in development.

Risks Related to the Commercialization of Setmelanotide

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

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

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

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

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

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

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

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

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

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

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

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

- the ability of setmelanotide to treat obesity caused by certain genetic deficiencies affecting the MC4 pathway and, if required by any competent authority in connection with the approval for these indications, to provide patients with incremental health benefits, as compared with other available treatments, therapies, devices or surgeries;

- the relative convenience and ease of SC injections as the necessary method of administration of setmelanotide, including as compared with other treatments for obese patients;

- the prevalence and severity of any adverse side effects associated with setmelanotide;

- limitations or warnings contained in the labeling approved, as well as the existence of a REMS, for setmelanotide by the FDA or the specific obligations imposed as a condition for marketing authorization imposed by other equivalent competent authorities in foreign jurisdictions, particularly by the European Commission;
- availability of alternative treatments, including a number of obesity therapies already approved or expected to be commercially launched in the near future;
- the size of the target patient population, and the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the ability of setmelanotide to treat the maximum range of pediatric patients, and any limitations on its indications for use, such as if the labeling limits the approved population to patients ages 12 and above;
- the strength of marketing and distribution support and timing of market introduction of competitive products;
- publicity concerning setmelanotide or competing products and treatments;
- pricing and cost effectiveness;
- the effectiveness of our sales and marketing strategies;
- our ability to increase awareness of setmelanotide through marketing efforts;
- our ability to obtain sufficient third-party coverage or reimbursement;
- the willingness of patients to pay out-of-pocket in the absence of third-party coverage; and
- the likelihood that the FDA or other equivalent competent authorities in foreign jurisdictions may require development of a REMS as a condition of approval or post-approval, may not agree with our proposed REMS or may impose additional requirements that limit the promotion, advertising, distribution or sales of setmelanotide.

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

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

Currently, there are no approved or effective current treatments for regulating hunger and hyperphagia related behaviors of patients with POMC deficiency obesity, LepR deficiency obesity, Bardet-Biedl syndrome, Alström syndrome, POMC heterozygous deficiency obesity, or POMC epigenetic disorders. Bariatric surgery is not a treatment option for these genetic disorders of obesity because the severe obesity and hyperphagia associated with these disorders are considered to be risk factors for bariatric surgery. While we are unaware of any competitive products in development

for the obesity and hyperphagia caused by MC4 pathway deficiencies specifically, new competitors may emerge which could limit our business opportunity in the future.

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

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

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

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

Risks Related to Our Dependence on Third Parties

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

We enter into agreements with third-party CROs to provide monitors for and to manage data for our ongoing clinical trials. We rely heavily on these parties for the execution of clinical trials for setmelanotide and control only certain

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

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

These factors may materially adversely affect the willingness or ability of third parties to conduct our clinical trials and may subject us to unexpected cost increases that are beyond our control. Nevertheless, we are responsible for ensuring that each of our studies is conducted in accordance with the applicable protocol, legal, regulatory and scientific standards, and our reliance on CROs does not relieve us of our regulatory responsibilities. We and our CROs are required to comply with current Good Clinical Practices, or cGCPs, which are guidelines enforced by the FDA, the Competent Authorities of the EU member states and equivalent competent authorities in foreign jurisdictions for any products in clinical development. The FDA enforces these regulations and cGCP guidelines through periodic inspections of clinical trial sponsors, principal investigators, and trial sites, and IRBs. If we or our CROs fail to comply with applicable cGCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or other equivalent competent authorities in foreign jurisdictions may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that, upon inspection, the FDA will determine that any of our clinical trials comply with cGCPs. In addition, our clinical trials must be conducted with products produced under current Good Manufacturing Practices, or cGMPs. Our failure or the failure of our CROs to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process and could also subject us to enforcement action up to and including civil and criminal penalties.

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

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

We do not currently have, nor do we plan to acquire, the infrastructure or capability to internally manufacture our clinical drug supply of setmelanotide, or any future product candidates, for use in the conduct of our preclinical studies and clinical trials, and we lack the internal resources and the capability to manufacture any product candidate on a clinical or commercial scale. The facilities used by our contract manufacturing organizations, or CMOs, to manufacture the active pharmaceutical ingredient, or API, and final drug product must pass inspection by the FDA and other equivalent competent authorities in foreign jurisdictions pursuant to inspections that would be conducted after we submit our NDAs or relevant

foreign regulatory submission to the other equivalent competent authorities in foreign jurisdictions. In addition, our clinical trials must be conducted with products produced under cGMP regulations. Our failure or the failure of our CROs or CMOs to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process and could also subject us to enforcement action, including civil and criminal penalties. If we import any drugs or drug substances, we would be subject to FDA and U.S. Bureau of Customs and Border Patrol, or CBP, import regulation requirements. Such enforcement for our failure or our CROs or CMOs' failure to comply with these regulations could result in import delays, detention of products, and, depending on criteria such as the history of violative activities, the FDA could place a foreign firm or certain drug substances or products on Import Alert and require that all such drug substances or products be subject to detention without physical examination, or DWPE, which could significantly impact the global supply chain for setmelanotide. FDARA provides that prescription drug products, with the exception of those on the FDA's drug shortage list or properly imported by individuals, may not be imported for commercial use if they were manufactured in a foreign country, unless they have been approved or are otherwise authorized to be marketed in the United States and are labeled accordingly.

We currently contract with a third party for the manufacture of setmelanotide and intend to continue to do so in the future. We have entered into a process development and manufacturing services agreement with Corden Pharma Brussels S.A, or Corden, formerly Peptisyntha SA prior to its acquisition by Corden, under which Corden will provide certain process development and manufacturing services in connection with the manufacture of setmelanotide. We have also entered into a process development and manufacturing services agreement with Recipharm Monts S.A.S, or Recipharm, under which Recipharm will provide certain process development and manufacturing services in connection with the manufacture of setmelanotide. Under our agreements, we pay both Corden and Recipharm for services in accordance with the terms of mutually agreed upon work orders, which we, Corden and Recipharm may enter into from time to time. The agreement with Corden also provides that, subject to certain conditions, for a period following each product launch date, we will source from Corden a portion of our requirements for that product being sourced from non-affiliate third parties. We may need to engage additional third-party suppliers to manufacture our clinical drug supplies. In the future, if we approach commercialization of setmelanotide or any future product candidate, we will need to engage other third parties to assist in, among other things, labeling, packaging, distribution, post-approval safety reporting, and pharmacovigilance activities. We cannot be certain that we can engage third-party suppliers on terms as favorable as those that are currently in place.

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

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

We do not have long-term supply agreements in place with our contractors, and each batch of setmelanotide is individually contracted under a quality and supply agreement. If we engage new contractors, such contractors must be

approved by the FDA and other equivalent competent authorities in foreign jurisdictions. We will need to submit information to the FDA and other equivalent competent authorities in foreign jurisdictions describing the manufacturing changes. If manufacturing changes occur post-approval, the FDA may have to approve these changes. We plan to continue to rely upon CMOs and, potentially, collaboration partners to manufacture commercial quantities of setmelanotide, if approved. Our current scale of manufacturing appears adequate to support all of our current needs for clinical trial supplies for setmelanotide. If setmelanotide is approved, we will need to identify CMOs or partners to produce setmelanotide on a larger scale.

Risks Related to Our Intellectual Property Rights

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

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

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

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

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

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

parties covered setmelanotide, our financial position and results of operations would also be materially and adversely impacted.

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

- any of our patents, or any of our pending patent applications, if issued, will include claims having a scope sufficient to protect setmelanotide;
- any of our pending patent applications will issue as patents;
- we will be able to successfully commercialize setmelanotide, if approved, before our relevant patents expire;
- we were the first to make the inventions covered by each of our patents and pending patent applications;
- we were the first to file patent applications for these inventions;
- others will not develop similar or alternative technologies that do not infringe our patents;
- any of our patents will be found to ultimately be valid and enforceable;
- any patents issued to us will provide a basis for an exclusive market for our commercially viable products, will provide us with any competitive advantages or will not be challenged by third parties;
- we will develop additional proprietary technologies or product candidates that are separately patentable; or
- our commercial activities or products will not infringe upon the patents of others.

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

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

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

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

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

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

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

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

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

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

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

- cease development and commercialization of setmelanotide;
- pay substantial damages for past use of the asserted intellectual property;

- obtain a license from the holder of the asserted intellectual property, which license may not be available on reasonable terms, if at all; and

- in the case of trademark claims, rename setmelanotide.

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

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

We may also be subject to claims that former employees, collaborators or other third parties have an ownership interest in our patents or other intellectual property. Litigation may be necessary to defend against these and other claims challenging inventorship or ownership. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, such intellectual property. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

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

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

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

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

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

Filing, prosecuting and defending patents on setmelanotide in all countries and jurisdictions throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States could be less extensive than those in the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our

technologies in jurisdictions where we have not obtained patent protection to develop their own products and further, may export otherwise infringing products to territories where we have patent protection, but enforcement is not as strong as that in the United States. These products may compete with our product and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

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

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

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

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

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

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

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

additional resources in an effort to identify a suitable substitute name that would qualify under applicable trademark laws, not infringe the existing rights of third parties and be acceptable to the FDA.

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

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

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

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

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

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

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

Our employees have been previously employed at other biotechnology or pharmaceutical companies, including our competitors or potential competitors. We may be subject to claims that these employees or we have inadvertently or otherwise used or disclosed trade secrets or other proprietary information of the former employers of our employees. Litigation may be necessary to defend against these claims. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to management. If we fail in defending such claims, in addition to paying money damages, we may lose valuable intellectual property rights or personnel. A loss of key personnel or their work product could hamper or prevent our ability to commercialize setmelanotide, which would materially adversely affect our commercial development efforts.

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

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

We currently have only one product candidate, setmelanotide, in clinical development, and our business depends entirely on its successful clinical development, regulatory approval and commercialization. We currently have no drug products for sale and may never be able to develop marketable drug products. Setmelanotide, which is currently in Phase 3 clinical development as a treatment for genetic deficiencies affecting the MC4 pathway, including POMC deficiency obesity and LepR deficiency obesity, and which will initiate Phase 3 clinical development in Bardet-Biedl syndrome in 2018, 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 raised from our IPO. When a sponsor relies exclusively or predominantly on foreign clinical data, the FDA may require a showing that those data are applicable to the U.S. population and U.S. medical practice, which in some cases may require bridging studies or other evidence. Of the large number of drugs in development in the United States and in other countries, only a small percentage will successfully complete the FDA regulatory approval process or the equivalent process in foreign jurisdictions and will be commercialized. In addition, we have not discussed all of our proposed development programs with the FDA of the competent authorities of foreign jurisdictions. Accordingly, even if we are able to obtain the requisite financing to continue to fund our development and clinical trials, we cannot assure you that setmelanotide will be successfully developed or commercialized.

We are not permitted to market setmelanotide in the United States until we receive approval of an NDA from the FDA, or in any foreign jurisdictions until we receive the requisite approval from such countries. We have two Phase 3 clinical trials underway, one each for the treatment of POMC deficiency obesity and LepR deficiency obesity, and plan to initiate a third Phase 3 trial for Bardet-Biedl syndrome in 2018. Under our current development program, we plan to conduct a single Phase 3 clinical trial for POMC deficiency obesity. To date, in our ongoing discussions with the FDA, the agency has not asked for additional Phase 3 trials in POMC deficiency obesity, but the agency could still require us to conduct additional Phase 3 clinical trials for this indication. Moreover, for POMC deficiency obesity, the FDA has provided clear advice in the past, but could at any time alter its previous advice on many aspects of the trial—the small size, the primary and key secondary endpoints, the open label design, the amount of past medical history available on individual patients, the statistical analysis plan, the definition of clinically-relevant success for the protocol, entry of patients ages six or over—all of which may impact the timing and ability to obtain FDA approval. For example, the FDA asked us in December 2017 to switch the order of our primary and key secondary endpoints for weight in our POMC deficiency Phase 3 protocol. While this might be favorable as the new primary endpoint has increased statistical power - the ability to produce a positive study result - this change occurred after the Phase 3 trial had started and may result in additional complexities such as more attention to compliance and retention. There are other aspects of the trial for which we have not received advice from the FDA, such as the number of U.S. versus non-U.S. patients and the number of patients with POMC gene defects versus the number of patients with PCSK1 defects, which could also impact the timing of and our ability to obtain FDA approval. We have received FDA comments that indicate the Phase 3 program for LepR deficiency can be similar to POMC deficiency, but we have not yet discussed with the FDA the protocol for a Phase 3 program for LepR deficiency obesity in detail. Therefore, the timeline for enrollment, availability of data, and cost of conducting such trials are less certain, and could be less favorable than those applicable to the POMC deficiency obesity program.

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

The FDA or other regulatory authorities and other equivalent competent authorities in foreign jurisdictions will also require that we conduct one or more pivotal trials for each other indication sought. In addition, we are not sure if one or more Phase 3 trials would be required for approval in each other indication. The need and length of placebo-controlled data in these pivotal trials and the number of patients required for these approvals is also unclear. We expect to seek an indication for obesity caused by monogenic deficiencies affecting the MC4 pathway. We are currently conducting Phase 3 trials for treatment of setmelanotide in POMC deficiency obesity and LepR deficiency obesity and initiating a Phase 3 trial for treatment of Bardet-Biedl syndrome.

We are currently conducting Phase 2 trials in Alström syndrome, POMC heterozygous deficiency obesity, and POMC epigenetic disorders. If the clinical data meet key primary and secondary endpoints for safety and efficacy, our overall clinical program may be less time consuming and require fewer patients than might a program for a broader obesity indication. We will be determining if the trial meets “proof of concept” in each of these indications in our own judgment. There is no certainty that the FDA, other competent authorities, or outside investors will agree with our determination, which might impact on the ability to transition to Phase 3 studies.

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

In the European Union we are currently conducting the Phase 3 clinical trial RM-493-015 in Germany, France, Netherlands, and the United Kingdom, in LepR deficiency obesity. We are also conducting this study in the United States. We have not obtained EMA scientific advice for the LepR deficiency indication.

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

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

Our plan is to expand our internal clinical development operations and capabilities so that we can continue to enroll and manage our Phase 2 clinical trials, and enroll and manage our Phase 3 clinical trials, such that, if the clinical trials are successful, we can file an NDA for POMC deficiency obesity in the United States by 2019 or early 2020. We believe we have finalized the design, timing and size of our Phase 3 trial for POMC deficiency obesity with the FDA but we cannot assure you that the trial will not be subject to further modification or that it will be completed on time. In addition, obtaining approval of an NDA and the approval of a marketing authorization application from the European Commission is a complex, lengthy, expensive and uncertain process, and the FDA, EMA or equivalent competent authorities in foreign jurisdictions may delay, limit or deny approval of setmelanotide for many reasons, including, among others:

- the FDA, the EMA, or other equivalent competent authorities in foreign jurisdictions may disagree with our interpretation of data from clinical trials, or may change the requirements for approval even after it has reviewed and commented on the design for our clinical trials;

- we may not be able to demonstrate to the satisfaction of the FDA, the EMA, or other equivalent competent authorities in foreign jurisdictions that setmelanotide is safe and effective in treating obesity caused by certain genetic deficiencies affecting the MC4 pathway;

- the results of our clinical trials may not be interpretable or meet the level of statistical or clinical significance required by the FDA, the EMA, or other equivalent competent authorities in foreign jurisdictions for marketing approval. For example, the potential unblinding of setmelanotide studies due to easily identifiable adverse events may raise the concern that potential bias has affected the clinical trial results;

- the FDA, the EMA, or other equivalent competent authorities in foreign jurisdictions may disagree with the number, size, conduct or implementation of our clinical trials;

- the FDA, the EMA, or other equivalent competent authorities in foreign jurisdictions may require that we conduct additional clinical trials or pre-clinical studies;

- the FDA, the EMA, or other equivalent competent authorities in foreign jurisdictions or the applicable foreign regulatory agency may identify deficiencies in our chemistry, manufacturing or controls of setmelanotide;

- the CROs that we retain to conduct our clinical trials may take actions outside of our control that materially adversely impact our clinical trials;

- the FDA, the EMA, or other equivalent competent authorities in foreign jurisdictions may find the data from preclinical studies and clinical trials insufficient to demonstrate that clinical and other benefits of setmelanotide outweigh its safety risks;

- the FDA, the EMA, or other equivalent competent authorities in foreign may disagree with our interpretation of data from our preclinical studies and clinical trials;

- the FDA, the EMA, or other equivalent competent authorities in foreign jurisdictions may not approve the formulation, labeling or specifications of setmelanotide;

- the FDA, the EMA, or other equivalent competent authorities in foreign may not accept data generated at our clinical trial sites;

- if and when our NDA or our marketing authorization application is submitted and reviewed by an advisory committee, the FDA, the EMA, or the equivalent competent authorities in foreign jurisdictions may have difficulties scheduling an advisory committee meeting in a timely manner or the advisory committee may recommend against approval of our application or may recommend that the FDA, the EMA, or the equivalent competent authorities in foreign jurisdictions require, as a condition of approval, additional preclinical studies or clinical trials, limitations on approved labeling or distribution and use restrictions;

- the FDA may require development of a REMS as a condition of approval or post-approval, or may not agree with our proposed REMS or may impose additional requirements that limit the promotion, advertising, distribution, or sales of setmelanotide. In addition, the European Commission may grant only conditional approval marketing authorization or impose specific obligations as a condition for marketing authorization, or may require us to conduct post authorization safety studies as a condition of grant of marketing authorization;

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

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

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

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

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

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

Even if we receive marketing approval for setmelanotide, regulatory authorities may impose significant restrictions on setmelanotide's indicated uses or marketing or impose ongoing requirements for potentially costly post approval studies. Setmelanotide will also be subject to ongoing requirements by the FDA, the EMA, and the competent authorities in the EU member states, governing labeling, packaging, storage, advertising, promotion, marketing, distribution, importation, exportation, post-approval changes, manufacturing, recordkeeping, and submission of safety and other post market information. The FDA and the other competent foreign authorities have significant post market authority, including, for example, the authority to require labeling changes based on new safety information and to require post market studies or clinical trials to evaluate serious safety risks related to the use of a drug. The FDA also has the authority to require, as part of an NDA or post approval, the submission of a REMS, which may include Elements to Assure Safe Use, or ETASU. Any REMS required by the FDA may lead to increased costs to assure compliance with new post approval regulatory requirements and potential requirements or restrictions on the sale of approved products, all of which could lead to lower sales volume and revenue.

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

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

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

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

In addition, EU legislation related to pharmacovigilance, or the assessment and monitoring of the safety of medicinal products, provides that the EMA and the competent authorities of the EU member states have the authority to require companies to conduct additional post-approval clinical efficacy and safety studies. The legislation also governs the obligations of marketing authorization holders with respect to additional monitoring, adverse event management and reporting. Under the pharmacovigilance legislation and its related regulations and guidelines, we may be required to conduct a labor intensive collection of data regarding the risks and benefits of marketed products and may be required to engage in ongoing assessments of those risks and benefits, including the possible requirement to conduct additional clinical studies, which may be time-consuming and expensive and could impact our profitability. Non-compliance with such

obligations can lead to the variation, suspension or withdrawal of marketing authorization or imposition of financial penalties or other enforcement measures.

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

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

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

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

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

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

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

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

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

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

- the Independent Payment Advisory Board, or IPAB, which has authority to recommend certain changes to the Medicare program to reduce expenditures by the program that could result in reduced payments for

prescription drugs. However, the IPAB implementation has been not been clearly defined. ACA provided that under certain circumstances, IPAB recommendations or recommendations of the Secretary of Health and Human Services will become law unless Congress enacts legislation that will achieve the same or greater Medicare cost savings; and

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

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

Legislative changes to or regulatory changes under the ACA have occurred in the 115th U.S. Congress and under the Trump administration. For example, the Tax Cuts and Jobs Act enacted on December 22, 2017, eliminated the shared responsibility payment for individuals who fail to maintain minimum essential coverage under section 5000A of the Internal Revenue Code of 1986, commonly referred to as the individual mandate, beginning in 2019. Further, in the Bipartisan Budget Act of 2018, the Medicare Part D coverage gap discount program was revised to increase drug manufacturers' discount levels under the program. Additional legislative changes to and regulatory changes under the ACA remain possible, but the nature and extent of such potential additional changes are uncertain at this time. We expect that the ACA, as currently enacted or as it may be amended in the future, and other healthcare reform measures that may be adopted in the future, could have a material adverse effect on our industry generally and on our ability to successfully commercialize our product candidates, if approved.

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

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

The pricing of prescription pharmaceuticals is also subject to governmental control outside the United States. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost effectiveness of setmelanotide to other available therapies. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our ability to generate revenues and become profitable could be impaired.

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

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

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

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

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

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

If we obtain marketing approval for setmelanotide, we will be subject to continual requirements of and review by the FDA and equivalent competent authorities in foreign jurisdictions. These requirements may include, but are not limited to, post-approval studies to be conducted which may include carcinogenicity studies, a QT interval prolongation study in one form or another, other Phase 1 trials, and ongoing natural history studies with patient registries. Other requirements may also include, among other things, restrictions governing promotion of an approved product, submissions of safety and other post-marketing information and reports, registration and listing requirements, cGMP requirements relating to manufacturing, quality control, quality assurance and corresponding maintenance of records and documents, and requirements regarding the distribution of samples to physicians and recordkeeping. The FDA and other federal and state agencies, including the Department of Justice and other equivalent competent authorities in foreign jurisdictions, closely regulate compliance with all requirements governing prescription drug products, including requirements pertaining to marketing and promotion of drugs in accordance with the provisions of the approved labeling and manufacturing of products in accordance with cGMP requirements. Violations of such requirements may lead to investigations alleging violations of the FDCA, and other statutes, including the False Claims Act and other federal and state health care fraud and abuse laws as well as state consumer protection laws.

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

In the European Union, the advertising and promotion of our products are subject to EU laws governing promotion of medicinal products, interactions with physicians, misleading and comparative advertising and unfair commercial practices. In addition, other legislation adopted by individual EU member states may apply to the advertising and promotion of medicinal products. These laws require that promotional materials and advertising in relation to medicinal products comply with the product's Summary of Product Characteristics, or SmPC, as approved by the competent authorities. The SmPC is the document that provides information to physicians concerning the safe and effective use of the medicinal product. It forms an intrinsic and integral part of the marketing authorization granted for the medicinal product. Promotion of a medicinal product that does not comply with the SmPC is considered to constitute off-label promotion. The off-label promotion of medicinal products is prohibited in the European Union. The applicable laws at European Union level and in the individual EU member states also prohibit the direct-to-consumer advertising of prescription-only medicinal products. Violations of the rules governing the promotion of medicinal products in the European Union could be penalized by administrative measures, fines and imprisonment. These laws may further limit or restrict the advertising and promotion of our products to the general public and may also impose limitations on our promotional activities with health care professionals.

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

Healthcare providers, physicians and others will play a primary role in the recommendation and prescription of setmelanotide, if approved. Our arrangements and interactions with healthcare professionals, third-party payors, patients

and others will expose us to broadly applicable fraud and abuse, anti-kickback, false claims and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute setmelanotide, if we obtain marketing approval. The U.S. federal and state healthcare laws and regulations that may affect our ability to operate include, but are not limited to:

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

- The federal civil False Claims Act prohibits individuals or entities from, among other things, knowingly presenting, or causing to be presented a false or fraudulent claim for payment of government funds, or knowingly making, using or causing to made or used a false record or statement material to an obligation to pay money to the government or knowingly concealing or knowingly and improperly avoiding, decreasing or concealing an obligation to pay money to the federal government. Actions under the False Claims Act may be brought by the Attorney General or as a qui tam action by a private individual in the name of the government. Many pharmaceutical manufacturers have been investigated and have reached substantial financial settlements with the federal government under the civil False Claims Act for a variety of alleged improper activities including causing false claims to be submitted as a result of the marketing of their products for unapproved and thus non-reimbursable uses, inflating prices reported to private price publication services which are used to set drug payment rates under government healthcare programs, and other interactions with prescribers and other customers including those that may have affected their billing or coding practices and submission to the federal government. The government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal civil False Claims Act. Pharmaceutical and other healthcare companies also are subject to other federal false claims laws, including, among others, federal criminal healthcare fraud and false statement statutes that extend to non-government health benefit programs.

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

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

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

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

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

Ensuring that our business arrangements and interactions with healthcare professionals, third-party payors, patients and others comply with applicable healthcare laws and regulations will require substantial resources. It is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations, including anticipated activities to be conducted by our sales and marketing team, were found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, imprisonment, damages, fines, exclusion from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations, any of which could substantially disrupt our operations. Although compliance programs can mitigate the risk of investigation and prosecution for violations of these laws, the risks cannot be entirely eliminated. Any action against us for violation of these laws or regulations, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business.

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

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

fines or other sanctions. Some of these laws and related risks are described under the risk factor "*We may be subject to federal and state healthcare laws and regulations. If we are unable to comply or have not fully complied with such laws and regulations, we could face criminal sanctions, damages, civil penalties, reputational harm and diminished profits and future earnings*" of this Quarterly Report on Form 10-Q.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Various laws, regulations and executive orders also restrict the use and dissemination outside of the United States, or the sharing with certain non-U.S. nationals, of information classified for national security purposes, as well as certain products and technical data relating to those products. If we expand our presence outside of the United States, it will require us to dedicate additional resources to comply with these laws, and these laws may preclude us from developing, manufacturing or selling certain product candidates and products outside of the United States, which could limit our growth potential and increase our development costs.

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

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

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

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

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

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

Risks Related to Preclinical Development and Clinical Development of RM-853

We have assumed sole responsibility for the global product development and commercialization of RM-853, which may distract our management team from pursuing regulatory approval of setmelanotide, and we may never complete preclinical development of RM-853 or file an IND with the FDA. Many of the risks we have faced in preclinical development and in clinical development of setmelanotide will also exist in preclinical development of RM-853 and clinical development, should we ever enter into clinical development of RM-853

In March 2018 we entered into a license agreement with Takeda Pharmaceutical Company Limited, which we refer to as Takeda, to develop and commercialize T-3525770, now known as RM-853. RM-853 is a potent, orally available ghrelin o-acyltransferase, or GOAT, inhibitor currently in preclinical development for PWS. Under the terms of the license agreement, we assumed sole responsibility for the global product development and commercialization of RM-853. This relationship may distract our management team from clinical development of setmelanotide and may require us to expend financial and other resources. PWS is a complex disease and companies have had difficulties in developing new therapies for PWS. In addition, many of the risks we have faced in preclinical development and in clinical development of setmelanotide will also exist in preclinical development of RM-853 and clinical development, should we ever enter into clinical development of RM-853, including:

- results from preclinical studies may not be predictive of later clinical trials of RM-853;
- failures or delays in the commencement or completion of preclinical studies or clinical trials could result in increased costs to us and could delay, prevent or limit our ability to generate revenue and continue our business;
- RM-853 could cause undesirable side effects that could result in significant negative consequences, including the inability to enter clinical development or receive regulatory approval;
- experience by others suggest that PWS patients are high risk for adverse experiences and for this, and many other reasons, clinical trials in that population are extremely challenging;
- other risks related to regulatory approval, and if ever received, marketing and commercialization of RM-853;
- potential product liability exposure;
- an inability to protect our intellectual property related to RM-853;
- risks related to our dependence on third parties, including in manufacturing RM-853 and conducting preclinical studies and clinical trials of RM-853; and
- the burden of complying with complex and changing foreign regulatory, tax, accounting and legal requirements.

Risks Related to Employee Matters and Managing Growth

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

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

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

We expect to increase our number of employees and the scope of our operations. In particular, we will need to transition from a research and development company to a commercial company. To manage our anticipated development and expansion, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Also, our management may need to divert a disproportionate amount of its attention away from their day-to-day activities and devote a substantial amount of time to managing these development activities. Due to our limited resources, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. This may result in weaknesses in our infrastructure, and give rise to operational mistakes, loss of business and commercial opportunities, loss of employees and reduced productivity among remaining employees. The physical expansion of our operations may lead to significant costs and may divert financial resources from other projects, such as the development of setmelanotide. If our management is unable to effectively manage our expected development and expansion, our expenses may increase more than expected, our ability to generate or increase our revenue could be reduced and we may not be able to implement our business strategy. Our future financial performance and our ability to commercialize setmelanotide, if approved, and compete effectively will depend, in part, on our ability to effectively manage the future development and expansion of our company.

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

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

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

Our internal computer systems and those of our third-party CROs, CMOs, and other contractors and consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. If such an event were to occur and cause interruptions in our operations, it could

result in a material disruption of our programs. For example, the loss of clinical trial data for setmelanotide could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach results in a loss of or damage to our data or applications or other data or applications relating to our technology or product candidate, or inappropriate disclosure of confidential or proprietary information, we could incur liabilities and the further development of setmelanotide could be delayed.

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

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

Risks Related to Our Common Stock

Our principal stockholders and management own a significant percentage of our stock and will be able to exert significant control over matters subject to stockholder approval.

Based on the number of shares outstanding as of March 31, 2018, our executive officers, directors, holders of 5% or more of our capital stock and their respective affiliates beneficially owned approximately 74% of our voting stock. These stockholders will have the ability to influence us through this ownership position. These stockholders may be able to determine all matters requiring stockholder approval. For example, these stockholders may be able to control elections of directors, amendments of our organizational documents, or approval of any merger, sale of assets, or other major corporate transaction. This may prevent or discourage unsolicited acquisition proposals or offers for our common stock that you may feel are in your best interest as one of our stockholders.

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.

An active market for our common stock may not be maintained.

Our stock only recently began trading on The NASDAQ Global Market and we can provide no assurance that we will be able to maintain an active trading market on The NASDAQ Global Market or any other exchange in the future. If an active market for our common stock does not develop or is not maintained, it may be difficult for our stockholders to sell shares without depressing the market price for the shares or at all. An inactive market may also impair our ability to

raise capital by selling shares and may impair our ability to acquire other businesses, applications or technologies using our shares as consideration.

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 currently have very limited research coverage by securities and industry analysts. If no additional securities or industry analysts commence coverage of our company, the trading price for our stock would be negatively impacted. If one or more of the analysts who covers us downgrades our stock, our stock price would likely decline. If one or more of these analysts issues unfavorable commentary or ceases to cover us or fails to regularly publish reports on us, interest in our stock could decrease, which could cause our stock price or trading volume to decline.

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

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

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

The market price for our common stock is likely to be volatile and 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 from our IPO. We may not use these proceeds effectively, which could affect our results of operations and cause our stock price to decline.

We have considerable discretion in the application of the net proceeds from our IPO. We intend to continue to use the net proceeds to fund development and manufacturing of setmelanotide through completion of our Phase 3 clinical trials and subsequent NDA submissions with the FDA for the treatment of POMC deficiency obesity and LepR deficiency obesity, the development of setmelanotide through our Phase 2 proof of concept clinical trials for Bardet-Biedl syndrome, Alström syndrome, POMC heterozygous deficiency obesity and POMC epigenetic disorders, as well as the initiation of our Phase 3 clinical trials for Bardet-Biedl syndrome, the preparation for commercialization of setmelanotide, initiatives to expand the diagnosis of genetic obesity, including research and scientific exchange related to our ongoing genotyping and genetic epidemiology studies and for working capital and general administrative expenses, additional research and development expenses, and other general corporate purposes. 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. 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 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 Code, a corporation is generally allowed a deduction for net operating losses, or NOLs, carried over from a prior taxable year. Under the Code, we can carry forward certain NOLs of our subsidiaries to offset future taxable income, if any, until such losses are used or, for NOLs arising in taxable years ending on or before December 31, 2017, until such NOLs expire. NOLs arising in taxable years ending after December 31, 2017 are not subject to expiration. NOLs arising in taxable years beginning after December 31, 2017 may only be used to offset up to 80% of the corporation's taxable income computed without taking into account NOL deductions. Other unused tax attributes, such as research tax credits may also be carried forward to offset future taxable income, if any, until such credits are used or expire. As of December 31, 2017, we had approximately $73.1 million and $3.8 million of unused federal and state carryforwards of NOLs, respectively, and approximately $1.9 million and $0.5 million of unused federal and state carryforwards of tax credits, respectively. Additionally, as of December 31, 2017, we had federal orphan drug credits related to qualifying research of $2.3 million.

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 our IPO may result in a limitation under Code 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 our existing stockholders sell, or indicate an intention to sell, substantial amounts of our common stock in the public market, the trading price of our common stock could decline. As of March 31, 2018, we had outstanding a total of approximately 27.3 million shares of common stock. Of these shares, approximately 7.2 million of the shares of our common stock sold in the IPO are freely tradable, without restriction, in the public market.

The lock-up agreements pertaining to our IPO expired on April 2, 2018, following which up to an additional 20.1 million shares of common stock became eligible for sale in the public market, of which approximately 13.3 million shares are held by current directors, executive officers and their respective affiliates and may be subject to Rule 144 under the Securities Act.

In addition, approximately 5.1 million shares of our common stock that are either subject to outstanding stock awards or reserved for future issuance under our 2017 Plan are eligible for sale in the public market to the extent permitted by the provisions of various vesting schedules and Rule 144 and Rule 701 under the Securities Act. If these additional shares of common stock are sold, or if it is perceived that they will be sold, in the public market, the trading price of our common stock could decline.

The holders of approximately 18.9 million shares of our common stock, or approximately 69% of our total outstanding common stock as of March 31, 2018 are entitled to rights with respect to the registration of their shares under the Securities Act, subject to vesting schedules. 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 trading price of our common stock.

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 our IPO, (b) in which we have total annual gross revenue of at least $1.07 billion, or (c) in which we are deemed to be a large accelerated filer, which means the market value of our common stock that is held by non-affiliates exceeds $700 million as of the prior June 30th, and (2) the date on which we have issued more than $1.0 billion in non-convertible debt during the prior three-year period.

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

As a public company, and particularly after we are no longer an emerging growth company, we will incur significant legal, accounting and other expenses that we did not incur as a private company. The Sarbanes-Oxley Act of

2002, or Sarbanes-Oxley, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of the NASDAQ Global Market and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel will need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations will increase our legal and financial compliance costs and will make some activities more time-consuming and costly. For example, we expect that these rules and regulations may make it more difficult and more expensive for us to obtain director and officer liability insurance, which in turn could make it more difficult for us to attract and retain qualified members of our board of directors.

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

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

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

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

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

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

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

Item 2. Unregistered Sales of Equity Securities and Use of Proceeds.

Unregistered Sales of Equity Securities

During the quarter ended March 31, 2018, we authorized the issuance and sale of 223,544 shares of common stock to Takeda pursuant to the Takeda license agreement.

Use of Proceeds

Shares of our common stock began trading on The NASDAQ Global Market on October 5, 2017. The offer and sale of all the shares in the IPO were registered under the Securities Act pursuant to a registration statement on Form S-1 (File No. 333-220337), which was declared effective by the SEC on October 4, 2017.

There has been no material change in the planned use of proceeds from our IPO as described in the Prospectus filed with the SEC pursuant to Rule 424(b) under the Securities Act on October 5, 2017.

Repurchased of Shares or of Company Equity Securities

None.

Item 3. Defaults Upon Senior Securities

Not applicable.

Item 4. Mine Safety Disclosure

Not applicable.

Item 5. Other Information

None

Item 6. Exhibits

		Incorporated by Reference		
Exhibit Number	Exhibit Description	Form	Date	Number
10.1*#	License Agreement dated March 30, 2018, by and between the Company and Takeda Pharmaceutical Company Limited.			
10.2*†	Summary of Non-Employee Director Compensation Policy.			
31.1*	Certification of the Chief Executive Officer, as required by Section 302 of the Sarbanes-Oxley Act of 2002 (18 U.S.C. 1350).			
31.2*	Certification of the Chief Financial Officer, as required by Section 302 of the Sarbanes-Oxley Act of 2002 (18 U.S.C. 1350).			
32.1*	Certification of the Chief Executive Officer, as required by Section 906 of the Sarbanes-Oxley Act of 2002 (18 U.S.C. 1350).			

32.2*	Certification of the Chief Financial Officer, as required by Section 906 of the Sarbanes-Oxley Act of 2002 (18 U.S.C. 1350).
101.INS*	XBRL Instance Document.
101.SCH*	XBRL Taxonomy Extension Schema Document.
101.CAL*	XBRL Taxonomy Extension Calculation Linkbase Document.
101.DEF*	XBRL Taxonomy Extension Definition Linkbase Document.
101.LAB*	XBRL Taxonomy Extension Label Linkbase Document.
101.PRE*	XBRL Taxonomy Extension Presentation Linkbase Document.

* Filed or furnished herewith

† 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 24b-2 of the Securities Act

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the Registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

RHYTHM PHARMACEUTICALS, INC.

Dated: May 14, 2018

By: /s/ Keith M. Gottesdiener
Name: Keith M. Gottesdiener
Title: Chief Executive Officer, President and Director
(Principal Executive Officer)

Dated: May 14, 2018

By: /s/ Hunter Smith
Name: Hunter Smith
Title: Chief Financial Officer and Treasurer
(Principal Financial and Accounting Officer)

EXHIBIT 10.1

RHYTHM PHARMACEUTICALS, INC. REQUESTS THAT THE MARKED PORTIONS OF THIS EXHIBIT BE GRANTED CONFIDENTIAL TREATMENT UNDER RULE 24B-2 OF THE SECURITIES EXCHANGE ACT OF 1934, AS AMENDED

EXECUTION VERSION

LICENSE AGREEMENT

BY AND BETWEEN

TAKEDA PHARMACEUTICAL COMPANY LIMITED

AND

RHYTHM PHARMACEUTICALS, INC.

CONFIDENTIAL

*CONFIDENTIAL TREATMENT REQUESTED.

LICENSE AGREEMENT

THIS LICENSE AGREEMENT (this "Agreement") is made effective as of March 30, 2018 (the "Effective Date") by and between Takeda Pharmaceutical Company Limited, a corporation incorporated under the laws of Japan, having its principal place of business at 1-1, Doshomachi 4-chome, Chuo-ku, Osaka 540-8645, Japan ("Takeda") and Rhythm Pharmaceuticals, Inc., a Delaware corporation having its principal place of business at 500 Boylston Street, 11th Floor, Boston, MA 02116 ("Licensee"). Licensee and Takeda are sometimes referred to herein individually as a "Party" and collectively as the "Parties."

RECITALS

WHEREAS, Takeda is a pharmaceutical company engaged in the research, development and commercialization of products useful in the amelioration, treatment or prevention of human diseases and conditions;

WHEREAS, Licensee is a biopharmaceutical company engaged in the development and commercialization of peptide therapeutics for the treatment of genetic deficiencies that result in life-threatening metabolic disorders; and

WHEREAS, Licensee wishes to be granted, and Takeda desires to grant, a license in the Territory (as defined below) under certain patents, patent applications, know-how, and other proprietary information for the further development and commercialization of the Compound (as defined below) and Products (as defined below).

NOW, THEREFORE, in consideration of the foregoing and the mutual agreements set forth below, and other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, the Parties agree as follows:

ARTICLE 1 – DEFINITIONS

1.1 "ADR" has the meaning set forth in Exhibit E.

1.2 "ADR Notice" has the meaning set forth in Exhibit E.

1.3 "Affiliate" means, with respect to a particular Party, a person, corporation, partnership, or other entity that controls, is controlled by or is under common control with such Party. For the purposes of this definition, the word "control" (including, with correlative meaning, the terms "controlled by" or "under the common control with") means the actual power, either directly or indirectly through one or more intermediaries, to direct or cause the direction of the management and policies of such entity, whether by the ownership of fifty percent (50%) or more of the voting stock of such entity, or by contract or otherwise.

1.4 "[ ]*" has the meaning set forth in Section 5.1.

1.5 "[ ]* Agreement" has the meaning set forth in Section 5.1.

1.6 "Applicable Law" means all applicable statutes, ordinances, regulations, rules, or orders of any kind whatsoever of any Governmental Authority, including the U.S. Food, Drug and Cosmetic Act, (21 U.S.C. §301 et seq.), Prescription Drug Marketing Act, the Generic Drug Enforcement Act of 1992 (21 U.S.C. §335a et seq.), U.S. Patent Act (35 U.S.C. §1 et seq.), Federal Civil False Claims Act (31 U.S.C. §3729 et seq.), and the Anti-Kickback Statute (42 U.S.C. §1320a-7b et seq.), all as amended from time to time, together with any rules, regulations, and compliance guidance promulgated thereunder.

1.7 [ ]* has the meaning set forth in Section 5.2.

1.8 [ ]* has the meaning set forth in Section 5.2.

1.9 "Bankruptcy Laws" has the meaning set forth in Section 13.5(b).

1.10 "Bayh-Doyle Act" means the Patent and Trademark Law Amendments Act of 1980, as amended, codified at 35 U.S.C. §§ 200-212, as well as any regulations promulgated pursuant thereto, including 37 C.F.R. Part 401, and any successor statutes or regulations.

1.11 "Breaching Party" has the meaning set forth in Section 13.2(a).

1.12 "Business Day" means a day other than Saturday, Sunday or any other day on which commercial banks located in the State of New York, U.S., or Tokyo, Japan, are authorized or obligated by Applicable Law to close.

1.13 "Calendar Quarter" means the respective periods of three (3) consecutive calendar months ending on March 31, June 30, September 30 and December 31; provided, however, that (a) the first Calendar Quarter of the Term shall extend from the Effective Date to the end of the first complete Calendar Quarter thereafter; and (b) the last Calendar Quarter of the Term shall end upon the expiration or termination of this Agreement.

1.14 "Calendar Year" means the twelve (12)-month period ending on December 31; provided however, that (a) the first Calendar Year of the Term shall begin on the Effective Date and end on December 31, 2018; and (b) the last Calendar Year of the Term shall end on the date of expiration or termination of this Agreement.

1.15 "Change of Control" means an event upon which: (a) any Third Party acquires directly or indirectly the beneficial ownership of any voting security of Licensee, or if the percentage ownership of such person or entity in the voting securities of Licensee is increased through stock redemption, cancellation or other recapitalization, and immediately after such acquisition or increase such Third Party is, directly or indirectly, the beneficial owner of voting securities representing more than fifty percent (50%) of the total voting power of all of the then-outstanding voting securities of Licensee; (b) the consummation of a merger, consolidation, recapitalization, or reorganization of Licensee, other than any such transaction, which would result in stockholders or equity holders of Licensee, or an Affiliate of Licensee existing immediately prior to such transaction, owning at least fifty percent (50%) of the outstanding securities of the surviving entity (or its parent entity) immediately following such transaction; (c) the stockholders or equity holders of Licensee approve a plan of complete liquidation of Licensee, or an agreement for the sale or

disposition by Licensee of all or a substantial portion of such Licensee's assets, other than pursuant to the transaction as described above or to an Affiliate; or (d) the sale or other transfer to a Third Party of all or substantially all of Licensee's assets which relate to this Agreement.

1.16 "Claim" has the meaning set forth in Section 15.1.

1.17 "Clinical Trial" means any human clinical study or trial of a Product in the Field in the Territory.

1.18 "Combination Product" has the meaning set forth in Section 1.85.

1.19 "Commercialization" means all activities undertaken in support of the promotion, marketing, strategy, pricing, physician targeting, reimbursement, branding, sale and distribution (including importing, exporting, transporting, customs clearance, warehousing, invoicing, handling and delivering the Products to customers) of the Products in the Field in the Territory. "Commercialize" means to engage in Commercialization activities.

1.20 "Commercially Reasonable Efforts" means (a) with respect to Licensee, its Affiliates or its Sublicensees, the efforts and resources typically used by biotechnology or pharmaceutical companies similar in size and scope to Licensee, its Affiliates or such Sublicensees, and (b) with respect to Takeda, [ ]*, in each case of (a) and (b), to perform the obligation at issue, which efforts will not be less than those efforts made with respect to other products at a similar stage of development or in a similar stage of product life, with similar developmental risk profiles, of similar market and commercial potential, taking into account the proprietary position of the products, the regulatory structure involved (including regulatory or data exclusivity), Regulatory Authority-approved labeling, product profile, the expected and actual profitability and return on investment of the applicable product, issues of safety and efficacy, the likely timing of the product's entry into the market, the likelihood of receiving Regulatory Approval, and other relevant scientific, technical, and commercial factors.

1.21 "Common Stock" has the meaning set forth in Section 7.1.

1.22 "Completion of a Phase 1 Clinical Trial for a Product" means the delivery by Licensee to Takeda of a copy of the final clinical study report for a Phase 1 Clinical Trial for a Product.

1.23 "Compound" means the Ghrelin O-acyltransferase inhibitor known as "T-3525770", claimed in the Takeda Patents or described in the Takeda Intellectual Property.

1.24 "Confidential Disclosure Agreement" means that certain Confidential Disclosure Agreement between Licensee and Millennium Pharmaceuticals, Inc., dated October 19, 2017.

1.25 "Confidential Information" means all non-public or proprietary Information disclosed by a Party or any of its Affiliates or any of its or their Representatives to the other Party or any of its Affiliates or any of its or their Representatives under this Agreement, without regard as to whether any of such Information is marked "confidential" or "proprietary," or disclosed in oral, written, graphic, or electronic form. Confidential Information shall include (a) the terms and conditions of

this Agreement and (b) all non-public or proprietary Information disclosed by a Party or its Affiliates or its or their Representatives pursuant to the Confidential Disclosure Agreement.

1.26 "Control" means (i) with respect to any Information, ownership or possession by a Party, or, where expressly provided, its Affiliates, of the ability (without taking into account any rights granted by one Party to the other Party under the terms of this Agreement) to grant access, a license or a sublicense to such Information without violating the terms of any agreement or other arrangement with, or necessitating the consent of, any Third Party, at such time that such Party or any of its Affiliates would be first required under this Agreement to grant the other Party such access, license or sublicense, and (ii) with respect to any Patent, trademark or other intellectual property right that does not constitute Information, ownership or possession by a Party, or, where expressly provided, its Affiliates, of the ability (without taking into account any rights granted by one Party to the other Party under the terms of this Agreement) to grant a license or a sublicense to such Patent, trademark or other intellectual property right without violating the terms of any agreement or other arrangement with, or necessitating the consent of, any Third Party, at such time that such Party or any of its Affiliates would be first required under this Agreement to grant the other Party such license or sublicense.

1.27 "Cover," "Covering," or "Covered" means, with respect to a particular subject matter at issue and the relevant Patent, that, but for a license granted to a Person under a claim included in such Patent, the manufacture, use, sale, offer for sale, or importation by such Person of the subject matter at issue would infringe such claim or, in the case of a Patent that is a patent application, would infringe a claim in such patent application if it were to issue as a patent in a particular country.

1.28 "CPR" has the meaning set forth in Exhibit E.

1.29 "CPR Rules" has the meaning set forth in Exhibit E.

1.30 "Creditable Payments" has the meaning set forth in Section 7.7(c).

1.31 "Cure Period" has the meaning set forth in Section 13.2(a).

1.32 "Development" means all non-clinical and clinical drug development activities, including toxicology, pharmacology, and other non-clinical efforts, statistical analysis, the performance of Clinical Trials, including the Manufacturing of the Product for use in the Clinical Trials, or other activities reasonably necessary in order to obtain or maintain, Regulatory Approval of the Product in the Field in the Territory, as detailed in a Development Plan for the Product, including the Initial Development Plan. When used as a verb, "Develop" means to engage in Development activities.

1.33 "Development Plan" means a written plan prepared by Licensee for the Development activities with respect to the Compound and the Products, which plan shall identify the Development objectives, projected timeline and activities to be conducted pursuant to this Agreement with respect to the Compound and the Products during the Term in a format and scope similar to that set forth in the Initial Development Plan. "Development Plan" includes the "Initial Development Plan".

1.34 "Disclosing Party" has the meaning set forth in Section 12.1.

1.35 "Dispute" or "Disputes" has the meaning set forth in Section 14.1.

1.36 "Equity Grant Shares" has the meaning set forth in Section 7.1.

1.37 "E.U." means all countries, possessions and territories in Austria, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Netherlands, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden and the United Kingdom (including all possessions and territories of any of the foregoing).

1.38 "Executive Officer" means, for Licensee, its Chief Executive Officer or his or her designee, and for Takeda, its Chief Medical and Scientific Officer or his or her designee, each with the appropriate responsibilities, seniority, and decision-making authority.

1.39 "Exercise Notice" has the meaning set forth in Section 8.1.

1.40 "Exercise Period" has the meaning set forth in Section 8.1.

1.41 "Existing Research Material" has the meaning set forth in Section 3.5(d).

1.42 "Exploit" or "Exploitation" means to research, make, have made, import, export, distribute, use, have used, sell, have sold, or offer for sale, including to Develop, Manufacture, Commercialize, register, modify, enhance, improve or otherwise dispose of.

1.43 "FDA" means the U.S. Food and Drug Administration, or any successor agency thereto.

1.44 "FFDCA" means the Federal Food, Drug and Cosmetic Act under United States Code, Title 21, as amended.

1.45 "Field" means the diagnosis, treatment and prevention of any and all indications.

1.46 "First Commercial Sale" means, on a country-by-country and Product-by-Product basis, the first sale of a Product by Licensee, its Affiliates or Sublicensees (or, at any time after Takeda has royalty payment obligations to Licensee pursuant to Section 13.6(j), by Takeda, its Affiliates, licensees or Sublicensees) to an end user or prescriber for use, consumption or resale of such Product in the applicable country in the Territory in the Field where Regulatory Approval of such Product has been obtained.

1.47 "Force Majeure" means any event beyond the reasonable control of the affected Party or any of its Affiliates, including embargoes; war or acts of war, including terrorism; insurrections, riots, or civil unrest; strikes, lockouts or other labor disturbances; epidemics, fire, floods, earthquakes or other acts of nature; acts, omissions or delays in acting by any Governmental Authority (other than delays incident to the ordinary course of drug development); and failure of plant or machinery (provided that such failure could not have been prevented by the exercise of skill, diligence, and prudence that would be reasonably and ordinarily expected from a skilled and

experienced person engaged in the same type of undertaking under the same or similar circumstances).

1.48 "GAAP" means generally accepted accounting principles current in the U.S.

1.49 "Generic Competition Percentage" means, with respect to a particular Product in a particular country in the Territory, [ ]*.

1.50 "Generic Product" means, on a country-by-country and Product-by-Product basis, any pharmaceutical product sold by a Person in the Territory (other than Licensee, any Affiliate of Licensee, or any Sublicensee under the license granted to Licensee under this Agreement) that: [ ]*.

For the purposes of this definition, [ ]* then-current edition of the FDA publication "Approved Drug Products With Therapeutic Equivalence Evaluations" ("Orange Book").

1.51 "Good Clinical Practices" or "GCP" means the then-current standards, practices and procedures promulgated or endorsed by the FDA as set forth in the guidelines adopted by the International Conference on Harmonization ("ICH"), titled "Guidance for Industry E6 Good Clinical Practice: Consolidated Guidance," (or any successor document) including related regulatory requirements imposed by the FDA, as they may be updated from time to time.

1.52 "Good Laboratory Practices" or "GLP" means the then-current standards, practices and procedures promulgated or endorsed by the FDA as set forth in 21 C.F.R. Part 58 (or any successor statute or regulation), including related regulatory requirements imposed by the FDA, as they may be updated from time to time, including applicable guidelines promulgated under the ICH.

1.53 "Governmental Authority" means any multi-national, federal, state, local, municipal or other government authority of any nature (including any governmental division, subdivision, department, agency, bureau, branch, office, commission, council, court or other tribunal).

1.54 "IFRS" means International Financial Reporting Standards.

1.55 "IND" means an Investigational New Drug application as defined in the FFDCA, as amended, and applicable regulations promulgated thereunder by the FDA, or a clinical trial authorization application for a product filed with a Regulatory Authority in any other regulatory jurisdiction outside the U.S., the filing of which is necessary to commence or conduct clinical testing of a pharmaceutical product in humans in such jurisdiction.

1.56 "Indemnitee" has the meaning set forth in Section 15.3(a).

1.57 "Indemnifying Party" has the meaning set forth in Section 15.3(a).

1.58 "Information" means information, inventions, concepts, discoveries, compounds, compositions, formulations, formulas, practices, procedures, processes, methods, knowledge, know-how, trade secrets, technology, techniques, designs, drawings, correspondence, computer programs, documents, apparatus, results, strategies, regulatory documentation, information and submissions pertaining to, or made in association with, filings with any Government Authority or

patent office, data, including pharmacological, toxicological, non-clinical and clinical data, analytical and quality control data, manufacturing data and descriptions, patent and legal data, market data, financial data or descriptions, devices, assays, chemical formulations, specifications, material, product samples and other samples, physical, chemical and biological materials and compounds, and the like, in written, electronic, oral or other tangible or intangible form, now known or hereafter developed (unless expressly provided otherwise), whether or not patentable.

1.59 "Initial Development Plan" means Licensee's initial Development Plan for the Product as approved by Licensee's board of directors, a copy of which is attached to this Agreement as Exhibit A.

1.60 "Inventions" means all inventions, discoveries and developments, whether or not patentable, made, conceived and/or reduced to practice in the course of performance of this Agreement whether made, conceived and/or reduced to practice solely by, or on behalf of, Takeda, Licensee, the Parties jointly, or any Affiliate of the same.

1.61 "Japan" means all countries, possessions, and territories in Japan (including all possessions and territories thereof).

1.62 "Japan License" has the meaning set forth in Section 8.1.

1.63 "Japan License Agreement" has the meaning set forth in Section 8.2.

1.64 "Japan RON" has the meaning set forth in Section 8.1.

1.65 "Japan RON Trigger Notice" has the meaning set forth in Section 8.1.

1.66 "Japan RON Period" means the period commencing on the Effective Date and ending on the earliest of: (a) the [ ]* anniversary of the Effective Date, (b) the consummation of a Change of Control, or (c) the consummation of Licensee's sublicense to a Third Party of all rights to the Compound and the Products in the Field in the Territory.

1.67 "Joint Committee" means the joint discussion committee established as set forth in Article 9.

1.68 "Joint Know-How" means (a) all Information that is necessary or useful to Exploit the Compound or any Product in the Field in the Territory that is jointly created by Licensee or any of its Affiliates and Takeda or any of its Affiliates under this Agreement and during the Term and (b) all Inventions jointly created by Licensee or any of its Affiliates and Takeda or any of its Affiliates under this Agreement and during the Term. "Joint Know-How" excludes any Information or Inventions contained within a Joint Patent.

1.69 "Joint Intellectual Property" means, collectively, Joint Know-How and Joint Patents.

1.70 "Joint Inventions" has the meaning set forth in Section 10.1.

1.71 "Joint Patents" means all Patents covering or claiming any Invention which is jointly conceived and/or reduced to practice by, or on behalf of, the Parties or their Affiliates under this Agreement and during the Term.

1.72 "Knowledge" means, as applied to a Party, that such Party shall be deemed to have knowledge of a particular fact or other matter to the extent that a person within the Knowledge Group had actual knowledge of such fact or other matter.

1.73 "Knowledge Group" means, with respect to each Party, the officers and directors of such Party, or any Affiliates of such Party. Knowledge Group also includes, with respect to Takeda's representations and warranties in Sections 11.2(c), (d), (e), (i) and (j), [ ]*.

1.74 "Licensee Covenant Beneficiaries" means, collectively, (i) Licensee, (ii) Licensee's Affiliates, (iii) Licensee's Sublicensees, (iv) any of the direct or indirect licensees, sublicensees, importers, exporters, suppliers, manufacturers, distributors, contractors, agents, or customers of Licensee or any of Licensee's Affiliates or Sublicensees, and (v) any successors or assigns of any of the Persons referred to in the foregoing clauses (i)-(iv) and this clause (v).

1.75 "Licensee Covenant Patent" means any Patent that Licensee or any of its Affiliates Controls or otherwise has the right to enforce at any time during the Term that (i) Covers the Development, Manufacture, or Commercialization of the Compound or any Product in the Field in the Territory at any time during the Term, and (ii) is not a Licensee Patent or a Joint Patent. Notwithstanding the foregoing, a Patent that is or becomes a Licensee Covenant Patent shall cease to be a Licensee Covenant Patent if, at any time thereafter, such Patent no longer Covers the Development, Manufacture or Commercialization of the Compound or any Product in the Field in the Territory.

1.76 "Licensee Indemnitee" has the meaning set forth in Section 15.2.

1.77 "Licensee Intellectual Property" means, collectively, Licensee Know-How and Licensee Patents.

1.78 "Licensee Know-How" means all Information and Inventions Controlled by Licensee or any of its Affiliates as of the Effective Date or during the Term (other than Takeda Know-How licensed to Licensee and Joint Know-How) that are necessary or useful to Exploit the Compound or any Product in the Field in the Territory. Licensee Know-How excludes any Information or Inventions contained within a Licensee Patent.

1.79 "Licensee Patents" means all Patents Controlled by Licensee or any of its Affiliates as of the Effective Date or during the Term (other than Takeda Patents licensed to Licensee and Joint Patents) that are necessary or useful to Exploit the Compound or any Product in the Field in the Territory.

1.80 "License Negotiation Period" has the meaning set forth in Section 8.2.

1.81 "Losses" has the meaning set forth in Section 15.1.

1.82 "MAA" means an application for Regulatory Approval filed with the European Medicines Agency.

1.83 "Manufacture" or "Manufacturing" means all activities related to the manufacturing of the Compound or any Product, or any ingredient thereof, including manufacturing for Development and Commercialization, labeling, packaging, in-process and finished Product testing, release of the Compound or the Product or any ingredient thereof, quality assurance activities related to manufacturing and release of the Compound or the Product, ongoing stability tests and regulatory activities related to any of the foregoing.

1.84 "NDA" means a New Drug Application or supplemental New Drug Application as contemplated by Section 505(b) of the FFDCA, as amended, and the regulations promulgated thereunder, submitted to the FDA pursuant to Part 314 of Title 21 of the U.S. C.F.R., including any amendments thereto. References herein to NDA shall include, to the extent applicable, any comparable applications filed in or for jurisdictions outside the U.S., such as an MAA with the European Medicines Agency.

1.85 "Net Sales" means, with respect to a Product, the gross amounts invoiced and/or received (whichever is the first to occur) by Licensee, its Affiliates and Sublicensees (or, with respect to Section 13.6(j)(iii) below only, by Takeda, its Affiliates, licensees and Sublicensees) for sales of such Product to Third Parties (other than [ ]*), less the following deductions, to the extent such deductions are paid, incurred or otherwise taken, reasonable and customary, provided to Third Parties, and actually allowed with respect to such sales:

(a) [ ]*;

(b) [ ]*;

(c) [ ]*;

(d) [ ]*; and

(e) [ ]*.

Notwithstanding the foregoing, amounts received or invoiced by the applicable Party, its Affiliates, licensees or Sublicensees for the sale of such Product among the applicable Party, its Affiliates, licensees or Sublicensees for resale shall not be included in the computation of Net Sales hereunder. In any event, any amounts received or invoiced by the applicable Party or its Affiliates shall be accounted for only once. For purposes of determining Net Sales, a Product shall be deemed to be sold when recorded by the applicable Party, its licensee, Sublicensee or Affiliate in accordance with GAAP or IFRS, as the case may be. Net Sales shall be accounted for in accordance with standard accounting practices, as practiced by the applicable Party, its Affiliates, licensees or Sublicensees in the relevant country in the Territory, but in any event in accordance with GAAP or IFRS, as consistently applied in such country in the Territory. For clarity, a particular deduction may only be accounted for once in the calculation of Net Sales. Net Sales shall exclude any samples of a Product transferred or disposed of at no cost for promotional, Development or educational purposes.

The Net Sales of any Product sold as a component of a combination or bundled product that consists of a Product (or the Compound) together with one or more other therapeutically active products or compounds (a "Combination Product") shall be calculated as follows:

(i) [ ]*;

(ii) [ ]*; and

(iii) [ ]*.

1.86 "Neutral Arbitrator" has the meaning set forth in Exhibit E.

1.87 "Non-Breaching Party" has the meaning set forth in Section 13.2(a).

1.88 "Panel" has the meaning set forth in Exhibit E.

1.89 "Party Arbitrator" has the meaning set forth in Exhibit E.

1.90 "Patent Proceeding" has the meaning set forth in Section 13.4.

1.91 "Patents" means all: (a) patents, including any utility or design patent; (b) patent applications, including provisionals, substitutions, divisionals, continuations, continuations in-part or renewals; (c) patents of addition, restorations, extensions, supplementary protection certificates, registration or confirmation patents, patents resulting from post-grant proceedings, re-issues and re-examinations; (d) other patents or patent applications claiming priority directly or indirectly to: (i) any such specified patent or patent application specified in (a) through (c), or (ii) any patent or patent application from which a patent or patent application specified in (a) through (c) claim direct or indirect priority; (e) inventor's certificates; (f) other rights issued from a Governmental Authority similar to any of the foregoing specified in (a) through (e); and (g) in each of (a) through (f), whether such patent, patent application or other right arises in the U.S. or any other jurisdiction in the Territory.

1.92 "Payments" has the meaning set forth in Section 7.10(a).

1.93 "Person" means an individual, sole proprietorship, partnership, limited partnership, limited liability partnership, corporation, limited liability company, business trust, joint stock company, trust, incorporated association, joint venture or similar entity or organization, including a government or political subdivision, department or agency of a government.

1.94 "Phase 1 Clinical Trial" means a study of a pharmaceutical product in human subjects or patients, which trial is designed to ascertain initial tolerance, safety, metabolism, pharmacological and/or pharmacokinetic information regarding such product in a manner that is generally consistent with 21 CFR § 312.21(a), as amended (or its successor regulation), for the purpose of enabling the design of a well-controlled, scientifically valid, Phase 2 Clinical Trial.

1.95 "Phase 2 Clinical Trial" means a study of a pharmaceutical product in human subjects or patients, which trial is designed to evaluate the initial effectiveness and dose range of the pharmaceutical product for a particular indication or indications in patients with the disease or

condition under study and to determine the common short-term side effects and risks associated with the drug, in a manner that is generally consistent with 21 CFR § 312.21(b), as amended (or its successor regulation), for the purpose of enabling the design of further clinical trials.

1.96 "Phase 3 Clinical Trial" means a pivotal clinical trial of a pharmaceutical product in human subjects or patients, with a defined dose or a set of defined doses, which trial is designed to ascertain efficacy and safety of such product, in a manner that is generally consistent with 21 CFR § 312.21(c), as amended (or its successor regulation), for the purpose of enabling the preparation and submission of an NDA with the FDA.

1.97 "Pricing Approval" means any governmental approval, agreement, determination, or decision establishing the prices for a Product that can be charged or reimbursed in regulatory jurisdictions where the Governmental Authorities approve or determine the price or reimbursement of pharmaceutical products.

1.98 "Product" means any pharmaceutical product, including all forms, presentations, strengths, doses and formulations (including any method of delivery), containing the Compound alone or in combination with other therapeutically active ingredients. "Product" shall include "Combination Products".

1.99 "Product IND" means any IND filed in the Territory pertaining to a Product, including any supplements or amendments thereto.

1.100 "Product Infringement" has the meaning set forth in Section 10.5(b)(i).

1.101 "Product Liabilities" means all losses, damages, fees, expenses and other liabilities incurred by, or on behalf of, a Party, its Affiliate or its Sublicensee and resulting from or relating to human use of Products, including use in Clinical Trials or Commercialization of the Products, in the Territory after the Effective Date. Product Liabilities include reasonable attorneys' and experts' fees and expenses relating to any claim or potential claim against a Party, its Affiliate, or its Sublicensee. Product Liabilities shall not include [ ]*.

1.102 "Product NDA" means any NDA filed in the Territory which seeks Regulatory Approval for a Product in the Field, including any supplements or amendments thereto.

1.103 "Receiving Party" has the meaning set forth in Section 12.1.

1.104 "Regulatory Approval" means all approvals (including supplement, amendment, or pre- and post-approval), licenses, registrations or authorizations of any national, regional, state or local Regulatory Authority, department, bureau, commission, council or other Governmental Authority, that are necessary for the Commercialization of the Product in a country or countries in the Territory, and in those countries and regulatory jurisdictions where required, any Pricing Approvals.

1.105 "Regulatory Authority" means any applicable Governmental Authority involved in granting Regulatory Approval, including in the U.S., the FDA and any other applicable Governmental Authority having jurisdiction over the Compound or a Product in the Territory.

1.106 "Regulatory Exclusivity" means any exclusive marketing rights or data protection or other exclusivity rights conferred by any Regulatory Authority with respect to a Product in a country or jurisdiction in the Territory, other than a Patent right, including orphan drug exclusivity, pediatric exclusivity, and rights conferred in the U.S. under the Drug Price Competition and Patent Term Restoration Act, 21 U.S.C. 355, as amended (the "Hatch-Waxman Act").

1.107 "Regulatory Materials" means all regulatory applications, submissions, notifications, registrations, Regulatory Approvals or other submissions, including any written correspondence or meeting minutes, made to, made with, or received from a Regulatory Authority in the Territory that are necessary or reasonably desirable in order to Develop, Manufacture, market, sell or otherwise Commercialize a Product in the Territory. Regulatory Materials include the Product INDs and the Product NDAs, and amendments and supplements thereto.

1.108 "Relationship Manager" has the meaning set forth in Section 9.6.

1.109 "Representatives" means officers, directors, employees, agents, advisors and consultants of each Party and its Affiliates.

1.110 "Research Material" means active pharmaceutical ingredient prepared according to a medicinal chemistry laboratory route and synthetic procedure, manufactured at a laboratory scale (i.e., batch sizes of up to approximately 100 grams) in a research facility, under technical (i.e., non-GMP) conditions, and analyzed according to limited research methods with no formal specifications applied. Research Material is not intended for use in GLP or GMP studies. "Research Material" includes the Existing Research Material and the [ ]*.

1.111 "Research Material Synthesis Activities" means the activities described in Section 5.2.

1.112 "Resolution Period" has the meaning set forth in Section 14.2.

1.113 "Review Period" has the meaning set forth in Section 12.7.

1.114 "Royalty Term" means, on a country-by-country and Product-by-Product basis, the period commencing on the First Commercial Sale of a Product in such country and continuing until the latest of:

(a) the expiration of the last to expire Valid Claim in a Takeda Patent Covering the composition or use of such Product in such country;

(b) the expiration of all Regulatory Exclusivity for such Product in such country; or

(c) [ ]* after the First Commercial Sale of such Product in such country.

1.115 "Sole Inventions" has the meaning set forth in Section 10.1.

1.116 "Subcontractor" has the meaning set forth in Section 2.4(e).

1.117 "Subject Licensee Intellectual Property" means the Licensee Intellectual Property used by Licensee, its Affiliates or Sublicensees at any time during the Term to Develop or Manufacture

(whether directly or indirectly) the Compound or any Product. Notwithstanding the foregoing, a Licensee Patent that is included within Subject Licensee Intellectual Property at any time during the Term shall cease to be included within Subject Licensee Intellectual Property on the effective date of termination of this Agreement if such Licensee Patent no longer Covers the Development or Manufacture of the Compound or any Product on the effective date of termination of this Agreement.

1.118 "Subject Licensee Patents" means Licensee Patents that claim Subject Licensee Intellectual Property.

1.119 "Sublicensee" means (a) any Third Party granted a sublicense by either Licensee or any other Person that is also a Sublicensee of any of the rights granted to Licensee by Takeda under Section 2.1, or (b) any Third Party granted a sublicense by either Takeda or any other Person that is also a Sublicensee of any of the rights granted to Takeda by Licensee under Section 2.2 or Section 13.6(d).

1.120 "Takeda California" has the meaning set forth in Section 3.5(d).

1.121 "Takeda Covenant Beneficiaries" means, collectively, (i) Takeda, (ii) Takeda's Affiliates, (iii) Takeda's Sublicensees, (iv) any of the direct or indirect licensees, sublicensees, importers, exporters, suppliers, manufacturers, distributors, contractors, agents, or customers of Takeda or any of Takeda's Affiliates or Sublicensees, and (v) any successors or assigns of any of the Persons referred to in the foregoing clauses (i)-(iv) and this clause (v).

1.122 "Takeda Covenant Patent" means any Patent that Takeda or any of its Affiliates Controls or otherwise has the right to enforce at any time during the Term that (i) Covers the Development, Manufacture, or Commercialization of the Compound or any Product in the Field in the Territory at any time during the Term, and (ii) is not a Takeda Patent or a Joint Patent. Notwithstanding the foregoing, a Patent that is or becomes a Takeda Covenant Patent shall cease to be a Takeda Covenant Patent if, at any time thereafter, such Patent no longer Covers the Development, Manufacture or Commercialization of the Compound or any Product in the Field in the Territory.

1.123 "Takeda Indemnitee" has the meaning set forth in Section 15.1.

1.124 "Takeda Intellectual Property" means, collectively, Takeda Know-How and Takeda Patents.

1.125 "Takeda Know-How" means all Information and Inventions Controlled by Takeda or any of its Affiliates as of the Effective Date that is necessary or useful to Exploit the Compound or any Product in the Field in the Territory. Takeda Know-How excludes any Information or Inventions contained within a Takeda Patent and any Information or Inventions that are not Controlled by Takeda or any of its Affiliates as of the Effective Date (even if such Information or Inventions is Controlled by Takeda or any of its Affiliates at any time during the Term after the Effective Date). Notwithstanding the foregoing, Takeda Know-How shall include all pre-clinical data, results and reports generated, and all Inventions conceived or reduced to practice, solely by or on behalf of Takeda or any of its Affiliates at any time during the Term in the course of Takeda's conduct of the Research Material Synthesis Activities.

1.126 "Takeda Patents" means all Patents Controlled by Takeda or any of its Affiliates as of the Effective Date that are necessary or useful to Exploit the Compound or any Product in the Field in the Territory. Takeda Patents are set forth on Exhibit B. "Takeda Patents" excludes any Patents that are not Controlled by Takeda or any of its Affiliates as of the Effective Date (even if such Patents are Controlled by Takeda or any of its Affiliates at any time during the Term after the Effective Date). Notwithstanding the foregoing, "Takeda Patents" shall include any Patent Controlled by Takeda or any of its Affiliates at any time during the Term that claims an Invention that is necessary or useful to Exploit the Compound or any Product in the Field in the Territory and is conceived and/or reduced to practice solely by, or on behalf of, Takeda or any of its Affiliates in the course of Takeda's conduct of the Research Material Synthesis Activities.

1.127 "Tax" or "Taxes" means any form of tax or taxation, levy, duty, charge, social security charge, contribution or withholding of whatever nature (including any related fine, penalty, surcharge or interest) imposed by, or payable to, any government, state or municipality, or any local, state, federal or other fiscal, revenue, customs, or excise authority, body or official in the Territory.

1.128 "TDCE" means Takeda Development Centre Europe Ltd.

1.129 "Territory" means all countries, jurisdictions and territories in the world.

1.130 "Term" has the meaning set forth in Section 13.1.

1.131 "Third Party" means a Person other than Takeda and Licensee and their respective Affiliates.

1.132 "Third Party License" has the meaning set forth in Section 7.7(a).

1.133 "Third Party Payments" has the meaning set forth in Section 7.7(a).

1.134 "U.S." means all countries, possessions and territories in the United States of America (including all possessions and territories thereof, including Puerto Rico).

1.135 "Valid Claim" means (a) a claim of an issued and unexpired Patent included within the Takeda Patents, the Licensee Patents or the Joint Patents, to the extent such claim has not been revoked, held invalid or unenforceable by a patent office, court or other governmental agency of competent jurisdiction in a final order, from which no further appeal can be taken, and which claim has not been disclaimed, denied or admitted to be invalid or unenforceable through reissue, re-examination or disclaimer; or (b) a claim of any patent application (where such claim was filed in good faith) within the Takeda Patents, the Licensee Patents or the Joint Patents, to the extent such claim has not been canceled, withdrawn, abandoned, or pending for more than seven (7) years from its earliest priority date.

ARTICLE 2 – LICENSES

2.1 **Licenses from Takeda to Licensee**. Subject to the terms and conditions of this Agreement, Takeda hereby grants to Licensee an exclusive (even as to Takeda and its Affiliates), nontransferable (except as provided in Section 16.4) license, with the right to grant sublicenses

solely in accordance with Section 2.4, under the Takeda Intellectual Property and Takeda's rights to the Joint Intellectual Property, to Exploit the Compound and the Products in the Field in the Territory.

2.2 **Licenses and Grant-Back Sublicenses from Licensee to Takeda.**

(a) Subject to the terms and conditions of this Agreement, Licensee hereby grants to Takeda a limited, non-exclusive, fully paid-up, royalty-free, non-transferable (except as provided in Section 16.4) license, with the right to grant sublicenses solely in accordance with Section 2.4 to Sublicensees for the sole purpose of performing as a subcontractor any of Takeda's activities under this Agreement during the Term, under the Subject Licensee Intellectual Property and Licensee's rights to the Joint Intellectual Property solely as, and to the extent necessary, to enable Takeda in the Field in the Territory, to exercise its express rights and perform its obligations under this Agreement during the Term.

(b) Subject to the terms and conditions of this Agreement, Licensee hereby grants-back to Takeda a limited, non-exclusive, fully paid-up, royalty-free, non-transferable (except as provided in Section 16.4) sublicense, with the right to further sublicense solely in accordance with Section 2.4 to Sublicensees for the sole purpose of performing as a subcontractor any of Takeda's activities under this Agreement during the Term, under the Takeda Intellectual Property and Takeda's rights to the Joint Intellectual Property solely as, and to the extent necessary, to enable Takeda in the Field in the Territory, to exercise its express rights and perform its obligations under this Agreement during the Term.

(c) Notwithstanding subsections (a) and (b) of this Section 2.2, and subject to the terms and conditions of this Agreement, as of the Effective Date, the Parties do not currently contemplate that Takeda will perform any Development, Manufacturing or Commercialization activities under this Agreement during the Term except as expressly set forth in Section 3.5, Section 5.1 or Section 5.2.

2.3 **Covenant Not to Sue**. Licensee, on behalf of itself and its Affiliates, hereby covenants not to assert or cause to be asserted, and will cause its Affiliates not to assert or cause to be asserted, against any Takeda Covenant Beneficiary any claim, including any claim of infringement, under any Licensee Covenant Patent with respect to the Development, Manufacturing, or Commercialization of the Compound or any Product, or the performance of the foregoing activities by, or on behalf of, any Takeda Covenant Beneficiary, in each case, in accordance with this Agreement. Takeda, on behalf of itself and its Affiliates, hereby covenants not to assert or cause to be asserted, and will cause its Affiliates not to assert or cause to be asserted, against any Licensee Covenant Beneficiary any claim, including any claim of infringement, under any Takeda Covenant Patent with respect to the Development, Manufacturing, or Commercialization of the Compound or any Product, or the performance of the foregoing activities by, on behalf of, any Licensee Covenant Beneficiary, in each case, in accordance with this Agreement. Each Takeda Covenant Beneficiary or Licensee Covenant Beneficiary, as the case may be, that is not a party to this Agreement is a third party beneficiary solely of this Section 2.3. If Licensee or any of its Affiliates sells, assigns, licenses, transfers, or otherwise grants any right under any Licensee Covenant Patent to a Third Party, then Licensee or such Affiliate, as applicable, will require such purchaser, assignee, licensee, or transferee to agree in writing to be bound by the same covenant to the same

extent as made by Licensee and its Affiliates in this Section 2.3. If Takeda or any of its Affiliates sells, assigns, licenses, transfers, or otherwise grants any right under any Takeda Covenant Patent to a Third Party, then Takeda or such Affiliate, as applicable, will require such purchaser, assignee, licensee, or transferee to agree in writing to be bound by the same covenant to the same extent as made by Takeda and its Affiliates in this Section 2.3.

2.4 **Sublicensing; Subcontracting**.

(a) Subject to the terms and conditions of this Agreement, Licensee shall have the right to grant sublicenses, through multiple tiers, under the rights granted by Takeda to Licensee under Section 2.1, to its Affiliates and to one or more Sublicensees. Licensee shall give prior written notice to Takeda of any grant by Licensee to a Sublicensee (other than a Sublicensee to whom Licensee grants any such sublicense for the sole purpose of performing as a subcontractor any of Licensee's activities under this Agreement). For clarity, Licensee's Sublicensees shall have the right, subject to and upon the terms and conditions of this Agreement, to grant further sublicenses under the rights granted by Takeda to Licensee under Section 2.1.

(b) Subject to the terms and conditions of this Agreement, Takeda shall have the limited right to grant one or more licenses or sublicenses, as the case may be, under the rights granted to Takeda under Section 2.2 to (i) its Affiliates, with the right to sublicense, to the extent necessary to exercise Takeda's express rights and perform its obligations under this Agreement during the Term, and/or (ii) one or more vendors, contract research organizations and the like, with the right to sublicense, in order to, on Takeda's behalf, carry out activities that Takeda is expressly permitted or required to perform under this Agreement during the Term.

(c) Each sublicense shall refer to and be subordinate to this Agreement and, except to the extent the Parties otherwise agree in writing, any such sublicense must be consistent in all material respects with the terms and conditions of this Agreement. Each Party shall remain responsible for the performance of this Agreement and the performance of its Sublicensees hereunder. Promptly after execution of any sublicense agreement with a Sublicensee (other than a Sublicensee with whom the sublicensing Party has executed such sublicense agreement for the sole purpose of enabling such Sublicensee to perform as a subcontractor any of the sublicensing Party's activities under this Agreement during the Term), the sublicensing Party shall provide a complete and correct copy of such sublicense agreement to the other Party.

(d) Upon termination of this Agreement pursuant to Section 13.2, Section 13.3 or Section 13.5, Takeda shall offer any Sublicensee (other than a Sublicensee with whom Licensee has executed such sublicense agreement for the sole purpose of enabling such Sublicensee to perform as a subcontractor any of Licensee's activities under this Agreement during the Term) under a sublicense granted directly by Licensee or any of its Affiliates to such Sublicensee pursuant to this Section 2.4 that was in effect on the effective date of termination of this Agreement the right to enter into a license agreement directly with Takeda on substantially the same terms and conditions under which such sublicense was granted to such Sublicensee, provided that such Sublicensee (i) is not then in breach of its sublicense, (ii) agrees to comply with all the terms of this Agreement to the extent applicable to the rights sublicensed to it by Licensee or any of its Affiliates, and (iii) such agreement does not impose any obligations upon Takeda that exceed the obligations of Takeda under this Agreement.

(e) Subject to the terms and conditions of this Agreement, each Party and its Affiliates and Sublicensees shall be permitted to use subcontractors (each a "Subcontractor") to perform activities that do not require a sublicense of the rights granted to such Party or its Affiliates or Sublicensees under Section 2.1, Section 2.2, Section 2.4(a) or Section 2.4(b), as applicable, and for which such Party is responsible under this Agreement or for which any Affiliate or Sublicensee of such Party is responsible under any applicable sublicense agreement. The granting of a subcontract hereunder shall not relieve a Party of any of its obligations hereunder or relieve any Affiliate or Sublicensee of such Party from any of the obligations of such Affiliate or Sublicensee under any applicable sublicense agreement, and such Party or, if applicable, each of its subcontracting Affiliates or Sublicensees shall require its Subcontractors to comply, and shall remain responsible for its Subcontractor's compliance, with all of the terms hereof applicable to such Subcontractor. Each Party shall ensure that, except to the extent otherwise agreed in writing by the other Party, its Subcontractors and the Subcontractors of any subcontracting Affiliates or Sublicensees of such Party shall (i) have obligations of confidentiality and restrictions on the use of Confidential Information that are no less restrictive than the obligations set forth in Article 12 and, (ii) agree in writing to assign or license (with the right to grant sublicenses) to such Party or such subcontracting Affiliate or Sublicensee, as the case may be, any inventions (and Patents Covering such inventions) made by such Third Party in performing such services for such subcontracting Party or such subcontracting Affiliate or Sublicensee, as the case may be.

2.5 **No Implied Licenses**. No license or other right is or shall be created or granted hereunder by implication, estoppel, or otherwise. All licenses and rights are or shall be granted only as expressly provided in this Agreement. All rights not expressly granted by a Party under this Agreement are reserved by the Party and may not be used by the other Party for any purpose.

ARTICLE 3 – DEVELOPMENT

3.1 **Development Responsibilities**. Except as otherwise set forth in Section 5.2, Licensee (itself or through its Affiliates or Sublicensees) shall be solely responsible for: (a) all activities related to the Development of the Compound and the Products in the Field in the Territory; and (b) all expenses, including Third Party expenses, related to such Development activities. Licensee may amend, supplement or update the Development Plan in writing from time to time; provided, however, that Licensee shall provide a copy of such amendment, supplement or update to the Joint Committee promptly following (but in no event more than ten (10) days following) such amendment, supplement or update.

3.2 **Development Standards**. Licensee (itself or through its Affiliates or Sublicensees) shall conduct all Development activities in compliance with Applicable Law, including GCP, GLP, and all legal and regulatory requirements pertaining to the design and conduct of Clinical Trials.

3.3 **Development Diligence**. Licensee shall use Commercially Reasonable Efforts to Develop [ ]* in the Field in the U.S. and in the E.U.

3.4 **Development Diligence in Japan**. Subject to Article 8, if Licensee grants to any Third Party a sublicense in Japan under the rights granted to Licensee pursuant to this Agreement, such sublicense agreement shall include an obligation for such Sublicensee to use Commercially Reasonable Efforts to Develop [ ]* in Japan.

3.5 **Transfer of Takeda Know-How and Existing Research Material**.

(a) Promptly (but in any event within [ ]* days) following the Effective Date, Takeda shall commence transferring to Licensee (or at Licensee's written instruction, to Licensee's Subcontractor or Sublicensee) all Takeda Know-How in the possession or Control of Takeda or any of its Affiliates, to the extent such Takeda Know-How has not previously been provided hereunder to Licensee.

(b) To the extent Takeda subsequently identifies any Takeda Know-How that should have been transferred as provided above, Takeda will promptly provide or make available such additional Takeda Know-How to Licensee (or at Licensee's written instruction, to Licensee's Subcontractor or Sublicensee).

(c) Any Takeda Know-How provided by Takeda pursuant to subsection (a) or (b) above shall be provided by Takeda to Licensee (or at Licensee's written instruction, to Licensee's Subcontractor or Sublicensee) in electronic or other format and in the language in which it exists as of the Effective Date. If such language is other than English, then the Parties will use good faith efforts to determine which Party is responsible for translation services, including costs thereof.

(d) As of the Effective Date, [ ]* Controls certain quantities of the Research Material as described on Exhibit C (the "Existing Research Material"). Promptly following the Effective Date, Takeda or its Affiliate shall (i) transfer and deliver, or instruct its Subcontractor or Sublicensee to transfer and deliver, to Licensee (or at Licensee's written instruction, to Licensee's Subcontractor or Sublicensee) the Existing Research Material and all Information in the possession of Takeda or any of its Affiliates relating to the Existing Research Material and (ii) use Commercially Reasonable Efforts to cause its Subcontractor or Sublicensee to transfer and deliver to Licensee (or at Licensee's written instruction, to Licensee's Subcontractor or Sublicensee) all Information in the possession of Takeda's Subcontractor or Sublicensee relating to the Existing Research Material to the extent not inconsistent with Takeda's or its Affiliate's written agreement with such Subcontractor or Sublicensee. Without limiting Section 11.5 below, THE EXISTING RESEARCH MATERIAL IS PROVIDED TO LICENSEE "AS-IS" AND WITHOUT ANY WARRANTY, EXPRESS OR IMPLIED, INCLUDING ANY WARRANTY WITH RESPECT TO COMPLETENESS, COMPLIANCE WITH REGULATORY STANDARDS OR REGULATIONS OR FITNESS FOR A PARTICULAR PURPOSE OR ANY WARRANTY THAT THE USE OF THE EXISTING RESEARCH MATERIAL WILL NOT INFRINGE OR VIOLATE ANY PATENT OR OTHER PROPRIETARY RIGHTS OF ANY THIRD PARTY, OR ANY OTHER KIND OF WARRANTY WHETHER EXPRESS OR IMPLIED.

(e) Each Party shall use Commercially Reasonable Efforts to complete its obligations under subsections (a) and (c) above within [ ]* days following the Effective Date.

(f) Subject to subsection (c) above, all out-of-pocket costs incurred by Takeda in connection with the activities performed pursuant to this Section 3.5 shall be at Licensee's expense. Takeda shall submit invoices to Licensee from time to time for out-of-pocket costs and expenses incurred by Takeda for activities performed pursuant to this Section 3.5. Licensee shall remit payment on any undisputed invoice within thirty (30) days following Licensee's receipt of such invoice.

* CONFIDENTIAL TREATMENT REQUESTED.

3.6 **Development and Regulatory Progress Reports**. At least [ ]* days prior to each of the start of each Calendar Year and July 1 of each Calendar Year, commencing with the Calendar Year of [ ]*, and ending with the Calendar Year in which the first Regulatory Approvals have been obtained for a Product in both the U.S. and the E.U., Licensee shall provide to Takeda a reasonably detailed written report consisting of (a) an update on the progress of Licensee's Development activities, including (i) key achievements or milestones to date in the reporting period, and (ii) studies that were run or are in process, (b) a summary of the planned Development activities for the upcoming reporting period and (c) an update on the progress of Licensee's regulatory activities, including a list of (1) any application(s) for Product INDs and Product NDAs, and amendments and supplements to such applications, submitted to a Regulatory Authority during the reporting period and (2) any responses received from a Regulatory Authority during the reporting period to any application(s) for Product INDs and Product NDAs. In addition to the foregoing, Licensee shall provide Takeda with updates on the progress of the Development activities pursuant to Article 9. At Takeda's written request, Licensee shall provide Takeda with a copy, in electronic form if reasonably practicable, of any of such applications and responses referred to in clauses (1) and (2) above.

ARTICLE 4 – REGULATORY

4.1 **Regulatory Responsibilities**. After the Effective Date, subject to this Article 4, Licensee shall have the sole right and responsibility for the conduct of all regulatory activities related to the development and submission of Regulatory Materials for the Compound and the Products in the Field in the Territory, including developing regulatory plans and strategies for the Compound and the Products, preparing, obtaining, and maintaining, as applicable, the Regulatory Materials, including the Product INDs and other submissions, and conducting communications with, and making all filings with, the relevant Regulatory Authorities, monitoring of all clinical experiences, maintaining the global safety database, safety monitoring, pharmacovigilance surveillance, compliance and filing of all required safety reports (including annual safety reports) with Regulatory Authorities in the Territory with respect to the Compound and the Products, and reporting on safety issues to safety boards of any nature, including urgent safety information, to investigators, and to applicable Regulatory Authorities. All Product INDs generated after the Effective Date with respect to the Products in the Field in the Territory under this Agreement shall be owned by, and shall be the sole property and held in the name of, Licensee or its designee.

4.2 **Notification of Regulatory Events**. After the Effective Date, Licensee shall notify the Joint Committee, as soon as reasonably practicable, of any action by, or notice or other information that Licensee or its Affiliates receives (directly or indirectly) from, any Third Party (including any Governmental Authority), which: (1) considered in light of all other information related to the Compound or any Product, raises any material concerns regarding the safety of the Product; (2) is reasonably likely to lead to a recall or clinical hold with respect to such Product; or (3) constitutes notice of an investigation, inspection or formal inquiry by any Regulatory Authority regarding such Product. At Takeda's written request, Licensee shall provide Takeda with copies of any documents issued by a Regulatory Authority to Licensee following any such investigation or formal inquiry.

4.3 **Regulatory Expenses**. Licensee shall bear all expenses incurred related to the preparation, maintenance, formatting and filing of the Regulatory Materials and any other regulatory activities related to the Compound and any Product.

ARTICLE 5– MANUFACTURING

5.1 **Assistance and Support Regarding [ ]***. After the Effective Date, Takeda or its Affiliates shall provide to Licensee reasonable assistance and support in securing a written agreement between Licensee or its Affiliate and [ ]* whereby [ ]* would perform Development activities related to the Manufacture of the Compound for Phase 1 Clinical Trials (the "[ ]* Agreement").

5.2 **[ ]* Research Material**. Prior to the Effective Date, Takeda or its Affiliate submitted a request form to [ ]* under that certain [ ]*, pursuant to which [ ]* agreed to perform chemical synthesis of the quantity of Research Material described on Exhibit C (the "[ ]* Research Material"). Promptly following [ ]* completion of such synthesis activities, (a) Takeda shall, or shall instruct [ ]* to, transfer and deliver to Licensee (or at Licensee's request, Licensee's Subcontractor or Sublicensee) the [ ]* and all Information in the possession of Takeda or any of its Affiliates relating to the [ ]* and (b) Takeda shall use Commercially Reasonable Efforts to cause [ ]* to transfer and deliver to Licensee (or at Licensee's written instruction, to Licensee's Subcontractor or Sublicensee) all Information in the possession of [ ]* relating to the [ ]* to the extent not inconsistent with Takeda's or its Affiliate's written agreement with [ ]*. Without limiting Section 11.5 below, THE [ ]* WILL BE PROVIDED TO LICENSEE "AS-IS" AND WITHOUT ANY WARRANTY, EXPRESS OR IMPLIED, INCLUDING ANY WARRANTY WITH RESPECT TO COMPLETENESS, COMPLIANCE WITH REGULATORY STANDARDS OR REGULATIONS OR FITNESS FOR A PARTICULAR PURPOSE OR ANY WARRANTY THAT THE USE OF THE [ ]* WILL NOT INFRINGE OR VIOLATE ANY PATENT OR OTHER PROPRIETARY RIGHTS OF ANY THIRD PARTY, OR ANY OTHER KIND OF WARRANTY WHETHER EXPRESS OR IMPLIED.

5.3 **Manufacturing Responsibilities**. Except as otherwise set forth in Section 5.1 and Section 5.2 above, Licensee (itself or through its Affiliates or Sublicensees) shall be solely responsible for the conduct of all activities related to the Manufacturing and supply of the Compound and the Products in the Field in the Territory and for all expenses, including Third Party expenses, relating to such Manufacturing activities.

ARTICLE 6 - COMMERCIALIZATION

6.1 **Commercialization Responsibilities.** Licensee (itself or through its Affiliates or Sublicensees) shall be solely responsible for: (a) all activities relating to the Commercialization of the Products in the Field in the Territory; and (b) all expenses, including Third Party expenses, related to such Commercialization activities.

6.2 **Commercialization Diligence**. Licensee (itself or through its Affiliates or Sublicensees) shall use Commercially Reasonable Efforts to Commercialize [ ]* in the Field in the U.S. and in the E.U. throughout the Term.

6.3 **Commercialization Diligence in Japan.** Subject to Article 8, if Licensee grants to any Third Party a sublicense in Japan under the rights granted to Licensee pursuant to this Agreement, such sublicense agreement shall include an obligation for such Third Party sublicensee to use Commercially Reasonable Efforts to Commercialize [ ]* in Japan throughout the Term.

6.4 **Commercialization Reports.** At least [ ]* days prior to the start of each Calendar Year, commencing with the Calendar Year immediately following the Calendar Year during which the First Commercial Sale occurs, Licensee shall provide to Takeda a reasonably detailed written report consisting of (a) an update on the progress of Licensee's Commercialization activities, including key achievements or milestones to date in the reporting period, and (b) a summary of the planned Commercialization activities for the upcoming reporting period, such as anticipated commercial launches in various countries and other commercial milestones.

ARTICLE 7– PAYMENT

7.1 **Initial Equity Issuance**. As a condition to and as partial consideration for Takeda entering into and granting the licenses and other rights to Licensee under this Agreement, Licensee shall issue to Takeda shares of Licensee's common stock, $0.001 par value per share (the "Common Stock"), having an equity value equal to Five Million Dollars ($5,000,000), calculated using the arithmetical average closing price for a share of Common Stock as reported by the NASDAQ stock exchange for the [ ]* trading days ending on (and including) the [ ]* trading day prior to the Effective Date (collectively, the "Equity Grant Shares"). Concurrently with this Agreement, Licensee and Takeda shall enter into a Stock Issuance Agreement, in the form attached hereto as Exhibit D, providing for the issuance of the Equity Grant Shares.

7.2 **Development Milestones**. Licensee shall owe to Takeda one-time milestone payments upon the first achievement of each of the events set forth below with respect to the first Product containing the Compound to achieve such event. Licensee shall promptly notify Takeda in writing following the achievement of each milestone event. Thereafter, Takeda shall submit to Licensee an invoice for the corresponding milestone payment set forth below. Within thirty (30) days following Licensee's receipt of any such invoice, Licensee shall remit the applicable milestone payment to Takeda. Each milestone payment by Licensee pursuant to this Section 7.2 shall be payable only once, regardless of the number of times that such milestone event is achieved for the Product. All payment amounts listed are in U.S. Dollars. The total maximum amount payable to Takeda under this Section 7.2 is [ ]*.

Development Milestones.

Milestone Event	**Payment Amount**
[ ]*	[ ]*
[ ]*	[ ]*
[ ]*	[ ]*
[ ]*	[ ]*

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[ ]*.

7.3 **Sales Milestones**. Licensee shall owe to Takeda one-time milestone payments upon the first achievement of each of the events set forth below. Licensee shall promptly notify Takeda in writing following the achievement of each milestone event. Thereafter, Takeda shall submit to Licensee an invoice for the corresponding milestone payment set forth below. Within ninety (90) days following the Calendar Year during which the applicable milestone event was met, Licensee shall remit the applicable milestone payment to Takeda. Each milestone payment by Licensee pursuant to this Section 7.3 shall be payable only once, regardless of the number of times that such milestone event is achieved. All payment amounts listed are in U.S. Dollars. The total maximum amount payable to Takeda under this Section 7.3 is [ ]*.

Sales Milestones.

Milestone Event	**Payment Amount**
[ ]*	[ ]*
[ ]*	[ ]*

[ ]*.

7.4 **Royalty**. Subject to Sections 7.5, 7.6 and 7.7 below, and during the applicable Royalty Term, Licensee shall pay to Takeda a running royalty on aggregate Net Sales of each Product in the Territory (calculated on a Product-by-Product basis) during each Calendar Year as further consideration for the rights granted hereunder as set forth below:

Annual Net Sales	**Rates**
On the portion of aggregate Net Sales of the applicable Product in a Calendar Year that is less than [ ]*	[ ]*
On the portion of aggregate Net Sales of the applicable Product in a Calendar Year that is greater than or equal to [ ]*	[ ]*

7.5 **Royalty Term**. Royalties under Section 7.4 shall be payable on Net Sales until the expiration of the Royalty Term in each country (at which time sales in such country shall be excluded from all calculations of aggregate Net Sales hereunder) on a Product-by-Product and country-by-country basis beginning upon the First Commercial Sale of the applicable Product in such country in the Territory.

7.6 **Royalty Reduction**. The royalty rate set forth in Section 7.4 for Net Sales of a particular Product in a particular country (after any previous reduction(s), if any, made pursuant to the next sentence of this Section 7.6) shall be reduced, on a Product-by-Product and country-by-country basis by: (i) [ ]* at the end of the first to occur Calendar Quarter during which either (a) the last to expire Valid Claim in a Takeda Patent Covering the composition or use of such Product in such

country expires or has expired and all applicable Regulatory Exclusivity for such Product in such country expires or has expired; or (b) the Generic Competition Percentage in such country of the Territory is greater than or equal to [ ]* and less than [ ]*; and (ii) [ ]* at the end of the first to occur Calendar Quarter during which the Generic Competition Percentage in such country of the Territory is greater than or equal to [ ]*. In addition, with respect to any Product being Commercialized in the U.S. during the applicable Royalty Term, (a) following expiration of the last to expire Valid Claim in a Takeda Patent published in the FDA's Orange Book, the royalty rate for such Product set forth in Section 7.4 for Net Sales in the U.S. (after any previous reduction(s), if any, made pursuant to this sentence or the first sentence of this Section 7.6) shall be reduced by [ ]* of such royalty rate until the end of such applicable Royalty Term; and (b) following expiration of the last to expire Valid Claim in a Takeda Patent in the U.S. not published in the FDA's Orange Book, the royalty rate for such Product set forth in Section 7.4 for Net Sales in the U.S. (after any previous reduction(s), if any, made pursuant to this sentence or the first sentence of this Section 7.6) shall be reduced by [ ]* of such royalty rate until the end of such applicable Royalty Term. Notwithstanding anything contained in this Agreement to the contrary, none of the reductions to royalties provided in this Section 7.6 shall, individually or in the aggregate, reduce the royalties payable with respect to Net Sales of any Product sold by Licensee, its Affiliates and its and their Sublicensees in any country during the applicable Royalty Term by more than [ ]* of the royalties otherwise owed to Takeda pursuant to Section 7.4.

7.7 **Payment for Third Party Licenses**.

(a) During the Term, Licensee or any of its Affiliates will have the right, following reasonable consultation with Takeda, to negotiate and obtain a license under one or more Patents from one or more Third Parties (each such Third Party license (including any license granted in settlement of any litigation as contemplated under Section 10.6) is referred to herein as a "Third Party License") if in the absence of a license under such Third Party Patents, the Exploitation of the Compound or Product would, in Licensee's good faith assessment, upon advice of legal counsel, infringe such Third Party Patents. Except as set forth in clause (c) of this Section 7.7 or as the Parties may otherwise agree in writing, Licensee or any of its Affiliates shall bear any upfront license fees, license option grant or exercise fees, license maintenance fees, milestone payments and royalties under any Third Party License provided that such upfront license fees, license option grant or exercise fees, license maintenance fees, milestone payments and royalties arise in connection with, or pertain to, the Exploitation of the Compound or Products by Licensee or any of its Affiliates or Sublicensees (collectively, the "Third Party Payments") and any other payments owed to any Third Party for such a Third Party License.

(b) In the event that Takeda disputes Licensee's determination that any Third Party Payments are properly subject to the milestone payment and/or royalty offset provided under this Section 7.7 or Licensee's allocation of any such Third Party Payments to a Product, Takeda may by written notice to Licensee require that such Dispute be resolved in accordance with Article 14 of this Agreement; provided that Licensee shall have the right to take milestone payment and/or royalty reductions pursuant to this Section 7.7 pending resolution of any such Dispute; provided further, that if any such Dispute is resolved in favor of Takeda, then within sixty (60) days of such resolution, Licensee shall pay to Takeda any adjustment in milestone payments and/or royalties due pursuant to this Section 7.7 as required by such resolution.

(c) Licensee may credit up to [ ]* of the amount of any Third Party Payments that consist of upfront license fees, license option grant or exercise fees, license maintenance fees or milestone payments paid by Licensee or any of its Affiliates under a Third Party License pursuant to clause (a) above (collectively, "Creditable Payments"), against any milestone payments that would otherwise be payable to Takeda under Section 7.2 or Section 7.3; provided, that in no event will such credit reduce any milestone payment that would otherwise be payable to Takeda under Section 7.2 or Section 7.3 by more than [ ]*. Licensee may credit (i) any amount that Licensee was unable to credit against milestone payments by virtue of the proviso in the immediately preceding sentence and (ii) up to [ ]* of the amount of any Creditable Payments that consist of royalties paid by Licensee or any of its Affiliates under a Third Party License pursuant to clause (a) above against any royalties that would otherwise be payable to Takeda under Section 7.4. Licensee may take such credit for Creditable Payments that consist of any such amount referred to in the foregoing clause (i) and/or royalties during a Calendar Quarter for which royalties are payable hereunder; provided, that in no event will such credit reduce the royalties payable to Takeda for such Calendar Quarter by more than [ ]*.

(d) This Section 7.7 shall not apply to any Third Party Payments payable by Licensee or any of its Affiliates or Sublicensees under any license or other agreement or understanding, written or oral, between Licensee or any of its Affiliates or Sublicensees, on the one hand, and any Third Party, on the other hand, in existence as of the Effective Date.

7.8 **Manner of Payment**. Beginning with the Calendar Quarter immediately following the Calendar Quarter during which the First Commercial Sale occurs, within three (3) Business Days following the end of each Calendar Quarter, Licensee shall provide Takeda with a written report containing Licensee's reasonable good faith estimate of the following information for the Calendar Quarter in order to allow Takeda to comply with internal accounting procedures: the amount of gross sales (U.S. dollars) of each Product in the Territory, an itemized calculation of Net Sales for each Product in the Territory showing deductions, to the extent practicable, provided for in the definition of "Net Sales," a calculation of the royalty payment due on such sales, an accounting of the number of units and prices for each Product sold, the application of the reductions, if any, made in accordance with this Article 7, and any other information reasonably required for the purpose of calculating royalties. Within forty-five (45) days following the end of each Calendar Quarter, Licensee shall provide Takeda with a report containing the information described above in respect of such Calendar Quarter for Takeda's review and confirmation within ten (10) Business Days from receipt. In the event that either Party determines that the calculation of Net Sales for a Calendar Quarter deviates from the amounts previously reported to Takeda for any reason (such as, on account of additional amounts collected or Product returns), Licensee and Takeda shall reasonably cooperate to reconcile any such deviations to the extent necessary under applicable legal or financial reporting requirements. Within the later of (a) sixty (60) days from the end of the Calendar Quarter, or (b) five (5) Business Days following Takeda's written confirmation of the applicable quarterly report, Licensee shall pay all amounts due to Takeda pursuant to this Article 7 with respect to Net Sales for such Calendar Quarter.

7.9 **Exchange Rate**. The rate of exchange to be used in computing the amount of currency equivalent in U.S. Dollars owed to a Party under this Agreement shall be the monthly average exchange rate between each currency of origin and U.S. Dollars as reported by the Wall Street

Journal East Coast Edition. The monthly average exchange rate shall be the average of (i) the exchange rate published on the last day of the month; and (ii) the exchange rate published on the last day of the preceding month.

7.10 **Taxes**

(a) The amounts payable pursuant to this Agreement ("Payments") shall not be reduced on account of any Taxes unless required by Applicable Law. Licensee shall deduct and withhold from the Payments any Taxes that it is required by Applicable Law to deduct or withhold. Notwithstanding the foregoing, if Takeda is entitled under any applicable tax treaty to a reduction of rate of, or the elimination of, or recovery of, applicable withholding Tax, it may deliver to Licensee or the appropriate Governmental Authority the prescribed forms necessary to reduce the applicable rate of withholding or to relieve Licensee of its obligation to withhold Tax. In such case, Licensee shall apply the reduced rate of withholding, or not withhold, as the case may be, provided that Licensee is in receipt of evidence, in a form reasonably satisfactory to Licensee (e.g., Takeda's delivery of all applicable documentation) at least two (2) weeks prior to the time that the Payments are due. If, in accordance with the foregoing, Licensee withholds any amount, it shall pay to Takeda the balance when due, make timely payment to the proper taxing authority of the withheld amount, and send Takeda proof of such payment within sixty (60) days following that payment.

(b) If a Party that owes a Payment under this Agreement assigns its rights and obligations to any Person and if, solely as a result of such assignment, the withholding or deduction of Taxes required by Applicable Law with respect to payments owed by such assignee under this Agreement is increased, then any amount payable under this Agreement shall be increased to take into account such withheld or deducted Taxes as may be necessary so that, after making all required Tax withholdings and deductions (including Tax withholdings and deductions on amounts payable under Section 7.10(a)), the payee receives an amount equal to the sum it would have received as of the Effective Date.

7.11 **Audit**. Licensee shall maintain complete and accurate records in sufficient detail to permit Takeda to confirm the accuracy of the calculation of royalty and other payments under this Agreement. Upon reasonable prior notice, such records shall be available during regular business hours for a period of [ ]* from the end of the Calendar Year to which they pertain for examination at Takeda's expense, and not more often than once each Calendar Year, by an independent certified public accountant selected by Takeda and reasonably acceptable to Licensee, for the sole purpose of verifying the accuracy of the financial reports furnished by Licensee pursuant to this Agreement. Any such auditor shall not disclose Licensee's Confidential Information, except to the extent such disclosure is necessary to verify the accuracy of the financial reports furnished by Licensee or the amount of payments due to Takeda under this Agreement during the prior [ ]*. Any amounts shown to be owed to Takeda but unpaid shall be paid within thirty (30) days from the auditor's report, plus interest (as set forth in Section 7.12) from the original due date. Any amounts shown to have been overpaid shall be refunded within thirty (30) days from the auditor's report. Takeda shall bear the full expense of such audit unless such audit discloses an underpayment by Licensee of more than [ ]* of the amount due, in which case Licensee shall bear the full expense of such audit.

7.12 **Manner of Payment; Late Payment**. All payments due to Takeda hereunder shall be made in U.S. Dollars by wire transfer of immediately available funds into an account designated by Takeda. If Takeda does not receive payment of any sum due to it on or before the due date, simple interest shall thereafter accrue on the sum due until the date of payment at the per annum rate of [ ]* over the then-current prime rate quoted by Citibank in New York City or the maximum rate allowable by Applicable Law, whichever is lower.

ARTICLE 8 – RIGHT OF NEGOTIATION FOR EXCLUSIVE LICENSE IN JAPAN

8.1 **Japan RON**. Licensee hereby grants Takeda a right of negotiation (the "Japan RON"), exercisable in accordance with this Article 8, to receive from Licensee an exclusive license (even as to Licensee and its Affiliates), with the right to sublicense through multiple tiers, under the Takeda Intellectual Property, the Licensee Intellectual Property and Licensee's rights to the Joint Intellectual Property, to Exploit the Compound and the Products in Japan (such license, the "Japan License"), but only if Licensee enters into discussions or negotiations with a Third Party for the grant by Licensee to such Third Party of a sublicense of any of the rights granted by Takeda to Licensee pursuant to Section 2.1 for purposes of allowing such Third Party to Exploit the Compound or the Product in Japan. If, during the Japan RON Period, Licensee so enters into discussions or negotiations with a Third Party for the grant of such sublicense to such Third Party, Licensee shall promptly (and in any event no later than [ ]* following commencement of such discussions or negotiations with such Third Party) notify Takeda in writing of such discussions or negotiations (the "Japan RON Trigger Notice"). At any time during the Japan RON Period after receipt of a Japan RON Trigger Notice (the "Exercise Period"), Takeda may exercise the Japan RON by delivering written notice thereof to Licensee (the "Exercise Notice") within [ ]* of receipt of the Japan RON Trigger Notice. If Takeda receives the Japan RON Trigger Notice within the Japan RON Period but less than [ ]* prior to expiration of the Japan RON Period pursuant to Section 1.65(a), then, the Exercise Period shall automatically extend until the date that is [ ]* following the date of Takeda's receipt of the Japan RON Trigger Notice.

8.2 **Japan License Negotiation**. If Takeda exercises the Japan RON by providing Licensee with the Exercise Notice during the Exercise Period (as may be extended pursuant to Section 8.1 above), then beginning on the date of Licensee's receipt of the Exercise Notice and continuing for a period of [ ]*, or such longer period agreed to by the Parties in writing (the "License Negotiation Period"), the Parties will enter into good faith negotiations regarding the terms and conditions of a definitive agreement or an amendment to this Agreement pursuant to which Takeda would receive from Licensee the Japan License ("Japan License Agreement"). In the Japan License Agreement, the Parties would amend certain other provisions of this Agreement as necessary to reflect the rights and responsibilities of the Parties following Licensee's grant of the Japan License to Takeda. Both Parties agree to extend the License Negotiation Period by no more than [ ]* where the Parties have reached agreement on all material terms and conditions of the Japan License Agreement prior to the expiration of the License Negotiation Period and only need additional time to finalize non-material terms or obtain final internal governance approvals.

8.3 **Terms of Third Party Agreements**. If the Parties fail to execute a Japan License Agreement during the License Negotiation Period (as may be extended pursuant to Section 8.2 above), Takeda's Japan RON will terminate, and Licensee shall have no further obligations to Takeda with respect to the Japan RON, and shall have all rights to enter into any sublicense or

other agreement with any Third Party for rights to Exploit the Compound and the Products in Japan; provided, however, that Licensee shall not grant to any Third Party any sublicense to Exploit the Compound or any Product in Japan unless the terms (when considered as a whole) offered by such Third Party for such sublicense or other agreement are more favorable to Licensee than the terms (when considered as a whole) offered by Takeda for the Japan License. Licensee shall use good faith in its consideration and comparison of the terms and conditions of the Japan License Agreement offered by Takeda and the terms and conditions of any sublicense or other agreement proposed by any Third Party.

8.4 **Termination of Discussions**. Notwithstanding any other provision of this Article 8, if Licensee determines at any time not to enter into, or to discontinue, any discussions or negotiations with any Third Parties for the grant of a sublicense to Exploit the Compound or the Product in Japan, then Licensee shall have the right to terminate such discussions or negotiations with such Third Parties if such discussions or negotiations are underway, and the right not to enter into, or to terminate, any discussions or negotiations with Takeda under this Article 8 for the grant to Takeda of the Japan License; provided, however, that if during the Japan RON Period, Licensee then subsequently again enters into discussion or negotiations with any Third Party for the grant by Licensee to such Third Party of a sublicense to Exploit the Compound or any Product in Japan, then Licensee shall provide the Japan RON Trigger Notice to Takeda in accordance with Section 8.1 above and the terms of this Article 8 shall again apply.

ARTICLE 9 - JOINT COMMITTEE; RELATIONSHIP MANAGERS

9.1 **Joint Committee Overview**. As set forth more fully below, the Parties agree that during the Term, the Joint Committee shall provide a forum for communication between the Parties, including the discussion of Licensee's progress of the Development of the Compound and the Products pursuant to the Development Plan, including any amendments, supplements or updates to such Development Plan, and Licensee's progress of material regulatory activities with respect to the Compound and the Products.

9.2 **Formation**. In accordance with this Article 9, the Parties agree to establish and convene the Joint Committee promptly after the Effective Date. The Joint Committee shall consist of an equal number of representatives designated by each Party and operate by the procedures in accordance with this Article 9. From time to time, each Party may replace any of its Joint Committee representatives by written notice to the other Party specifying the prior representative(s) and their replacement(s). Either Party may designate substitutes for its Joint Committee representatives if one (1) or more of such Party's designated representatives is unable to be present at a meeting. Each Party shall ensure that its Joint Committee representatives and other meeting participants are subject to confidentiality and non-use obligations at least as restrictive as those set forth in this Agreement prior to participation in any Joint Committee meeting.

9.3 **Meetings**. Unless the Joint Committee otherwise determines, the Joint Committee shall meet twice every Calendar Year and at such other times as the Joint Committee or the Parties may agree. The first meeting of the Joint Committee shall be held as soon as reasonably practicable. Meetings may be held in person, telephonically or by means of videoconference, as the Parties may mutually agree. Additional non-members of the Joint Committee having relevant experience

may from time to time be invited to participate in a Joint Committee meeting. Non-member participants shall only be allowed to attend if: (1) the other Party's representatives have consented to the attendance (such consent not to be unreasonably withheld, delayed or conditioned); and (2) such non-member participant is subject to confidentiality and non-use obligations at least as restrictive as those set forth in this Agreement. Each Party shall remain responsible for any failure by its representatives and invitees to comply with the confidentiality and non-use obligations contained in this Agreement. The Parties agree that the costs incurred by each Party in connection with its (and its representatives' and invitees') participation at any meetings under this Article 9 shall be borne solely by such Party.

9.4 **Authority**. The Joint Committee shall have no decision-making authority and shall not have any power to amend, modify or waive compliance with this Agreement.

9.5 **Dissolution of the Joint Committee**. The Joint Committee shall be dissolved upon the expiration or termination of this Agreement.

9.6 **Relationship Managers**. Promptly after the Effective Date, each Party shall appoint (and notify the other Party of the identify of) a senior representative having a general understanding of pharmaceutical development and commercialization issues to act as its relationship manager (each, a "Relationship Manager"). From time to time, each Party may replace its Relationship Manager with any other senior representative having a general understanding of pharmaceutical development and commercialization issues by written notice to the other Party specifying the replacement. Each Party shall ensure that its Relationship Manager is subject to confidentiality and non-use obligations at least as restrictive as those set forth in Article 12 hereof. Each Party shall remain responsible for any failure by its Relationship Manager to comply with the confidentiality and non-use obligations contained in this Agreement. The Relationship Managers shall serve as the contact points between the Parties to (i) facilitate the exchange of information related to the progress of Licensee's Development and Commercialization of the Compound and the Products, (ii) promote communication and coordination between the Parties, (iii) seek consensus within the respective Party's organization and with the other Party regarding key issues; (iv) facilitate the review of external corporate communications; (v) facilitate the transfer activities contemplated by Section 3.5 above, and (vi) raise cross-Party and/or cross-functional disputes in a timely manner. The Relationship Managers shall have no decision-making authority and shall not have any power to amend, modify or waive compliance with this Agreement.

ARTICLE 10 - INTELLECTUAL PROPERTY MATTERS

10.1 **Ownership of Inventions**. Inventorship shall be determined in accordance with U.S. patent laws. Each Party shall own any Inventions made solely by its own employees, agents, or independent contractors in the course of conducting any activities under this Agreement, together with all intellectual property rights therein (the "Sole Inventions"). The Parties shall jointly own any Inventions that are made jointly by employees, agents, or independent contractors of each Party in the course of performing activities under this Agreement, together with all intellectual property rights therein (the "Joint Inventions"). The Parties shall also jointly own any Information that is jointly generated or developed by the employees, agents, or independent contractors of each Party in the course of performing activities under this Agreement, together with all intellectual property rights therein (the "Joint Information"). Subject to the terms and conditions of this

Agreement (including the licenses granted by either Party to the other Party pursuant to this Agreement), each Party shall have the right to disclose, use and exploit Joint Inventions and Joint Information, in each case without the consent of the other Party and without having to account to the other Party for any such disclosure, use or exploitation. Notwithstanding the foregoing, neither Party shall disclose, use or Exploit any Joint Invention or Joint Information to the detriment of the other Party if such Joint Invention or Joint Information directly relates to the Compound or any Product.

10.2 **Disclosure of Inventions**. Each Party shall promptly disclose to the other Party any invention disclosures, or other similar documents, submitted to it by its employees, agents or independent contractors describing Inventions that such Party believes are patentable Joint Inventions.

10.3 **Prosecution of Patents**.

(a) **Takeda Patents**. Beginning on the Effective Date, and except as otherwise provided in this Section 10.3(a), as between the Parties, Licensee shall have the sole right and authority to prepare, file, prosecute and maintain the Takeda Patents on a worldwide basis using outside counsel that is mutually acceptable to both Parties. Licensee shall bear all expenses of preparation, filing, prosecution and maintenance of Takeda Patents in the Territory. Licensee shall provide Takeda a reasonable opportunity to review and comment on material communications from any patent authority regarding the Takeda Patents and drafts of any material filings or responses to be made to such patent authorities in advance of submitting such filings or responses. Licensee shall consider Takeda's comments regarding such communications and drafts in good faith, but Licensee shall have the final decision-making authority with respect to such communications and drafts, except that, during the Japan RON Period, Takeda shall have final decision-making authority in Japan with respect to such communications and drafts. If Licensee determines in its sole discretion to abandon or not maintain any Takeda Patent(s) that is being prosecuted or maintained by Licensee in one or more countries in the Territory, then Licensee shall provide Takeda with written notice of such determination within a period of time reasonably necessary to allow Takeda to determine, on a terminated country-by-country basis in its sole discretion, its interest in assuming the primary right and authority to prosecute and maintain such Takeda Patent(s) in such terminated country(ies) at Takeda's sole cost and expense (which notice by Licensee shall be given no later than sixty (60) days prior to the final deadline for any pending action or response that may be due with respect to such Takeda Patent(s) with the applicable patent authority). In the event Takeda provides written notice expressing its interest to assume the primary right and authority to prosecute and maintain such Takeda Patent(s) in such terminated country(ies), all rights in such Takeda Patents granted to Licensee under this Agreement shall terminate with respect to such terminated country(ies). Licensee and Takeda shall take all action necessary and execute and deliver all documents or instruments required to enable Takeda to assume the primary right and authority to prosecute and maintain such Takeda Patent(s) in the terminated country(ies). If Takeda assumes the primary right and authority to prosecute and maintain any Takeda Patent(s) in accordance with this subsection (a), Takeda may determine in its sole discretion to abandon or not maintain any such Takeda Patents.

(b) **Licensee Patents**. Licensee shall have the sole right and authority to prepare, file, prosecute and maintain the Licensee Patents on a worldwide basis at its own expense. Licensee

shall provide an updated list of Subject Licensee Patents at least annually at a Joint Committee meeting. If Licensee or any of its Affiliates sells, assigns, licenses, transfers, or otherwise grants any right under any Subject Licensee Patent to a Third Party, then Licensee or such Affiliate, as applicable, will require such purchaser, assignee, licensee, or transferee to agree in writing to recognize Takeda's rights under, and be bound to the same extent as Licensee by, Section 2.2, Article 8 and Section 13.6, with respect to such Subject Licensee Patent. Any sale, assignment, license, transfer or grant by Licensee or any of its Affiliates in violation of the terms of the foregoing sentence shall be null, void and of no legal effect.

(c) **Joint Patents**. Except as otherwise provided in this Section 10.3(c), Licensee shall have the primary right and authority to prepare, file, prosecute and maintain Joint Patents on a worldwide basis at its own expense using outside counsel that is mutually acceptable to both Parties. The Parties shall confer and mutually agree to a filing strategy and Licensee shall provide Takeda a reasonable opportunity to review and comment on material communications from any patent authority regarding the Joint Patents and drafts of any material filings or responses to be made to such patent authorities in advance of submitting such filings or responses. Licensee shall consider Takeda's comments regarding such communications and drafts in good faith, but Licensee shall have the final decision-making authority with respect to such communications and drafts to the extent that the subject matter of the Joint Patents is necessary or useful to Exploit the Compound or any Product in the Field in the Territory, except that, during the Japan RON Period, Takeda shall have final decision-making authority in Japan with respect to such communications and drafts to the extent that the subject matter of the Joint Patents is necessary or useful to Exploit the Compound or any Product in the Field in Japan. If Licensee determines in its sole discretion to abandon or not maintain any Joint Patent(s), then Licensee shall provide Takeda with written notice of such determination within a period of time reasonably necessary (which notice from Licensee shall be given no later than sixty (60) days prior to any final deadline for any pending action or response that may be due with respect to such Joint Patent(s) with the applicable patent authority) to allow Takeda and Licensee to determine and mutually agree what to do with such Joint Patent(s) and, absent any such mutual agreement by Takeda and Licensee, to allow Takeda to determine its interest in assuming the primary right and authority to prosecute and maintain such Joint Patent(s). In the event that Takeda and Licensee do not agree in writing on a course of action with respect to such Joint Patent(s) and that Takeda provides written notice to Licensee expressing its interest to assume the primary right and authority to prosecute and maintain such Joint Patent(s), (i) Licensee and Takeda shall take all action necessary and execute and deliver all documents or instruments required to enable Takeda to assume the primary right and authority to prosecute and maintain such Joint Patent(s) and (ii) Takeda shall thereafter have the right and authority to prosecute and maintain such Joint Patents at its cost; provided, however, that Licensee shall reimburse Takeda for [ ]* of the reasonable expenses actually incurred by Takeda in prosecuting and maintaining such Joint Patents promptly following Takeda's presentation of invoices detailing such expenses if, but only if, such reasonable expenses are actually incurred by Takeda during any portion of the Term that such Joint Patent or Joint Patents in respect of which Takeda incurs such reasonable expenses Covered the Exploitation of the Compound or any Product and no Takeda Patent, Subject Licensee Patent or Joint Patent in respect of which Licensee is prosecuting and maintaining at Licensee's sole cost and expense Covers the Exploitation of the Compound or any Product. If Licensee fails to make any reimbursement payment within thirty (30) days following Takeda's presentation of invoices, then Licensee shall free of charge assign and transfer to Takeda

the ownership of, and interest in, such Joint Patent(s) in the applicable country, and Licensee shall cooperate with Takeda for the assignment and transfer to Takeda of such Joint Patent(s) in such country and all rights of Licensee in such Joint Patent(s) under this Agreement shall terminate. If Takeda assumes the primary right and authority to prosecute and maintain any Joint Patent(s) in accordance with this subsection (c), Takeda may determine in its sole discretion to abandon or not maintain any such Joint Patent(s).

(d) **Cooperation in Prosecution**. Each Party shall provide the other Party reasonable assistance and cooperation in the Patent prosecution efforts provided above in this Section 10.3, including providing any necessary powers of attorney and executing any other required documents or instruments for such prosecution, as well as further actions as set forth below.

(i) Licensee shall prepare, file, maintain and prosecute the Takeda Patents, Licensee Patents and Joint Patents as set forth in, and subject to, this Section 10.3. As used herein, "prosecution" of such Patents shall include all communication and other interaction with any patent office or patent authority having jurisdiction over a patent application in connection with pre-grant proceedings.

(ii) All communications between the Parties relating to the preparation, filing, prosecution or maintenance of the Takeda Patents, the Licensee Patents and the Joint Patents, including copies of any draft or final documents or any communications received from or sent to patent offices or patenting authorities with respect to such Patents, shall be considered Confidential Information and subject to the confidentiality provisions of Article 12.

(iii) Assignments to Licensee Patents and Joint Patents shall be effected as follows: (1) employees or agents of Licensee that are named as inventors on Licensee Patents shall assign their interest in such Patents to Licensee; and (2) employees or agents of Takeda or Licensee that are named as inventors on Joint Patents shall assign their interest in such Patents to their respective employer.

10.4 **Orange Book Listing**. Subject to Section 10.3, Licensee shall be solely responsible for listing and maintaining all appropriate Takeda Patents, Licensee Patents and Joint Patents in the Orange Book, including payment of all expenses related to such maintenance incurred after the Effective Date. Upon request of Licensee, Takeda shall cooperate with Licensee to file appropriate information with the FDA for listing any Takeda Patents and any Joint Patents in the Orange Book. The obligations of Licensee under this Section 10.4 with respect to Takeda Patents and Joint Patents shall only be applicable for those Patents for which Licensee has the primary right and authority to prosecute and maintain in the U.S. pursuant to, and in accordance with, the provisions of Section 10.3.

10.5 **Infringement of Patents by Third Parties**.

(a) **Notification**. Each Party shall promptly notify the other Party in writing of any existing, alleged or threatened infringement of the Takeda Patents, Joint Patents or Licensee Patents in the Field in the Territory of which it becomes aware, and shall provide all Information in such Party's possession or control demonstrating such infringement.

(b) **Infringement Action**.

(i) Licensee shall have the right, but not the obligation, to bring an appropriate suit or other action against any Third Party engaged in any existing, alleged or threatened infringement of any Takeda Patent or Joint Patent related to the making, using, importing, offering for sale or selling a Product in the Field in the Territory (a "Product Infringement"), subject to Section 10.5(b)(ii) through 10.5(b)(iv), below.

(ii) Licensee shall notify Takeda of its election to take any action in accordance with Section 10.5(b)(i) at least ten (10) days before any time limit set forth in an Applicable Law or regulation, including the time limits set forth under the Hatch-Waxman Act (21 U.S.C. § 355). In the event Licensee does not so elect, Licensee shall so notify Takeda in writing, and Takeda shall have the right, but not the obligation, to commence a suit or take action to enforce the applicable Takeda Patent or Joint Patent against such Third Party perpetrating such Product Infringement in the Territory at its own expense. If one Party elects to bring suit or take action against the Product Infringement, then the other Party shall have the right, prior to commencement of the trial, suit or action, to join any such suit or action at such other Party's expense.

(iii) Each Party shall provide to the Party enforcing any such rights under this Section 10.5(b) reasonable assistance in such enforcement, at such enforcing Party's request and expense, including joining such action as a party plaintiff if required by Applicable Law to pursue such action. The enforcing Party shall keep the other Party regularly informed of the status and progress of such enforcement efforts, shall reasonably consider the other Party's comments on any such efforts, including determination of litigation strategy and filing of important papers to the competent court.

(iv) Subject to this Section 10.5(b)(iv), the enforcing Party shall be solely responsible for all expenses arising from a suit or action against a Product Infringement. For the avoidance of doubt, the enforcing Party shall not be responsible for the other Party's internal expenses (e.g., FTEs) incurred as a result of the other Party's cooperation with the enforcement action as provided in Section 10.5(b)(iii). The Party not bringing an action with respect to Product Infringement in the Territory under this Section 10.5(b) shall be entitled to separate representation in such matter by legal counsel of its own choice and at its own expense, but such Party shall at all times cooperate fully with the Party bringing such action.

(c) **Settlement**. Neither Party shall settle any claim, suit or action that it brought under this Section 10.5 with respect to any Takeda Patent or Joint Patent without the prior written consent of the other Party (which consent shall not be unreasonably withheld, conditioned or delayed).

(d) **Allocation of Proceeds**. If either Party recovers monetary damages from any Third Party in a suit or action brought under Sections 10.5(b), or any settlement proceeds from any settlement in accordance with the provisions of 10.5(c), or any fees, payments or royalties from a license agreement with a Third Party related to any alleged Product Infringement, whether such damages, settlement proceeds or fees, payments or royalties result from the infringement of Takeda Patents or Joint Patents, such recovery shall be allocated first to the reimbursement of any expenses incurred by the Parties in such litigation, action or license, and any remaining amounts shall be split as follows: (i) if such suit or action is initiated or defended by Licensee, such amounts shall

be retained by Licensee and treated as Net Sales for purposes of the royalties due to Takeda under this Agreement or (ii) if such suit or action was initiated or defended by Takeda, such amounts shall be retained by Takeda.

10.6 **Infringement of Third Party Rights in the Territory**. Notwithstanding Section 7.7:

(a) **Notice**. If any Product used or sold by Licensee, its Affiliates, or Sublicensees becomes the subject of a Third Party's claim or assertion of infringement of a Patent granted in the Territory, the Party first having notice of the claim or assertion shall promptly notify the other Party, the Parties shall agree on and enter into an "identity of interest agreement" wherein such Parties agree to their shared, mutual interest in the outcome of such potential dispute, and thereafter, the Parties shall promptly meet to consider the claim or assertion and the appropriate course of action.

(b) **Defense**. Pursuant to, and in accordance with, Section 15.3, Licensee shall have the obligation to defend any such Third Party claim or assertion of infringement of a Patent as described in Section 10.6(a) above, at Licensee's expense. Takeda, at Licensee's expense, shall reasonably cooperate with Licensee's defense of the claim or assertion, including if required to conduct such defense, furnishing a power of attorney. The obligations of Licensee under this Section 10.6(b) may be performed or discharged by Licensee directly or through Affiliates or Sublicensees of Licensee. If Licensee recovers monetary damages from any such Third Party asserting such a claim of infringement as a result of counter claims brought by such defending Party based on any Takeda Patent or Joint Patent, or any royalties from a license agreement with such Third Party, such recovery shall be allocated in accordance with the provisions of Section 10.5(d).

(c) **Settlement; Licenses**. Neither Party shall enter into any settlement of any claim described in this Section 10.6 that affects the other Party's rights or interests without such other Party's written consent, which consent shall not be unreasonably withheld, conditioned or delayed.

(d) **No Duty to Investigate or Inquire**. Nothing in this Section 10.6 shall be construed or interpreted as imposing on either Party any express or implied duty to investigate or make inquiry regarding intellectual property rights of Third Parties.

10.7 **Patent Oppositions and Other Proceedings.**

(a) **Third-Party Patent Rights**. If either Party desires to bring an opposition, action for declaratory judgment, nullity action, interference, declaration for non-infringement, reexamination or other attack upon the validity, title or enforceability of a Patent owned or controlled by a Third Party and having one or more claims that covers a Product, or the use, sale, offer for sale or importation of a Product (except insofar as such action is a counterclaim to or defense of, or accompanies a defense of, a Third Party's claim or assertion of infringement under Section 10.6, in which case the provisions of Section 10.6 shall govern), such Party shall so notify the other Party and the Parties shall promptly confer to determine whether to bring such action or the manner in which to settle such action. Licensee shall have the exclusive right, but not the obligation, to bring at its own expense and in its sole control such action in the Territory. If Licensee does not bring such an action in the Territory, within ninety (90) days of notification

thereof pursuant to this Section 10.7(a) (or earlier, if required by the nature of the proceeding), then Takeda shall have the right, but not the obligation, to bring, at Takeda's sole expense, such action. The Party not bringing an action under this Section 10.7(a) shall be entitled to separate representation in such proceeding by legal counsel of its own choice and at its own expense, and shall cooperate fully with the Party bringing such action.

(b) **Parties' Patent Rights**. If any Takeda Patent, Joint Patent or Licensee Patent becomes the subject of any proceeding commenced by a Third Party within the Territory in connection with an opposition, reexamination request, action for declaratory judgment, nullity action, interference or other attack upon the validity, title or enforceability thereof (except insofar as such action is a counterclaim to or defense of, or accompanies a defense of, an action for infringement against a Third Party under Section 10.5, in which case the provisions of Section 10.5 shall govern), then the Party responsible for filing, preparing, prosecuting and maintaining such Patent as set forth in Section 10.3 hereof, shall control such defense at its own expense. The controlling Party shall permit the non-controlling Party to participate in the proceeding to the extent permissible under Applicable Law, and to be represented by its own legal counsel in such proceeding, at the non-controlling Party's expense. If either Party decides that it does not wish to defend against such action, then the other Party shall have a backup right to assume defense of such Third-Party action at its own expense. Any awards or amounts received in defending any such Third-Party action shall be allocated between the Parties as provided in Section 10.5(d).

ARTICLE 11 – REPRESENTATIONS AND WARRANTIES

11.1 **Mutual Representations, Warranties and Covenants**. Each of the Parties hereby represents and warrants to the other Party as of the Effective Date and covenants that:

(a) **Organization**. It is a corporation duly organized, validly existing, and in good standing under the laws of the jurisdiction of its organization, and has all requisite power and authority, corporate or otherwise, to execute, deliver, and perform this Agreement.

(b) **Binding Agreement**. This Agreement is a legal and valid obligation binding upon such Party and enforceable in accordance with its terms, subject to the effects of bankruptcy, insolvency, or other laws of general application affecting the enforcement of creditor rights, judicial principles affecting the availability of specific performance, and general principles of equity (whether enforceability is considered in a proceeding at law or equity).

(c) **Authorization**. The execution, delivery, and performance of this Agreement by such Party have been duly authorized by all necessary corporate action and do not conflict with any agreement, instrument, or understanding, oral or written, to which it is a party or by which it is bound, nor violate any Applicable Law or any order, writ, judgment, injunction, decree, determination, or award of any court or governmental body, or administrative or other agency presently in effect applicable to such Party.

(d) **No Further Approval**. It is not aware of any government authorization, consent, approval, license, exemption of or filing or registration with any court or governmental department, commission, board, bureau, agency or instrumentality, domestic or foreign, under any Applicable Law, currently in effect, necessary for, or in connection with, the transactions

contemplated by this Agreement or any other agreement or instrument executed in connection herewith, or for the performance by it of its obligations under this Agreement and such other agreements (save for Regulatory Approvals and similar authorizations from Regulatory Authorities necessary for the Exploitation of the Compound and any Product as contemplated hereunder).

(e) **No Inconsistent Obligations**. Neither Party nor any of its Affiliates is under any obligation, contractual or otherwise, to any Person that conflicts with or is inconsistent in any material respect with the terms of this Agreement, or that would impede the diligent and complete fulfillment of its obligations hereunder.

(f) **Transparency Reporting**. Each Party shall be responsible for tracking and reporting transfers of value initiated and controlled by its and its Affiliates' employees, contractors, and agents pursuant to the requirements of the marketing reporting laws of any Government Authority in the Territory, including Section 6002 of the Patient Protection and Affordable Care Act, commonly referred to as the "Sunshine Act."

11.2 **Additional Representations, Warranties and Covenants of Takeda**. Takeda represents and warrants as of the Effective Date and covenants to Licensee that:

(a) Takeda has all rights necessary to grant the licenses under the Takeda Intellectual Property existing as of the Effective Date that it grants to Licensee in this Agreement. As of the Effective Date, there are no Regulatory Materials.

(b) As of the Effective Date, the Patents set forth in Exhibit B represent all Patents that Takeda or any of its Affiliates owns or Controls that claim or disclose any invention necessary or useful for the Exploitation of the Compound or any Product in the Field in the Territory. Takeda is the sole and exclusive owner of the entire right, title and interest in the Takeda Patents free of any encumbrance, lien, or claim of ownership by any Third Party.

(c) To Takeda's Knowledge, there is no actual or threatened infringement or misappropriation of the Takeda Intellectual Property by any Person in the Territory.

(d) The Takeda Patents are being diligently prosecuted in the Territory in accordance with Applicable Law. To Takeda's Knowledge, the Takeda Patents have been filed and maintained properly and correctly and all applicable fees have been paid on or before the due date for payment.

(e) To Takeda's Knowledge, each of the Takeda Patents properly identifies each and every inventor of the claims thereof as determined in accordance with Applicable Law of the jurisdiction in which such Takeda Patent is issued or such application is pending.

(f) To Takeda's Knowledge, the confidential Takeda Know-How has been kept confidential or has been disclosed to Third Parties only under terms of confidentiality. To the Knowledge of Takeda, no breach of such confidentiality has been committed by any Third Party.

(g) The Inventions claimed or disclosed by the Takeda Patents (i) were not conceived, discovered, developed, or otherwise made in connection with any research activities funded, in

whole or in part, by the federal government of the U.S. or any agency thereof, (ii) are not a "subject invention" as that term is described in 35 U.S.C. Section 201(f), and (iii) are not otherwise subject to the provisions of the Bayh-Dole Act.

(h) Takeda has not been debarred by the FDA, and is not subject to any such debarment or similar sanction by any other Regulatory Authorities in the Territory, and neither Takeda nor any of its Affiliates has used, or will engage, in any capacity, in connection with this Agreement, any Person who either has been debarred by such a Regulatory Authority, or is the subject of a conviction described in Section 306 of the FFDCA. Takeda shall inform Licensee in writing promptly if it or any Person engaged by Takeda or any of its Affiliates who is performing activities under this Agreement is debarred or is the subject of a conviction described in Section 306 of the FFDCA, or if any action, suit, claim, investigation or legal or administrative proceeding is pending or, to Takeda's Knowledge, is threatened, relating to the debarment or conviction of Takeda or any such Person performing activities hereunder.

(i) To Takeda's Knowledge, there are no material claims, judgments, or settlements against, or amounts with respect thereto, owed by Takeda or any of its Affiliates to any Third Parties relating to the Takeda Intellectual Property in the Territory.

(j) No claim or litigation in the Territory has been brought or, to Takeda's Knowledge, threatened by any Person alleging, and Takeda has no Knowledge of any claim, whether or not asserted: (i) that any of the Takeda Patents is invalid or unenforceable, (ii) that the Takeda Intellectual Property, or the disclosing, copying, making, assigning, or licensing of the Takeda Intellectual Property, violates, infringes, or otherwise conflicts or interferes with, or would violate, infringe, or otherwise conflict or interfere with, any intellectual property or proprietary right of any Person; or (iii) related to the Development of the Product, as of the Effective Date.

(k) To the extent permissible under Applicable Law, all employees of Takeda or its Affiliates performing activities under this Agreement shall be under an obligation to assign all right, title and interest in and to their inventions and other know-how, whether or not patentable, and intellectual property rights therein, to Takeda or its Affiliate(s) as the sole owner thereof. Licensee shall have no obligation to contribute to any remuneration of any inventor employed or previously employed by Takeda or any of its Affiliates in respect of any such inventions, Information and discoveries and intellectual property rights therein. Takeda will pay all such remuneration, if any, due to such inventors with respect to such inventions and other know-how and intellectual property rights therein.

(l) In performing its obligations under this Agreement, or any ancillary agreements (if any), Takeda shall, and shall cause its Affiliates to, comply with all Applicable Law, including any applicable anti-corruption or anti-bribery laws or regulation, of any Governmental Authority with jurisdiction over the activities performed by Takeda or its Affiliates in furtherance of such obligations.

11.3 **Additional Representations, Warranties and Covenants of Licensee**. Licensee represents and warrants as of the Effective Date and covenants to Takeda that:

(a) Licensee has not been debarred by the FDA, and is not subject to any such debarment or similar sanction by any other Regulatory Authorities in the Territory, and neither Licensee nor any of its Affiliates has used, or will engage, in any capacity, in connection with this Agreement, any Person who either has been debarred by such a Regulatory Authority, or is the subject of a conviction described in Section 306 of the FFDCA. Licensee shall inform Takeda in writing promptly if it or any Person engaged by Licensee or its Affiliates who is performing activities under this Agreement is debarred or is the subject of a conviction described in Section 306 of the FFDCA, or if any action, suit, claim, investigation or legal or administrative proceeding is pending or, to Licensee's Knowledge, is threatened, relating to the debarment or conviction of Licensee or any such Person performing activities hereunder.

(b) To the extent permissible under Applicable Law, all employees of Licensee or its Affiliates performing activities under this Agreement shall be under an obligation to assign all right, title and interest in and to their inventions and other know-how, whether or not patentable, and intellectual property rights therein, to Licensee or its Affiliate(s) as the sole owner thereof. Takeda shall have no obligation to contribute to any remuneration of any inventor employed or previously employed by Licensee or any of its Affiliates in respect of any such inventions, Information and discoveries and intellectual property rights therein that are so assigned to Licensee or its Affiliate(s). Licensee will pay all such remuneration, if any, due to such inventors with respect to such inventions and other know-how and intellectual property rights therein.

(c) In performing its obligations under this Agreement, or any ancillary agreements (if any), Licensee shall, and shall cause its Affiliates to, comply with all Applicable Law, including any applicable anti-corruption or anti-bribery laws or regulation, of any Governmental Authority with jurisdiction over the activities performed by Licensee or its Affiliates in furtherance of such obligations.

11.4 **No Other Representations or Warranties**. EXCEPT AS EXPRESSLY SET FORTH IN THIS ARTICLE 11, THE PARTIES MAKE NO REPRESENTATIONS OR WARRANTIES OF ANY KIND WHATSOEVER, EITHER EXPRESS OR IMPLIED, WRITTEN OR ORAL, EITHER IN FACT OR BY OPERATION OF LAW, BY STATUTE OR OTHERWISE, AND EACH PARTY SPECIFICALLY DISCLAIMS ANY OTHER WARRANTIES, INCLUDING ANY EXPRESS OR IMPLIED WARRANTY OF QUALITY, MERCHANTABILITY, FITNESS FOR A PARTICULAR PURPOSE, OR WARRANTY OF NON-INFRINGEMENT OR AS TO THE VALIDITY OF ANY PATENTS IN THE TERRITORY.

11.5 **Research Material**. SUBJECT TO THE EXPRESS TERMS OF THIS AGREEMENT, LICENSEE ACKNOWLEDGES AND AGREES THAT THE EXISTING RESEARCH MATERIAL AND THE [ ]* PROVIDED TO LICENSEE BY OR ON BEHALF OF TAKEDA OR ANY OF ITS AFFILIATES IN CONNECTION WITH THIS AGREEMENT ARE EXPERIMENTAL IN NATURE AND MAY HAVE UNKNOWN CHARACTERISTICS. LICENSEE SHALL USE PRUDENCE AND REASONABLE CARE IN THE USE, HANDLING, STORAGE, TRANSPORTATION, DISPOSITION, AND CONTAINMENT OF THE EXISTING RESEARCH MATERIAL AND THE [ ]*. EXCEPT AS OTHERWISE EXPRESSLY SET FORTH HEREIN, WITHOUT LIMITING THE FOREGOING, THE EXISTING RESEARCH MATERIAL AND THE [ ]* IS MADE AVAILABLE ON AN "AS-IS" BASIS, WITHOUT WARRANTY WITH RESPECT TO COMPLETENESS, COMPLIANCE

WITH REGULATORY STANDARDS OR REGULATIONS OR FITNESS FOR A PARTICULAR PURPOSE OR ANY WARRANTY THAT THE USE OF THE EXISTING RESEARCH MATERIAL OR THE [ ]* WILL NOT INFRINGE OR VIOLATE ANY PATENT OR OTHER PROPRIETARY RIGHTS OF ANY THIRD PARTY, OR ANY OTHER KIND OF WARRANTY WHETHER EXPRESS OR IMPLIED.

ARTICLE 12 – CONFIDENTIALITY

12.1 **Nondisclosure**. Each Party agrees that, during the Term and for a period of [ ]* thereafter, a Party (the "Receiving Party") receiving Confidential Information of the other Party (the "Disclosing Party") shall (a) maintain in confidence such Confidential Information using not less than the efforts such Receiving Party uses to maintain in confidence its own confidential or proprietary information of similar kind and value, (b) not disclose such Confidential Information to any Third Party without the prior written consent of the Disclosing Party, except for disclosures expressly permitted below, and (c) not use such Confidential Information for any purpose except those permitted by this Agreement (it being understood that this Section 12.1 shall not create or imply any rights or licenses not expressly granted under this Agreement). Notwithstanding anything to the contrary in the foregoing, the obligations of confidentiality and non-use with respect to any trade secret (to the extent understood by a Party to be a trade secret) within such Confidential Information shall survive such [ ]* period for so long as such Confidential Information remains protected as a trade secret under Applicable Law.

12.2 **Exceptions**. The obligations in Section 12.1 shall not apply with respect to any portion of the Confidential Information that the Receiving Party can show by competent evidence:

(a) is publicly disclosed by the Disclosing Party or any of its Affiliates, either before or after it is disclosed to the Receiving Party hereunder;

(b) is known to the Receiving Party or any of its Affiliates, without any obligation to keep it confidential or any restriction on its use, prior to disclosure by the Disclosing Party;

(c) is subsequently disclosed to the Receiving Party or any of its Affiliates on a non-confidential basis by a Third Party that, to the Receiving Party's Knowledge, is not bound by a similar duty of confidentiality or restriction on its use;

(d) is now, or hereafter becomes, through no act or failure to act on the part of the Receiving Party or any of its Affiliates, generally known or available, either before or after it is disclosed to the Receiving Party;

(e) is independently discovered or developed by or on behalf of the Receiving Party or any of its Affiliates without the use of or access to Confidential Information belonging to the Disclosing Party; or

(f) is the subject of written permission to disclose provided by the Disclosing Party.

12.3 **Authorized Disclosure**. The Receiving Party may disclose Confidential Information belonging to the Disclosing Party only to the extent such disclosure is reasonably necessary in the following instances:

(a) filing or prosecuting Patents as permitted by this Agreement;

(b) filing Regulatory Materials in order to obtain or maintain Regulatory Approvals;

(c) prosecuting or defending litigation, including responding to a subpoena in a Third Party litigation;

(d) complying with Applicable Law or regulations or court or administrative orders;

(e) to its Affiliates, licensees, prospective licensees, Sublicensees or prospective Sublicensees, subcontractors or prospective subcontractors, payors, consultants, agents and advisors on a "need-to-know" basis in order for the Receiving Party to exercise its rights or fulfill its obligations under this Agreement, each of whom prior to disclosure must be bound by obligations of confidentiality and restrictions on use of such Confidential Information that are no less restrictive (except for the duration of such restrictions, which shall be no less than five (5) years) than those set forth in this Article 12; provided, however, that, in each of the above situations, the Receiving Party shall remain responsible for any failure by any Person who receives Confidential Information pursuant to this Section 12.3(e) to treat such Confidential Information as required under this Article 12; or

(f) to its actual or prospective lenders, investors, acquirers, merger-partners, and to any investment advisors, each of whom prior to disclosure must be bound by obligations of confidentiality and restrictions on use of such Confidential Information that are no less restrictive than those set forth in this Article 12 (except for the duration of such restrictions which shall be no less than five (5) years solely in the case of Confidential Information that consists of the existence of this Agreement and the terms hereof, if and only if the Receiving Party uses reasonable efforts to obtain a term of such obligations equal to that herein); provided, however, that, in each of the above situations, the Receiving Party shall remain responsible for any failure by any Person who receives Confidential Information pursuant to this Section 12.3(f) to treat such Confidential Information as required under this Article 12.

(g) If and whenever any Confidential Information is disclosed in accordance with this Section 12.3, such disclosure shall not cause any such information to cease to be Confidential Information except to the extent that such disclosure results in a public disclosure of such information (other than by breach of this Agreement). Notwithstanding the foregoing, in the event a Party is required to make a disclosure of the other Party's Confidential Information pursuant to clauses (a) through (d) of this Section 12.3, it shall, except where impracticable, give reasonable advance notice to the other Party of such disclosure and use not less than the same efforts to secure confidential treatment of such information as it would to protect its own confidential information from disclosure and shall be jointly and severally liable for any breach of this Article 12 by such Person.

12.4 **Terms of this Agreement**. The Parties acknowledge that this Agreement and all of the respective terms of this Agreement shall be treated as Confidential Information of both Parties.

12.5 **Publicity**. Each Party agrees not to issue any press release or other public statement disclosing the execution of this Agreement and any other information relating to this Agreement or the transactions contemplated hereby without the prior written consent of the other Party, not to be unreasonably withheld, conditioned or delayed. Notwithstanding the foregoing, disclosures (including press releases or public statements) required by Applicable Law or regulations or court or administrative orders shall not be prohibited by this Section 12.5 if such disclosures are subject to Section 12.3(d) above, and disclosures (including press releases or public statements) required to comply with a Party's disclosure obligations under applicable securities laws, the rules and regulations of the Securities and Exchange Commission or the national securities exchange in which a Party's equity securities may be listed for trading shall not be prohibited by this Section 12.5 but shall be subject to Section 12.6.

12.6 **Securities Filings**. Notwithstanding anything to the contrary in this Article 12, in the event either Party proposes to file with the Securities and Exchange Commission or the securities regulators of any state or other jurisdiction a registration statement or any other disclosure document that describes or refers to the terms and conditions of this Agreement or any related agreements between the Parties, such Party shall notify the other Party of such intention and shall provide the other Party with a copy of relevant portions of the proposed filing promptly (and in any event, at least five (5) Business Days (or such shorter time to meet any filing deadline where it is not practical to provide the other Party with such notice) prior to such filing (and any revisions to such portions of the proposed filing a reasonable time prior to the filing thereof), including any exhibits thereto that refer to the other Party or the terms and conditions of this Agreement or any related agreements between the Parties; provided, however, that if such Party proposes to file this Agreement as an exhibit to any such filing and to request confidential treatment for portions of this Agreement in connection with any such filing, then such Party shall provide the other Party with a copy of the relevant portions of the proposed filing at least ten (10) Business Days prior to such filing. The Party making such filing shall cooperate in good faith with the other Party to seek confidential treatment of the terms and conditions of this Agreement or any related agreements between the Parties that the other Party requests to be kept confidential or otherwise afforded confidential treatment and for which confidential treatment is available under applicable securities laws, rules and regulations, and shall only disclose Confidential Information that it is reasonably advised by legal counsel is legally required to be disclosed. No such notice shall be required if the description of or reference to this Agreement or a related agreement between the Parties contained in the proposed filing has been included in any previous filing made by the either Party in accordance with this Section 12.6 or otherwise approved by the other Party or disclosed in a prior press release by the Parties or other prior public disclosure made by a Party in accordance with the terms of this Article 12.

12.7 **Publication**. Neither Party shall submit for publication or presentation, or publish or present, any academic, scientific or medical abstract, publication or presentation disclosing the Takeda Know-How (other than Information or Inventions with respect to the Compound or any Product) or Joint Know-How that relates solely to the Compound or the Products or any Joint Inventions without first submitting such proposed abstract, publication or presentation to the other

Party, and complying with the provisions set forth below in this Section 12.7. Written copies of any proposed publication or presentation required to be submitted by a Party hereunder shall be submitted to the other Party no later than forty-five (45) days before submission for publication or presentation (the "Review Period"). The other Party shall provide its comments with respect to such publications and presentations within thirty (30) days following its receipt of such written copy. The Review Period may be extended for an additional thirty (30) days in the event the other Party can, within ten (10) days following receipt of the written copy, demonstrate reasonable need for such extension including for the preparation and filing of patent applications. All publications relating to the use of the Compound and/or a Product in the Field by a Party shall be prepared, presented and/or published in accordance with pharmaceutical industry accepted guidelines including: (a) International Committee of Medical Journal Editors (ICMJE) guidelines, (b) Uniform Requirements for Manuscripts Submitted to Biomedical Journals: Writing and Editing for Biomedical Publication, (c) Pharmaceutical Research and Manufacturers of America (PhRMA) guidelines, and (d) Principles on Conduct of Clinical Trials.

12.8 **Equitable Relief**. Given the nature of the Confidential Information and the competitive damage that could result to a Party upon unauthorized disclosure, use or transfer of its Confidential Information to any Third Party, the Parties agree that monetary damages may not be a sufficient remedy for any breach of this Article 12. In addition to all other remedies, a Party shall be entitled to seek specific performance and injunctive and other equitable relief as a remedy for any breach or threatened breach of this Article 12.

ARTICLE 13 – TERM AND TERMINATION

13.1 **Term**. This Agreement shall become effective as of the Effective Date and shall continue in full force and effect until the expiration of this Agreement as described in this Section 13.1, unless earlier terminated pursuant to this Article 13 (the "Term"). This Agreement shall expire as follows:

(a) on a country-by-country and Product-by-Product basis, upon the expiration of the Royalty Term with respect to each Product in each country in the Territory, as applicable; or

(b) in its entirety, upon the expiration of the Royalty Term with respect to the last Product Commercialized in the last country in the Territory.

Upon expiration of this Agreement pursuant to Section 13.1(a) with respect to a Product in a country of the Territory, subject to the terms and conditions of this Agreement and except to the extent any rights are granted to or retained by Takeda pursuant to Article 8, Licensee will have a perpetual, irrevocable, exclusive, fully-paid and royalty-free license, with the right to grant sublicenses, under the Takeda Intellectual Property and Takeda's rights to the Joint Intellectual Property to Exploit such Product in the Field in such country of the Territory. Upon expiration of this Agreement in its entirety pursuant to Section 13.1(b), subject to the terms and conditions of this Agreement and except to the extent any rights are granted to or retained by Takeda pursuant to Article 8, Licensee will have a perpetual, irrevocable, exclusive, fully-paid and royalty-free license, with the right to grant sublicenses, under the Takeda Intellectual Property and Takeda's rights to the Joint Intellectual Property to Exploit any and all Products in the Field in all countries in the Territory.

13.2 **Termination for Material Breach**.

(a) Either Party (the "Non-Breaching Party") may terminate this Agreement in its entirety in the event the other Party (the "Breaching Party") has materially breached this Agreement, and such material breach has not been cured within [ ]* (other than any breach for failure to pay, which shall be [ ]*) after receipt of written notice of such breach by the Breaching Party from the Non-Breaching Party (the "Cure Period"). The written notice describing the alleged material breach shall provide sufficient detail to put the Breaching Party on notice of such material breach. Any termination of this Agreement pursuant to this Section 13.2(a) shall become effective at the end of the Cure Period, unless the Breaching Party has cured any such material breach prior to the expiration of such Cure Period, or unless such allegedly breaching Party disputes such breach in accordance with Section 13.2(b). The right of either Party to terminate this Agreement as provided in this Section 13.2(a) shall not be affected in any way by such Party's waiver of or failure to take action with respect to any previous breach under this Agreement.

(b) If the Parties reasonably and in good faith disagree as to whether there has been a material breach, including whether such breach was material, the Party that disputes whether there has been a material breach may contest the allegation in accordance with Article 14. Notwithstanding anything to the contrary contained in Section 13.2(a), the Cure Period for any Dispute shall run from the date that written notice was first provided to the Breaching Party by the Non-Breaching Party through the resolution of such Dispute pursuant to Article 14, and it is understood and acknowledged that, during the pendency of a Dispute pursuant to this Section 13.2(b), all of the terms and conditions of this Agreement shall remain in effect, and the Parties shall continue to perform all of their respective obligations under this Agreement.

13.3 **Termination by Licensee**. Licensee shall have the right to terminate this Agreement for any or no reason upon providing [ ]* prior written notice to Takeda. Notwithstanding the foregoing, in the event that Licensee provides such a notice of termination, Takeda may, in its sole discretion, reduce the applicable notice period set forth above by providing written notice thereof to Licensee.

13.4 **Termination for Patent Challenge**. Takeda may terminate this entire Agreement at any time upon written notice to Licensee, if Licensee, or any of Licensee's Affiliates, or its or their Sublicensees, directly, or indirectly through assistance granted to a Third Party, commences any interference or opposition proceeding, challenges the validity or enforceability of, or opposes any extension of or the grant of a supplementary protection certificate with respect to (a "Patent Proceeding") any Takeda Patent or any other Patent Controlled by Takeda that claims or discloses the composition of matter or the method of making or using the Compound or any Product anywhere in the Territory except for a country in the Territory in which this Agreement has been terminated prior to the commencement of any such Patent Proceeding. However, Takeda's right to terminate this Agreement under this Section 13.4 shall not apply to any Affiliate of Licensee that first becomes an Affiliate of Licensee after the Effective Date of this Agreement in connection with a merger or acquisition event, or any Sublicensee, where such Affiliate or Sublicensee was undertaking activities in connection with a Legal Proceeding prior to such merger or acquisition event or the grant of such sublicense, provided such Affiliate or Sublicensee promptly ceases all activities in the furtherance of such Patent Proceeding and withdraws or terminates with prejudice

any such Patent Proceeding within [ ]* days of such merger or acquisition event or grant of sublicense.

13.5 **Termination for Insolvency**.

(a) Either Party may terminate this Agreement in its entirety upon providing written notice to the other Party on or after the time that such other Party makes a general assignment for the benefit of creditors, files an insolvency petition in bankruptcy, petitions for or acquiesces in the appointment of any receiver, trustee or similar officer to liquidate or conserve its business or any substantial part of its assets, commences under the laws of any jurisdiction any proceeding involving its insolvency, bankruptcy, reorganization, adjustment of debt, dissolution, liquidation or any other similar proceeding for the release of financially distressed debtors, or becomes a party to any proceeding or action of the type described above, and such proceeding or action remains un-dismissed or un-stayed for a period of more than sixty (60) days.

(b) All rights and licenses granted under or pursuant to this Agreement are, and shall otherwise be deemed to be, for purposes of Section 365(n) of Title 11 of the United States Code and other similar laws in any other jurisdiction outside of the Territory (collectively, the "Bankruptcy Laws"), licenses of rights to "intellectual property" as defined under the Bankruptcy Laws. If a case is commenced during the Term by or against a Party under Bankruptcy Laws then, unless and until this Agreement is rejected as provided pursuant to such Bankruptcy Laws, such Party (in any capacity, including debtor-in-possession) and its successors and assigns (including a Title 11 trustee) shall perform all of the obligations in this Agreement intended to be performed by such Party. If a case is commenced during the Term by or against a Party under the Bankruptcy Laws, this Agreement is rejected as provided for under the Bankruptcy Laws, and the non-bankrupt Party elects to retain its rights hereunder as provided for under the Bankruptcy Laws, then the Party subject to such case under the Bankruptcy Laws (in any capacity, including debtor-in-possession) and its successors and assigns (including a Title 11 trustee), shall provide to the non-bankrupt Party copies of all Patents and Information necessary for the non-bankrupt Party to prosecute, maintain and enjoy its rights under the terms of this Agreement. All rights, powers and remedies of the non-bankrupt Party as provided herein are in addition to and not in substitution for any and all other rights, powers and remedies now or hereafter existing at law or in equity (including the Bankruptcy Laws) in the event of the commencement of a case by or against a Party under the Bankruptcy Laws. In particular, it is the intention and understanding of the Parties to this Agreement that the rights granted to the Parties under this Section 13.5 are essential to the Parties' respective businesses and the Parties acknowledge that damages are not an adequate remedy.

13.6 **Effects of Termination**. All of the following effects of termination are in addition to the other rights and remedies that may be available to either of the Parties under this Agreement and shall not be construed to limit any such rights or remedies. Upon the termination of this Agreement (other than as a result of the expiration of the Term pursuant to Section 13.1):

(a) Notwithstanding anything contained in this Agreement to the contrary, all rights and licenses granted herein to Licensee shall terminate and Licensee shall cease any and all Development and Commercialization activities with respect to the Compound and the Products;

(b) Except as otherwise expressly set forth in this Agreement, all payment and other obligations hereunder shall terminate, other than those that are accrued and unpaid as of the effective date of such termination;

(c) Takeda shall thereafter have all rights, on a fully paid-up and royalty-free basis, previously licensed to Licensee hereunder;

(d) Subject to Section 13.6(j), upon the termination of this Agreement (other than any termination of this Agreement by Licensee pursuant to Section 13.2 or Section 13.5), Licensee hereby grants to Takeda, effective as of the effective date of such termination, an exclusive (even as to Licensee), transferable, fully paid-up, royalty-free, license with the right to sublicense through multiple tiers in the Field in the Territory, under the Subject Licensee Intellectual Property and Licensee's rights in the Joint Intellectual Property, to Exploit the Compound and the Products in the Field in the Territory; and upon termination, Licensee shall provide Takeda with a listing of all Subject Licensee Patents subject to this obligation. Notwithstanding anything express or implied in this Agreement to the contrary, for purposes of this Section 13.6(d) and Section 13.6(j), the Subject Licensee Intellectual Property shall not include any Licensee Intellectual Property that, pursuant to any license agreement between Licensee or any of its Affiliates and a Third Party that provides Licensee or any of its Affiliates with in-licenses of any intellectual property rights from such Third Party, would require any of Licensee or its Affiliates to make any payment or payments to such Third Party at any time and from time to time from and after the effective date of termination of this Agreement in connection with the Exploitation of the Compound or any Product in the Field in the Territory, unless and until Licensee and Takeda shall have entered into a written agreement agreeing that (1) such Licensee Intellectual Property shall be included in the Subject Licensee Intellectual Property and (2) Takeda shall make payment to Licensee or such Third Party of all of such payment or payments to which such Third Party is entitled from Licensee or any of its Affiliates;

(e) Licensee shall in good faith coordinate the wind-down of Licensee's efforts under this Agreement, and Licensee, as soon as reasonably practical after the effective date of such termination, shall provide to Takeda, as applicable and to the extent permitted under any applicable Third Party contract (i) any Information, including copies of all Clinical Trial data and results, and the like developed by or for the benefit of Licensee relating to the Compound or any Product and any unused Research Material, and (ii) other documents to the extent relating to the Compound or any Product that are necessary in the continued Development, Commercialization or Manufacture of the Compound or any Product (including material documents and agreements relating to the sourcing and Manufacture of a Product for sale, promotion, distribution, or use of the Compound or any Product). Licensee shall cooperate with Takeda to provide a transfer of such material Information and documents. At Takeda's request, Licensee shall assign to Takeda any and all agreements to which Licensee, or any of its Affiliates, and a Third Party are parties, and that govern the Development, Commercialization or Manufacturing activities conducted in connection with the Compound or any Product prior to such termination, or if such assignment is not permitted under the relevant agreement, (A) grant to Takeda other rights to provide to Takeda the benefit of such non-assignable agreement, at Takeda's expense, to the extent permitted under the terms of such non-assignable agreement; or (B) to the extent not permitted under the terms of such non-assignable agreement, the Parties shall discuss in good faith an alternative solution to enable

Takeda to receive, at Takeda's expense, the benefit of the terms of such non-assignable agreement. All costs and expenses incurred by Licensee in connection with Licensee's activities under this Section 13.6(e), Section 13.6(g) or Section 13.6(h) shall be borne or reimbursed by Takeda; provided, however, that notwithstanding the foregoing, (1) if Takeda terminates this Agreement pursuant to Section 13.2 or 13.4, then all costs and expenses incurred by Takeda or Licensee in connection with any activities contemplated by this Section 13.6 shall be borne or reimbursed by Licensee, and (2) if Licensee terminates this Agreement pursuant to Section 13.3, then all costs and expenses incurred by each Party in connection with any activities contemplated by this Section 13.6 shall be borne by such Party;

(f) Subject to the payment of all amounts required under Section 13.6(b) above, Licensee shall have the right to sell or otherwise dispose of any inventory of the Products on hand at the time of such termination or in the process of Manufacturing; provided, however, Licensee shall, at Takeda's election, either destroy or return to Takeda any Products that have not been sold or used within [ ]* months following such termination;

(g) Licensee shall transfer and assign to Takeda any and all Regulatory Materials directly and solely related to the Compound and the Products, including Product INDs and Product NDAs and, upon Takeda's request, shall make available to Takeda any other relevant information reasonably related to such Regulatory Materials including inspection reports developed by Licensee with respect to any Third Party who is conducting Development, Manufacturing or Commercialization activities on Licensee's behalf;

(h) Takeda shall have the right (but not the obligation) to assume all prosecution, maintenance, and enforcement activities under Article 10 with respect to Takeda Patents and Joint Patents at Takeda's sole cost and expense. Licensee shall cooperate with Takeda and provide Takeda with reasonable assistance and cooperation with the prosecution, maintenance, and enforcement activities with respect to Takeda Patents and Joint Patents;

(i) The provisions in Section 2.4(d) shall apply in the case of a termination of this Agreement pursuant to Section 13.2, Section 13.3 or Section 13.5;

(j) If (A) a license is granted to Takeda pursuant to Section 13.6(d), other than due to Takeda's termination of this Agreement pursuant to Section 13.4, and (B) Licensee has achieved Completion of a Phase 1 Clinical Trial for a Product prior to the date it delivers notice of termination to Takeda, then in addition to the other provisions of this Section 13.6:

(i) Takeda shall owe to Licensee one-time milestone payments upon the first achievement of each of the events set forth below with respect to the first Product containing the Compound to achieve such event (but only if the event had not yet been achieved prior to the effective date of such termination). Takeda shall promptly notify Licensee in writing following the achievement of each milestone event. Thereafter, Licensee shall submit to Takeda an invoice for the corresponding milestone payment set forth below. Within [ ]* days following Takeda's receipt of any such invoice, Takeda shall remit the applicable milestone payment to Licensee. Each milestone payment by Takeda pursuant to this Section 13.6(j)(i) shall be payable only once, regardless of the number of times that such milestone event is achieved for the Product. All

payment amounts listed are in U.S. Dollars. The total maximum amount payable to Licensee under this Section 13.6(j)(i) is [ ]*.

Development Milestones.

Milestone Event	**Payment Amount**
[ ]*	[ ]*
[ ]*	[ ]*
[ ]*	[ ]*
[ ]*	[ ]*

(ii) Takeda shall owe to Licensee one-time milestone payments upon the first achievement of each of the events set forth below (but only if the event had not yet been achieved prior to the effective date of such termination). Takeda shall promptly notify Licensee in writing following the achievement of each milestone event. Thereafter, Licensee shall submit to Takeda an invoice for the corresponding milestone payment set forth below. Within ninety (90) days following the Calendar Year during which the applicable milestone event was met (but only if the event had not yet been achieved prior to the effective date of such termination), Takeda shall remit the applicable milestone payment to Licensee. Each milestone payment by Takeda pursuant to this Section 13.6(j)(ii) shall be payable only once, regardless of the number of times that such milestone event is achieved. All payment amounts listed are in U.S. Dollars. The total maximum amount payable to Takeda under this Section 13.6(j)(ii) is [ ]*.

Sales Milestones.

Milestone Event	**Payment Amount**
[ ]*	[ ]*
[ ]*	[ ]*

(iii) Subject to Subsections (iv), (v) and (vi) of this Section 13.6(j), and during the applicable Royalty Term, Takeda shall pay to Licensee a running royalty on aggregate Net Sales of each Product in the Territory (calculated on a Product-by-Product basis) during each Calendar Year as further consideration for the rights granted hereunder as set forth below:

Annual Net Sales Rates

[ ]*	[ ]*
[ ]*	[ ]*

Solely for purposes of this Section 13.6(j)(iii), Section 13.6(j)(iv) and Section 13.6(j)(v), the definition of the term Royalty Term is hereby modified so that the reference in clause (a) of such

definition to the words “Takeda Patent” is hereby replaced with the words “Takeda Patent or Subject Licensee Patent”. In addition, for purposes of this Section 13.6(j), Subject Licensee Patent(s) shall not include any Licensee Patent(s) that is or are not included in Subject Licensee Intellectual Property pursuant to, and in accordance with, Section 13.6(d).

(iv) Royalties under Section 13.6(j)(iii) shall be payable on Net Sales until the expiration of the Royalty Term in each country (at which time sales in such country shall be excluded from all calculations of aggregate Net Sales hereunder) on a Product-by-Product and country-by-country basis beginning upon the First Commercial Sale of the applicable Product in such country in the Territory.

(v) The royalty rate set forth in Section 13.6(j)(iii) for Net Sales of a particular Product in a particular country (after any previous reduction(s), if any, made pursuant to the next sentence of this Section 13.6(j)(v)) shall be reduced, on a Product-by-Product and country-by-country basis by: (i) [ ]* at the end of the first to occur Calendar Quarter during which either (a) the last to expire Valid Claim in a Takeda Patent or Subject Licensee Patent Covering the composition or use of such Product in such country expires or has expired and all applicable Regulatory Exclusivity for such Product in such country expires or has expired; or (b) the Generic Competition Percentage in such country of the Territory is greater than or equal to [ ]* and less than [ ]*; and (ii) [ ]* at the end of the first to occur Calendar Quarter during which the Generic Competition Percentage in such country of the Territory is greater than or equal to [ ]*. In addition, with respect to any Product being Commercialized in the U.S. during the applicable Royalty Term, (a) following expiration of the last to expire Valid Claim in a Takeda Patent or Subject Licensee Patent published in the FDA’s Orange Book, the royalty rate for such Product set forth in Section 13.6(j)(iii) for Net Sales in the U.S. (after any previous reduction(s), if any, made pursuant to this sentence or the first sentence of this Section 13.6(j)(v)) shall be reduced by [ ]* of such royalty rate until the end of such applicable Royalty Term; and (b) following expiration of the last to expire Valid Claim in a Takeda Patent or Subject Licensee Patent in the U.S. not published in the FDA’s Orange Book, the royalty rate for such Product set forth in Section 13.6(j)(iii) for Net Sales in the U.S. (after any previous reduction(s), if any, made pursuant to this sentence or the first sentence of this Section 13.6(j)(v)) shall be reduced by [ ]* of such royalty rate until the end of such applicable Royalty Term. Notwithstanding anything contained in this Agreement to the contrary, none of the reductions to royalties provided in this Section 13.6(j)(v) shall, individually or in the aggregate, reduce the royalties payable with respect to Net Sales of any Product sold by Takeda, its Affiliates, its licensees and its and their Sublicensees in any country during the applicable Royalty Term by more than [ ]* of the royalties otherwise owed to Licensee pursuant to Section 13.6(j)(iii).

(vi) If Takeda is required to pay royalties to Licensee pursuant to Section 13.6(j)(iii), then all of the provisions of Sections 7.7 –7.12 shall also be applicable with respect to such royalties required to be paid by Takeda to Licensee pursuant to Section 13.6(j)(iii), except that any reference in Sections 7.7-7.12 to Licensee shall be deemed to be a reference to Takeda and any reference in Sections 7.7-7.12 to Takeda shall be deemed to be a reference to Licensee.

(vii) For the avoidance of doubt, if this Agreement is terminated other than by Licensee pursuant to Section 13.3 above or Licensee has not achieved Completion of a Phase 1

Clinical Trial for a Product prior to the date it delivers notice of termination to Takeda, then Takeda shall not owe any amounts set forth in this Section 13.6(j) to Licensee.

13.7 **Remedies**. Notwithstanding anything to the contrary in this Agreement, except as otherwise set forth in this Agreement, termination or expiration of this Agreement shall not relieve the Parties of any liability or obligation which accrued hereunder prior to the effective date of such termination or expiration, nor prejudice either Party's right to obtain performance of any obligation. Each Party shall be free, pursuant to Article 14, to seek, without restriction as to the number of times it may seek, damages, expenses and remedies that may be available to it under Applicable Law or in equity and shall be entitled to offset the amount of any damages and expenses obtained against the other Party in a final determination under Section 14.3, against any amounts otherwise due to such other Party under this Agreement.

13.8 **Survival**. The following provisions shall survive any expiration or termination of this Agreement for the period of time specified therein (or, if no such period is specified, indefinitely): Articles 1, 7 (but only to the extent relating to milestone events occurring on or prior to the date of expiration or termination, or only with respect to royalties owed, if any, on Products sold prior to the date of expiration or termination, or sold after such termination to the extent expressly permitted under this Agreement), 12, 13, 14, 15 and 16 and Sections 2.4(d), 2.5, 10.1, 10.2 (with respect to any disclosure obligations that arise on or prior to expiration or termination), 10.3(c) (with respect to Licensee's obligation to notify Takeda of Licensee's decision to abandon or not maintain Joint Patents), 10.3(d)(ii), 10.3(d)(iii) and 10.5(d) (to the extent any suit or action under that section is still pending upon expiration or termination).

ARTICLE 14 – DISPUTE RESOLUTION

14.1 **Exclusive Dispute Resolution Mechanism**. The Parties agree that the procedures set forth in this Article 14 shall be the exclusive mechanism for resolving any dispute, controversy, or claim between the Parties arising out of or relating to this Agreement, including the breach, termination or validity thereof, and the Parties' rights and obligations hereunder (each, a "Dispute", and collectively, the "Disputes") which are not resolved through good faith negotiation between the Parties.

14.2 **Resolution by Executive Officers**. Except as otherwise provided in this Section 14.2, in the event of any Dispute, the Parties shall first attempt in good faith to resolve such Dispute by negotiation and consultation between themselves. In the event that such Dispute is not resolved on an informal basis within [ ]* Business Days after receipt of written notice of such Dispute by a Party, either Party may, by written notice to the other Party, refer the Dispute to the Executive Officers (or their designees) for attempted resolution by good faith negotiation for a period of [ ]* days after such notice is received (the "Resolution Period"). Each Party may, in its sole discretion, seek resolution of any Dispute that is not resolved within the Resolution Period in accordance with Section 14.3; *provided, however*, that except as set forth in Sections 14.4 and 14.5, neither Party shall seek resolution of any Dispute in accordance with Section 14.3 unless such Dispute has been referred to the Executive Officers under this Section 14.2 and the Resolution Period with respect to such Dispute has expired.

14.3 **Alternative Dispute Resolution**. The Parties desire that any Dispute be resolved in an efficient, speedy, and economical manner via an alternative dispute resolution process. To achieve that end, any Dispute the Parties are unable to resolve informally, or pursuant to Section 14.2 above, shall be resolved by arbitration pursuant to the Alternative Dispute Resolution provisions set forth on Exhibit E, the result of which shall be binding upon the Parties. The Parties shall have the right to be represented by counsel in such proceeding.

14.4 **Preliminary Injunctions**. Notwithstanding anything in this Agreement to the contrary, a Party may seek a temporary restraining order and/or a preliminary injunction from any court of competent jurisdiction in order to prevent immediate and irreparable injury, loss, or damage on a provisional basis prior to the decision of the Panel on the ultimate merits of the Dispute.

14.5 **Patent and Trademark Disputes**. Notwithstanding anything in this Agreement to the contrary, any and all issues regarding the scope, construction, validity, and enforceability of any Patent or trademark relating to the Product that is the subject of this Agreement shall be determined in a court or other tribunal, as the case may be, of competent jurisdiction under the applicable patent or trademark laws of the country in which such Patent or trademark rights were granted or arose.

14.6 **Payment Tolling**. During the pendency of any Dispute resolution proceeding between the Parties under this Article 14, the obligation to make any payment under this Agreement from one Party to the other Party, which payment is the subject, in whole or in part, of a proceeding under this Article 14, shall be tolled until the final outcome of such Dispute has been established.

14.7 **Confidentiality**. Any activities conducted under this Article 14, including any proceedings and decisions under Section 14.3, shall be deemed Confidential Information of each of the Parties, and shall be subject to Article 12.

ARTICLE 15 – INDEMNIFICATION

15.1 **Indemnification by Licensee**. Subject to, and upon, the terms, conditions and limitations set forth in this Article 15, Licensee hereby agrees to defend, indemnify and hold harmless Takeda and its Affiliates, and each of their respective directors, officers, employees, agents and representatives (each, a "Takeda Indemnitee") from and against any and all claims, suits, actions, demands, liabilities, expenses and/or losses, including reasonable legal expense and attorneys' fees (collectively, the "Losses"), to which any Takeda Indemnitee may become subject as a result of any claim, demand, action or other proceeding by any Third Party (each, a "Claim") to the extent such Losses arise directly or indirectly out of: (a) the practice by Licensee or any of its Affiliates of any license granted to it under Article 2; (b) the use, handling, storage, sale or other disposition of the Existing Research Material, the [ ]*, the Compound or any Product by Licensee, any of its Affiliates or any of its Sublicensees or Subcontractors, including any use of the Existing Research Material, the [ ]*, the Compound or any Product by Licensee or any of its Affiliates, Sublicensees or Subcontractors for Development and Commercialization or other Exploitation; (c) the breach by Licensee of any warranty, representation, covenant or agreement made by Licensee in this Agreement; (d) the alleged or actual negligence, gross negligence or willful misconduct (including to the extent such negligence, gross negligence or willful misconduct gives rise to Product Liabilities under any legal theory) of Licensee, any of its Affiliates or any of its Sublicensees or

Subcontractors, or any officer, director, employee, agent or representative thereof; or (e) the [ ]* Agreement, if any, and the use, handling, storage, sale or other disposition of the Compound or any Information produced in connection with the [ ]* Agreement, by Licensee, any of its Affiliates or any of its Sublicensees or Subcontractors, including any use of the Compound or any such Information by Licensee or any of its Affiliates, Sublicensees or Subcontractors for Development and Commercialization or other Exploitation; except, with respect to each of subsections (a) through (e) above, to the extent such Losses arise directly or indirectly from (i) the negligence, gross negligence or willful misconduct of any Takeda Indemnitee or (ii) the breach by Takeda of any warranty, representation, covenant or agreement made by Takeda in this Agreement.

15.2 **Indemnification by Takeda**. Subject to, and upon, the terms, conditions and limitations set forth in this Article 15, Takeda hereby agrees to defend, indemnify and hold harmless Licensee and its Affiliates and each of their respective directors, officers, employees, agents and representatives (each, a "Licensee Indemnitee") from and against any and all Losses to which any Licensee Indemnitee may become subject as a result of any Claim to the extent such Losses arise directly or indirectly out of: (a) the practice by Takeda or any of its Affiliates or Sublicensees of any rights licensed to Takeda under Section 13.6(d) or Article 2 (except for any Losses arising directly or indirectly out of or otherwise relating to the Existing Research Material, the [ ]*, the Compound produced in connection with the [ ]* Agreement or any Information produced in connection with the [ ]* Agreement, unless and to the extent that Takeda is required to indemnify for any of such Losses due to a breach of covenant under clause (c) below); (b) the use, handling, storage, sale or other disposition of the Compound or any Product by Takeda or any of its Affiliates, Third Party licensees, Sublicensees or Subcontractors, including any use of the Compound or any Product by Takeda or any of its Affiliates, Third Party licensees, Sublicensees or Subcontractors for Development and Commercialization or other Exploitation after the Term under Section 13.6(d); (c) the breach by Takeda of any warranty, representation, covenant or agreement made by Takeda in this Agreement; or (d) the alleged or actual negligence, gross negligence or willful misconduct (including to the extent such negligence, gross negligence or willful misconduct gives rise to Product Liabilities under any legal theory) of Takeda or any of its Affiliates, Takeda's licensees (other than Licensee or any of its Affiliates, or any of its or their Sublicensees or Subcontractors), Takeda's Sublicensees or Takeda's Subcontractors, or any officer, director, employee, agent or representative thereof; except, with respect to each of subsections (a) through (d) above, to the extent such Losses arise directly or indirectly from (i) the negligence, gross negligence or willful misconduct of any Licensee Indemnitee, or (ii) the breach by Licensee of any warranty, representation, covenant or agreement made by Licensee in this Agreement.

15.3 **Indemnification Procedures**.

(a) **Notice**. Promptly after a Takeda Indemnitee or a Licensee Indemnitee (each, an "Indemnitee") receives notice of a pending or threatened Claim, such Indemnitee shall give written notice of the Claim to the Party from whom the Indemnitee is entitled to receive indemnification pursuant to Section 15.1 or 15.2, as applicable (the "Indemnifying Party"). However, an Indemnitee's delay in providing or failure to provide such notice shall not relieve the Indemnifying Party of its indemnification obligations, except to the extent it can demonstrate prejudice due to the delay or lack of notice.

(b) **Defense**. Upon receipt of notice under Section 15.3(a) from the Indemnitee, the Indemnifying Party shall have the duty to either compromise or defend, at its own expense and by legal counsel (reasonably satisfactory to Indemnitee), such Claim. The Indemnifying Party shall promptly (and in any event not more than twenty (20) days after receipt of the Indemnitee's original notice) notify the Indemnitee in writing that it acknowledges its obligation to indemnify the Indemnitee with respect to the Claim pursuant to this Article 15 and of its intention either to compromise or defend such Claim. Once the Indemnifying Party gives such notice to the Indemnitee, the Indemnifying Party is not liable to the Indemnitee for the fees of other legal counsel or any other expenses subsequently incurred by the Indemnitee in connection with such defense, other than the Indemnitee's reasonable expenses of investigation and cooperation. However, the Indemnitee shall have the right to employ separate legal counsel and to control the defense of a Claim at its own expense.

(c) **Cooperation**. The Indemnitee shall cooperate fully with the Indemnifying Party and its legal representatives in the investigation and defense of any Claim. The Indemnifying Party shall keep the Indemnitee informed on a reasonable and timely basis as to the status of such Claim (to the extent the Indemnitee is not participating in the defense of such Claim) and conduct the defense of such Claim in a prudent manner.

(d) **Settlement**. If an Indemnifying Party assumes the defense of a Claim, no compromise or settlement of such Claim may be effected by the Indemnifying Party without the Indemnitee's written consent (which consent shall not be unreasonably withheld, conditioned or delayed), unless: (i) there is no finding or admission of any violation of law or any violation of the rights of any person and no effect on any other claims that may be made against the Indemnitee; (ii) the sole relief provided is monetary damages that are paid in full by the Indemnifying Party; and (iii) the Indemnitee's rights under this Agreement are not adversely affected. If the Indemnifying Party fails to assume defense of a Claim within a reasonable time, the Indemnitee may settle such Claim on such terms as it deems appropriate with the consent of the Indemnifying Party (which consent shall not be unreasonably withheld, conditioned or delayed), and the Indemnifying Party shall be obligated to indemnify the Indemnitee for such settlement as provided in this Article 15.

15.4 **Insurance**. Each Party shall, at its own expense, procure and maintain during the Term and for a period of [ ]* thereafter (or, if later, [ ]* after such Party is not practicing or using the intellectual property of the other Party pursuant to this Agreement), insurance policy/policies, including product liability insurance, adequate to cover its obligations hereunder and which are consistent with normal business practices of prudent companies similarly situated. Such insurance shall not be construed to create a limit of a Party's liability with respect to its indemnification obligations under this Article 15. Each Party shall provide the other Party with prompt written notice of cancellation, non-renewal or material change in such insurance that could materially adversely affect the rights of such other Party hereunder, and shall provide such notice within thirty (30) days after any such cancellation, non-renewal or material change. The Parties acknowledge and agree that Takeda may meet its obligations under this Section 15.4 through self-insurance.

15.5 **Limitation of Liability**. NEITHER PARTY WILL BE LIABLE FOR SPECIAL, INCIDENTAL, INDIRECT, CONSEQUENTIAL OR PUNITIVE DAMAGES ARISING OUT OF THIS AGREEMENT, OR THE EXERCISE OF ITS RIGHTS OR THE PERFORMANCE OF

ITS OBLIGATIONS HEREUNDER, INCLUDING LOST PROFITS ARISING FROM OR RELATING TO ANY BREACH OF THIS AGREEMENT, REGARDLESS OF ANY NOTICE OF SUCH DAMAGES, EXCEPT AS A RESULT OF A (A) PARTY'S GROSS NEGLIGENCE OR WILLFUL MISCONDUCT, OR (B) BREACH OF ARTICLE 12 (CONFIDENTIALITY). NOTHING IN THIS SECTION 15.5 (LIMITATION OF LIABILITY) IS INTENDED TO LIMIT OR RESTRICT THE INDEMNIFICATION RIGHTS OR OBLIGATIONS OF EITHER PARTY UNDER THIS AGREEMENT.

ARTICLE 16– MISCELLANEOUS

16.1 **Notice**. Any notice, request, or other communication permitted or required under this Agreement shall be in writing, shall refer specifically to this Agreement and shall be hand delivered or sent by a recognized overnight delivery service, expenses prepaid, or by facsimile (with transmission confirmed), to the following addresses or to such other addresses as a Party may designate by written notice in accordance with this Section 16.1:

If to Takeda:

Takeda Pharmaceutical Company Limited
1-1, Doshomachi 4-chome
Chuo-ku, Osaka 540-8645
Attention: [ ]*
Facsimile: [ ]*

with copies (which shall not constitute notice) to:

Takeda Pharmaceuticals U.S.A., Inc.
One Takeda Parkway
Deerfield, IL 60015
Attention: [ ]*
Facsimile: [ ]*

Polsinelli PC
150 N. Riverside Plaza, Suite 3000
Chicago, IL 60606
Attention: James R. Asmussen
Facsimile: (312) 873-2997

If to Licensee:

Rhythm Pharmaceuticals, Inc.
500 Boylston Street
11th Floor
Boston, MA 02116
Attention: Keith Gottesdiener, CEO
Facsimile: (857) 264-4299

with a copy (which shall not constitute notice) to:

Morgan Lewis
One Federal St.
Boston, MA 02110-1726
Attention: Julio E. Vega
Facsimile: (617) 345-5016

16.2 **Designation of Affiliates**. Each Party may discharge any obligations and exercise any rights hereunder through delegation of its obligations or rights to any of its Affiliates. Each Party hereby guarantees the performance by its Affiliates of such Party's obligations under this Agreement, and shall cause its Affiliates to comply with the provisions of this Agreement in connection with such performance. Any breach by a Party's Affiliate of any of such Party's obligations under this Agreement shall be deemed a breach by such Party, and the other Party may proceed directly against such Party without any obligation to first proceed against such Party's Affiliate.

16.3 **Force Majeure**. Both Parties shall be excused from the performance of their obligations under this Agreement to the extent that such performance is prevented by Force Majeure and the nonperforming Party promptly provides notice of the prevention to the other Party. Such excuse shall be continued so long as the condition constituting Force Majeure continues and the nonperforming Party takes reasonable efforts to remove the condition. Notwithstanding the foregoing, a Party shall not be excused from making payments owed hereunder because of a Force Majeure affecting such Party. If a Force Majeure persists for more than ninety (90) days, then the Parties shall discuss in good faith the modification of the Parties' obligations under this Agreement in order to mitigate the delays caused by such Force Majeure.

16.4 **Assignment**. Neither Party may assign or transfer this Agreement or any rights or obligations hereunder without the prior written consent of the other, except that a Party may assign this Agreement without the other Party's consent to any Affiliate or to a successor to all or substantially all of the business of such Party to which this Agreement relates, whether in a merger, sale of stock or units, sale of assets or other transaction. Any other assignment or transfer shall require the prior written consent of the other Party. Any successor or assignee of rights and/or obligations permitted hereunder shall, in writing to the other Party, expressly assume performance of such rights and/or obligations. Any permitted assignment shall be binding on the successors of the assigning Party. Any assignment or attempted assignment by either Party in violation of the terms of this Section 16.4 shall be null, void and of no legal effect. Any permitted assignment by either Party in accordance with the terms of this Section 16.4 shall not operate to release or relieve such Party of its liabilities or obligations under this Agreement unless otherwise agreed by the other Party in writing.

16.5 **Severability**. If any one or more of the provisions of this Agreement is held to be invalid or unenforceable by any court of competent jurisdiction from which no appeal can be or is taken, the provision shall be considered severed from this Agreement and shall not serve to invalidate any remaining provisions hereof. The Parties shall make a good faith effort to replace any invalid

or unenforceable provision with a valid and enforceable one such that the objectives contemplated by the Parties when entering this Agreement may be realized.

16.6 **Waiver and Non-Exclusion of Remedies**. Any term or condition of this Agreement may be waived at any time by the Party that is entitled to the benefit thereof, but no such waiver shall be effective unless set forth in a written instrument duly executed by or on behalf of the Party waiving such term or condition. The waiver by either Party hereto of any right hereunder or of the failure to perform or of a breach by the other Party shall not be deemed a waiver of any other right hereunder or of any other breach or failure by such other Party whether of a similar nature or otherwise. The rights and remedies provided herein are cumulative and do not exclude any other right or remedy provided by Applicable Law or otherwise available except as expressly set forth herein.

16.7 **Further Assurance**. Each Party shall duly execute and deliver, or cause to be duly executed and delivered, such further instruments and do and cause to be done such further acts and things, including the filing of such assignments, agreements, documents, and instruments, as may be necessary or as the other Party may reasonably request in connection with this Agreement or to carry out more effectively the provisions and purposes hereof.

16.8 **Relationship of the Parties**. It is expressly agreed that Takeda, on the one hand, and Licensee, on the other hand, shall be independent contractors and that the relationship between the two Parties shall not constitute a partnership, joint venture or agency, including for Tax purposes. Neither Takeda nor Licensee shall have the authority to make any statements, representations or commitments of any kind, or to take any action that shall be binding on the other, without the prior written consent of the other Party to do so. All persons employed by a Party shall be employees of that Party and not of the other Party and all expenses and obligations incurred by reason of such employment shall be for the account and expense of such Party.

16.9 **Counterparts**. This Agreement may be executed in two (2) or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument. This Agreement may be executed by facsimile, .pdf or other electronically transmitted signatures and such signatures shall be deemed to bind each Party hereto as if they were the original signatures.

16.10 **Construction**. Except where the context otherwise requires, wherever used, the singular shall include the plural, the plural the singular, and the use of any gender shall be applicable to all genders. Whenever this Agreement refers to a number of days, such number refers to calendar days. The captions of this Agreement are for the convenience of reference only and in no way define, describe, extend, or limit the scope or intent of this Agreement or the intent of any provision contained in this Agreement. The terms “including,” “include,” or “includes” as used herein shall mean “including, but not limited to,” and shall not limit the generality of any description preceding such term. The language of this Agreement shall be deemed to be the language mutually chosen by the Parties and no rule of strict construction shall be applied against either Party hereto. Each Party represents that it has been represented by legal counsel in connection with this Agreement and acknowledges that it has participated in the drafting hereof. In interpreting and applying the terms and provisions of this Agreement, the Parties agree that no presumption will apply against the Party which drafted such terms and provision.

16.11 **Governing Law**. This Agreement was prepared in the English language, which language shall govern the interpretation of, and any Dispute regarding, the terms of this Agreement. This Agreement and all Disputes arising out of or related to this Agreement or any breach hereof shall be governed by and construed under the laws of the State of New York, without giving effect to any choice of law principles that would require the application of the laws of a different state.

16.12 **Entire Agreement**. This Agreement, including the Exhibits hereto, sets forth the complete, final and exclusive agreement and all the covenants, promises, agreements, warranties, representations, conditions and understandings between the Parties hereto with respect to the subject matter hereof and supersedes, as of the Effective Date, all prior agreements and understandings between the Parties with respect to the subject matter hereof. There are no covenants, promises, agreements, warranties, representations, conditions or understandings, either oral or written, between the Parties other than as are set forth herein and therein. No subsequent alteration, amendment, change or addition to this Agreement shall be binding upon the Parties unless reduced to writing and signed by an authorized officer of each Party. In the event of any inconsistency between the body of this Agreement and the Exhibits to this Agreement or any subsequent agreements ancillary to this Agreement, unless otherwise expressly stated to the contrary in such Exhibit or subsequent ancillary agreement, the terms contained in this Agreement shall control.

16.13 **Headings**. The headings of each Article and Section in this Agreement have been inserted for convenience of reference only and are not intended to limit or expand on the meaning of the language contained in the particular Article or Section.

SIGNATURE PAGE FOLLOWS

IN WITNESS WHEREOF, the Parties have signed this Agreement as of the Effective Date.

TAKEDA PHARMACEUTICAL COMPANY LIMITED

By: /S/ Misako Hirose

Name: Misako Hirose

Title: Director, Global Alliances

Date: March 23, 2018

RHYTHM PHARMACEUTICALS, INC.

By: /S/ Keith M. Gottesdiener

Name: Keith M. Gottesdiener

Title: Chief Executive Officer

Date: March 30, 2018

EXHIBIT A

Initial Development Plan

See attached.

[ ]*

* CONFIDENTIAL TREATMENT REQUESTED.

EXHIBIT B

Takeda Patents

[ ]*

CONFIDENTIAL

* CONFIDENTIAL TREATMENT REQUESTED.

EXHIBIT C

Research Material

[ ]*

CONFIDENTIAL

* CONFIDENTIAL TREATMENT REQUESTED.

EXHIBIT D

Form of Stock Issuance Agreement

See attached.

CONFIDENTIAL

* CONFIDENTIAL TREATMENT REQUESTED.

STOCK ISSUANCE AGREEMENT

This STOCK ISSUANCE AGREEMENT (this "Agreement") is made as of this 30th day of March, 2018 (the "Effective Date"), by and between Rhythm Pharmaceuticals, Inc., a Delaware corporation, having its principal place of business at 500 Boylston Street, 11th floor, Boston, Massachusetts 02116 USA (the "Company"), and Takeda Pharmaceutical Company Limited, a corporation organized under the laws of Japan, having its principal place of business at 1-1 Doshomachi 4-chome, Chuo-ku, Osaka, Japan ("Takeda").

RECITALS

WHEREAS, in connection with the execution of that certain License Agreement as of the Effective Date by and between the Company and Takeda (the "License Agreement"), and as partial consideration for the licenses and other rights granted to the Company by Takeda pursuant to the License Agreement, the Company desires to issue to Takeda and Takeda desires to receive from the Company, pursuant to the terms set forth herein, shares of the Company's common stock, $0.001 par value per share (the "Common Stock").

NOW, THEREFORE, in consideration of the foregoing premises and the mutual covenants hereinafter set forth, and for other good and valuable consideration, the receipt, adequacy, and sufficiency of which are hereby acknowledged, the parties hereto agree as follows:

I. ISSUANCE OF STOCK.

a. Issuance. Subject to and upon the terms of this Agreement, the Company hereby agrees to issue to Takeda 223,544 shares of Common Stock (the "Shares"), as partial consideration for the licenses and other rights granted to the Company by Takeda pursuant to the License Agreement, the receipt and sufficiency of which the Company hereby acknowledges. The number of Shares was calculated by dividing Five Million Dollars ($5,000,000) by the arithmetical average closing price for a share of Common Stock as reported by the NASDAQ stock exchange for the [ ]* prior to the date hereof. The Company shall issue or cause to be issued the Shares to Takeda on the second (2nd) trading day after the date hereof.

b. Delivery of Evidence of Issuance. The Company shall cause ComputerShare, the Company's transfer agent, to deliver to Takeda on the second (2nd) trading day after the day hereof evidence of the book entry reflecting the issuance of the Shares to Takeda pursuant to this Agreement.

c. Lockup Agreement. Simultaneously with the execution and delivery of this Agreement, Takeda is executing and delivering the form of lockup agreement that was executed and delivered by officers, directors and certain stockholders of the Company in connection with the Company's initial public offering.

II. REPRESENTATIONS AND WARRANTIES OF TAKEDA. Takeda hereby represents and warrants to the Company as follows:

a. Formation; Authorization.

1. Takeda has been duly formed as a corporation and is validly existing in good standing under the laws of Japan. Takeda has the requisite power and authority to enter into and perform its obligations under this Agreement.

2. The execution and delivery of this Agreement and the consummation of the transactions contemplated hereby have been duly and validly authorized by all requisite action on the part of Takeda. This Agreement has been duly and validly executed and delivered by Takeda, and constitutes a legal, valid and binding obligation of Takeda, enforceable against Takeda in accordance with its terms, subject to applicable bankruptcy, insolvency, fraudulent conveyance, reorganization, moratorium and similar laws affecting creditors' rights generally and subject, as to enforceability, to general principles of equity.

3. Neither the execution and delivery by Takeda of this Agreement nor the issuance of the Shares will breach, conflict with, or result in the violation of or default under (i) any instrument, judgment, order, writ, decree, or contract to which Takeda is party or by which it is bound, or (ii) any provision of Takeda's certificate of incorporation or bylaws (or relevant Japanese equivalent), both as in existence as of the date hereof.

b. Accredited Investor. Takeda is an "accredited investor" as that term is defined in Rule 501 of Regulation D promulgated under the Securities Act of 1933, as amended (the "Securities Act"). Takeda (i) has such knowledge and experience in financial and business matters as to be capable of evaluating the merits and risks of an investment in the Shares; (ii) has the ability to bear the economic risk associated with such investment; and (iii) can bear the total loss of such investment therein. Takeda acknowledges that the Company has made available to Takeda the opportunity to ask questions of, and to receive answers from the Company's management, and has had access to all of the information Takeda considers necessary or appropriate to evaluate the risks and merits of an investment in the Shares.

c. Acquisition for Investment. The Shares are being acquired for Takeda's own account, only for investment purposes and not with a view to, or for resale in connection with, any public distribution or public offering thereof within the meaning of the Securities Act.

d. No General Solicitation. Takeda acknowledges that the Shares will not be acquired as a result of or subsequent to any general or public solicitation, including (i) any advertisement, article, notice or other communication published in any newspaper, magazine, or similar media, or broadcast over television or radio, or (ii) any seminar or meeting to which Takeda or its affiliates were invited by any of the forgoing means of communication.

e. Restricted Securities.

1. Takeda understands that the Shares will not be registered under the Securities Act or any state securities laws, by reason of a specific exemption from the registration provisions thereof which depends upon, among other things, the bona fide nature of the investment intent and the accuracy of Takeda's representations as expressed herein. Takeda understands that the Shares will be "restricted securities" under applicable United States federal and state securities laws and that, pursuant to these laws, Takeda must hold indefinitely the Shares, unless sold pursuant to a registration statement that has been declared effective under the

Securities Act or in compliance with Rule 144 promulgated thereunder, and subject to compliance with applicable state and foreign securities laws, in each case to the extent applicable. As a result, Takeda acknowledges that the Shares will be subject to the following legend or a similar legend reflecting the restrictions on the transfer of the Shares:

> THESE UNCERTIFICATED SHARES HAVE NOT BEEN REGISTERED UNDER THE SECURITIES ACT OF 1933, AND HAVE BEEN ACQUIRED FOR INVESTMENT AND NOT WITH A VIEW TO, OR IN CONNECTION WITH, THE SALE OR DISTRIBUTION THEREOF. NO SUCH TRANSFER MAY BE EFFECTED WITHOUT AN EFFECTIVE REGISTRATION STATEMENT RELATED THERETO OR AN OPINION OF COUNSEL IN A FORM SATISFACTORY TO THE COMPANY THAT SUCH REGISTRATION IS NOT REQUIRED UNDER THE SECURITIES ACT OF 1933.
>
> THESE UNCERTIFICATED SHARES ARE SUBJECT TO A LOCK-UP AGREEMENT THAT RESTRICTS THE TRANSFER OF THESE SHARES BEFORE APRIL 2, 2018. COPIES OF SUCH AGREEMENT MAY BE OBTAINED UPON WRITTEN REQUEST OF THE COMPANY.

2. Takeda understands that no U.S. federal or state agency or any governmental authority has passed upon or made any recommendation or endorsement of any of the Shares.

III. REPRESENTATIONS AND WARRANTIES OF THE COMPANY. The Company hereby represents and warrants to Takeda as follows:

a. Formation; Authorization; No Conflicts.

1. The Company has been duly formed and is validly existing in good standing under the laws of the state of Delaware. The Company has the requisite power and authority to enter into and perform its obligations under this Agreement.

2. The execution and delivery of this Agreement and the consummation of the transactions contemplated hereby have been duly and validly authorized by all requisite action on the part of the Company. This Agreement has been duly and validly executed and delivered by the Company, and constitutes a legal, valid and binding obligation of the Company, enforceable against the Company in accordance with its terms, subject to applicable bankruptcy, insolvency, fraudulent conveyance, reorganization, moratorium and similar laws affecting creditors' rights generally and subject, as to enforceability, to general principles of equity.

3. Neither the execution and delivery by the Company of this Agreement nor the issuance of the Shares will breach, conflict with, or result in the violation of or default under (i) any instrument, judgment, order, writ, decree, or contract to which the Company is party or by which it is bound, or (ii) any provision of the Company's certificate of incorporation or bylaws, both as in existence as of the date hereof.

4. As of the date hereof, the Company (i) has filed with the Securities and Exchange Commission (the "Commission") in a timely manner all reports and other documents required of the Company under the Securities Act and the Securities Exchange Act of 1934, as amended (the "Exchange Act"), since the time the Company became subject to such reporting requirements. Each such filing, as of the date thereof, complied as to form in all material respects with all applicable requirements of the Securities Act and the Exchange Act, as the case may be, and the rules and regulations of the Commission thereunder that are applicable to the Company, and no such filing, as of the date thereof, contained any untrue statement of material fact or omitted to state a material fact required to be stated therein or necessary in order to make the statements therein, in light of the circumstances under which they were made, not misleading; and (ii) has satisfied the current public information requirements contained in Rule 144(c)(1) under the Securities Act.

b. Valid Issuance. The Shares, when issued to Takeda in accordance with the terms and conditions of this Agreement, will be duly authorized and validly issued, fully paid and nonassessable, and will be free and clear from all liens and restrictions on transfer other than restrictions on transfer under applicable state and federal securities laws. Assuming the accuracy of the representations of Takeda set forth in this Agreement, the Shares will be issued in compliance with all applicable federal and state securities laws.

IV. RULE 144 COMPLIANCE. With a view to making available to Takeda the benefits of Rule 144 under the Securities Act and any other rule or regulation of the Commission that may at any time permit Takeda to sell the Shares to the public without registration, the Company shall:

a. make and keep public information available, as those terms are understood and defined in Rule 144 under the Securities Act, at all times after the date hereof, and otherwise satisfy the current public information requirements contained in Rule 144(c)(1) under the Securities Act;

b. use commercially reasonable efforts to file with the Commission in a timely manner all reports and other documents required of the Company under the Securities Act and the Exchange Act;

c. furnish to Takeda, so long as Takeda holds all or a portion of the Shares, promptly upon request, a written statement by the Company as to its compliance with the reporting requirements of Rule 144 under the Securities Act and of the Securities Act and the Exchange Act, a copy of the most recent annual or quarterly report of the Company, and such other reports and documents so filed or furnished by the Company as Takeda may reasonably request in connection with the sale of Shares without registration; and

d. upon written request of Takeda, cooperate with Takeda to transfer the Shares pursuant to Rule 144 and use best efforts to promptly remove any restrictive legends from the Shares, so long as the Shares are not otherwise restricted.

V. GENERAL PROVISIONS.

a. Survival. The warranties, representations, and covenants of the Company and Takeda contained in or made pursuant to this Agreement shall survive the execution and delivery of this Agreement.

b. Successors and Assigns. Except as otherwise expressly provided herein, all covenants and agreements contained in this Agreement by or on behalf of any of the parties hereto shall bind and inure to the benefit of the respective successors or permitted assigns of the parties hereto, whether or not so expressed. Notwithstanding the forgoing or anything to the contrary herein, neither party may assign this Agreement or its obligations hereunder without the prior written consent of the other party.

c. Notices. Any notice, demand, request or other communication hereunder to any party shall be deemed to be sufficient if contained in a written instrument delivered in person or duly sent by first class registered, certified or overnight mail, postage prepaid, or telecopier with a confirmation copy by regular, certified or overnight mail, postage prepaid, to such party at the address or telecopier number, as the case may be, set forth below or such other address or telecopier number, as the case may be, as may hereafter be designated in writing by the addressee to the addressor:

If to the Company:

Rhythm Pharmaceuticals, Inc.
500 Boylston Street, 11th floor
Boston, MA 02116 USA
Attention: CEO
Fax:
Email: kgottesdiener@rhythmtx.com

with a copy (which shall not constitute notice) to:

Morgan Lewis
One Federal St.
Boston, MA 02110-1726
Attention: Julio E. Vega
Fax: (617) 345-5016
Email: Julio.vega@morganlewis.com

If to Takeda:

Takeda Pharmaceutical Company Limited
1-1, Doshomachi 4-chome
Chuo-ka, Osaka 540-8645
Attention: [ ]*
Fax: [ ]*

with copies (which shall not constitute notice) to:

Takeda Pharmaceuticals U.S.A., Inc.
One Takeda Parkway
Deerfield, IL 60015
Attention: [ ]*
Fax: [ ]*

Polsinelli PC
150 N. Riverside Plaza, Suite 3000
Chicago, IL 60606
Attention: James R. Asmussen
Fax: (312) 873-2997
Email: jasmussen@polsinelli.com

d. Amendments and Waivers. No amendment of any provision of this Agreement shall be valid unless the same shall be in writing and signed by the Company and Takeda. No waiver by any party of any default, misrepresentation, or breach of warranty or covenant hereunder, whether intentional or not, shall be deemed to extend to any prior or subsequent default, misrepresentation, or breach of warranty or covenant hereunder or affect in any way any rights arising by virtue of any prior or subsequent such occurrence.

e. Counterparts; Facsimile. This Agreement may be executed in any number of counterparts, each of which when so executed shall be deemed to be an original and all of which taken together shall constitute one and the same instrument. This Agreement or any counterpart may be executed and delivered via facsimile, electronic mail (including pdf or any electronic signature complying with the U.S. federal ESIGN Act of 2000, *e.g.*, www.docusign.com) or other transmission method and any counterpart so delivered shall be deemed to have been duly and validly delivered and be valid and effective for all purposes.

f. Governing Law; Consent to Jurisdiction; Waiver of Jury Trial. This Agreement shall for all purposes be deemed to be made under and shall be construed in accordance with the laws of the State of New York. The parties hereby agree that any action, proceeding or claim arising out of or relating in any way to this Agreement shall be brought and enforced in the courts of the State of New York or the United States District Court for the Southern District of New York, and irrevocably submit to such jurisdiction, which jurisdiction shall be exclusive. The parties hereby waive any objection to such exclusive jurisdiction and agree not to plead or claim that such courts represent an inconvenient forum. EACH PARTY HEREBY WAIVES ANY RIGHT TO A JURY TRIAL.

g. Third Party Beneficiaries. This Agreement is intended for the benefit of the parties hereto and their respective permitted successors and assigns, and is not for the benefit of, nor may any provision hereof be enforced by, any other person.

h. Severability. In case any provision of this Agreement shall be found by a court of law to be invalid, illegal, or unenforceable, the validity, legality, and enforceability of the remaining provisions of this Agreement shall not in any way be affected or impaired thereby.

i. Headings. The section headings contained in this Agreement are for reference purposes only and shall not affect in any way the meaning or interpretation of this Agreement.

j. Entire Agreement. This agreement and the other documents delivered pursuant hereto constitute the full and entire understanding and agreement between the parties with regard to the subject matter hereof and thereof and they supersede, merge, and render void every other prior written and/or oral understanding or agreement among or between the parties hereto.

[*Signature Page Follows*]

IN WITNESS WHEREOF, the parties hereto have executed this Agreement as of the Effective Date.

RHYTHM PHARMACEUTICALS, INC.

By: _____
Name: Keith M. Gottesdiener
Title: Chief Executive Officer

TAKEDA PHARMACEUTICAL COMPANY LIMITED
By: _____
Name:
Title:

EXHIBIT E

Alternative Dispute Resolution ("ADR") Proceedings

All references to "days" in this Schedule are to calendar days.

1. To begin an ADR proceeding, a Party shall provide a detailed written notice to the other Party of the issues to be resolved by ADR and a demand for the relief requested (the "ADR Notice"). Within [ ]* days after its receipt of the ADR Notice, the other Party shall provide a written response to the Party initiating the ADR which shall add any additional issues to be resolved within the same ADR along with its requested relief.

2. The ADR proceeding shall be administered by the International Institute for Conflict Prevention and Resolution (the "CPR") in accordance with the International Institute for Conflict Prevention and Resolution Rules for Administered Arbitration (the "CPR Rules") in effect on the date of the ADR Notice and in accordance with the terms of this Agreement.

2.1 The ADR proceeding shall be presided over by a panel of [ ]* arbitrators (the "Panel"). Within [ ]* days following receipt of the original ADR notice, each Party shall designate a party arbitrator (each, a "Party Arbitrator"). Within fourteen (14) days thereafter, the Party Arbitrators shall confer and select a qualified neutral arbitrator ("Neutral Arbitrator") who has significant knowledge and experience in the subject matter at issue in the Dispute who will preside over the Panel. If the Party Arbitrators are unable to agree on a mutually acceptable Neutral Arbitrator within such period, either Party may request that the President of the CPR select the Neutral Arbitrator pursuant to the following procedures:

2.2 The CPR shall submit to the Party Arbitrators a list of not less than [ ]* qualified candidates within [ ]* days after receipt of the request, or as soon thereafter as possible, along with a curriculum vitae for each candidate. No candidate shall be an employee, consultant, advisor, contractor, officer, director or shareholder of either Party or any of its Affiliates, or an employee, consultant, advisor, contractor, officer, director or shareholder of any Third Party who has been engaged by either Party to provide services to such Party during the [ ]* year period prior to the date of initiation of the ADR proceeding.

2.3 Such list shall include a statement of disclosure by each candidate of any circumstances likely to affect his or her impartiality.

2.4 Each Party Arbitrator shall number the candidates in order of preference (with the number one signifying the greatest preference) and shall deliver the list to the CPR within [ ]* days following receipt of the list of candidates. If a Party Arbitrator believes a conflict of interest exists regarding any of the candidates, that Party Arbitrator shall provide a written explanation of the conflict to the CPR along with its list showing its

order of preference for the candidates. Any Party Arbitrator failing to return a list of preferences on time shall be deemed to have no order of preference. The CPR shall then select the available candidate who is most highly preferable to both Parties.

2.5 If all candidates submitted by the CPR are found to have conflicts, then within [ ]* days, the CPR shall submit an additional list of six candidates to the Party Arbitrators and the process set forth beginning in Section 2.1 of this Exhibit E shall be repeated until a Neutral Arbitrator is selected.

3. No earlier than [ ]* days or later than [ ]* days after selection, the Panel shall hold a hearing to resolve each of the issues identified by the Parties. The ADR proceeding shall take place at a location agreed upon by the Parties. If the Parties cannot agree, the Panel shall designate a location other than the principal place of business of either Party. Commencing on the date at least [ ]* days after receipt of the initial ADR Notice described in Section 1 of this Exhibit E, the Parties shall be entitled to engage in reasonable discovery under procedures of the Federal Rules of Civil Procedure and in proportion to the amount in controversy; provided, however, that a Party may not take more than [ ]* depositions which shall be limited to five (5) hours of testimony each. There shall not be any, and the Panel shall not permit any, discovery within [ ]* days of the hearing. The Panel shall decide any disputes between the Parties related to discovery, including ruling on the scope of discovery that will be permitted and reasonable requests to expedite discovery, taking into account the applicable period of time for discovery.

4. At least [ ]* days prior to the hearing, each Party shall submit the following to the other Party and the Panel:

4.1 A copy of all exhibits on which such Party intends to rely in any oral or written presentation to the Panel;

4.2 A list of any witnesses such Party intends to call at the hearing, and a short summary of the anticipated testimony of each witness;

4.3 A proposed ruling on each issue to be resolved, together with a request for a specific damage award or other remedy for each issue. The proposed rulings and remedies shall not contain any recitation of the facts or any legal arguments and shall not exceed one (1) page per issue.

4.4 A brief in support of such Party's proposed rulings and remedies; provided, that, the brief shall not exceed [ ]* pages. This page limitation shall apply regardless of the number of issues raised in the ADR proceeding.

5. The hearing shall be conducted on [ ]* consecutive days and shall be governed by the following rules:

5.1 Each Party shall be entitled to [ ]* hours of hearing time to present its case. The Panel shall determine whether each Party has had the [ ]* hours to which it is entitled.

5.2 Each Party shall be entitled, but not required, to make an opening statement, to present regular and rebuttal testimony, documents or other evidence, to cross-examine witnesses, and to make a closing argument. Cross-examination of witnesses shall occur immediately after their direct testimony, and cross-examination time shall be charged against the Party conducting the cross-examination.

5.3 The Party initiating the ADR shall begin the hearing and, if it chooses to make an opening statement, shall address not only issues it raised but also any issues raised by the responding Party. The responding Party, if it chooses to make an opening statement, also shall address all issues raised in the ADR. Thereafter, the presentation of regular and rebuttal testimony and documents, other evidence, and closing arguments shall proceed in the same sequence.

5.4 Prior to testifying, witnesses shall be excluded from the hearing.

5.5 Settlement negotiations, including any statements made therein, shall not be admissible under any circumstances. Affidavits prepared for purposes of the ADR hearing also shall not be admissible. As to all other matters, the Panel shall have sole discretion regarding the admissibility of any evidence.

6. Within [ ]* days following completion of the hearing, each Party may submit to the other Party and the Panel a post-hearing brief in support of its proposed rulings and remedies; provided that such brief shall not contain or discuss any new evidence and shall not exceed [ ]* pages. This page limitation shall apply regardless of the number of issues raised in the ADR proceeding.

7. The Panel shall rule on each disputed issue in writing within [ ]* days following completion of the hearing, or such longer time as justice may require although the Panel shall endeavor to providing a ruling as promptly as possible. Such ruling shall adopt in its entirety the proposed ruling and remedy of one of the Parties on each disputed issue but may adopt one Party's proposed rulings and remedies on some issues and the other Party's proposed rulings and remedies on other issues. The Panel may issue a written ruling but shall not issue any written opinion or otherwise explain the basis of the ruling in writing.

8. The Panel shall be paid a reasonable fee plus expenses. These fees and expenses, along with the fees and expenses of a court reporter, and any expenses for a hearing room, shall be paid as follows:

8.1 If the Panel rules in favor of one Party on all disputed issues in the ADR, the losing Party shall pay one hundred percent (100%) of such reasonable fees and expenses.

8.2 [ ]*.

9. The ADR process, or arbitration, shall be governed by the Federal Arbitration Act, 9 U.S.C. §§ 1 et seq. The Panel's decision will be final and binding upon the Parties, and judgment upon the award rendered by the Panel may be entered by any court of competent jurisdiction by the prevailing Party if it is necessary to effect enforcement of the judgment.

10. Except as provided in Section 9 of this Exhibit E or as required by law, the existence of the Dispute, any settlement negotiations, the ADR process and hearing, any submissions (including exhibits, testimony, transcripts, proposed rulings, and briefs), and the rulings shall be deemed Confidential Information as set forth in Article 12 of this Agreement. The Panel shall have the authority to impose sanctions for unauthorized disclosure of confidential information.

Summary of Non-Employee Director Compensation Policy

Under the Company's non-employee director compensation policy, all non-employee directors will be paid an annual retainer fee of $35,000 and such additional fees as are set forth in the following table. All payments will be made quarterly in arrears.

Non-Employee Director	Annual Fee
Lead Director	$ 25,000
Non-Executive Chair	$ 30,000
Chairman of the audit committee	$ 15,000
Member of the audit committee (other than chairman)	$ 7,500
Chairman of the compensation committee	$ 10,000
Member of the compensation committee (other than chairman)	$ 5,000
Chairman of the governance and nominating committee	$ 8,000
Member of the governance and nominating committee (other than chairman)	$ 4,000

Under the policy, each individual who is initially appointed or elected to the board of directors will be eligible to receive an option to purchase up to 20,000 shares of our common stock under the Plan on the date he or she first becomes a non-employee director. These option grants will vest annually over a three-year period from the date of grant, subject to continued service as a non-employee director through that vesting date. In addition, on the date of the annual meeting of stockholders, each continuing non-employee director who has served on the board of directors for a minimum of six months will be eligible to receive an option grant to purchase up to 10,000 shares of our common stock, which will vest in full upon the earlier of the first anniversary of the date of grant or the date of the next annual meeting of stockholders. The exercise price for each of these option grants will be equal to the fair market value of our common stock on the date of grant. These new director grants and annual grants will be subject to approval by our board of directors at the time of grant. The share numbers set forth herein will be appropriately adjusted for any split or recapitalization of the Company's securities.

Exhibit 31.1

CERTIFICATION OF PRINCIPAL EXECUTIVE OFFICER
PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Keith M. Gottesdiener, certify that:

1. I have reviewed this quarterly report on Form 10-Q of Rhythm Pharmaceuticals, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) for the registrant and have:

(a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

(b) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

(c) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

(a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

(b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: May 14, 2018

/s/ Keith M. Gottesdiener
Name: Keith M. Gottesdiener
Title: Chief Executive Officer, President and Director
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATION OF PRINCIPAL FINANCIAL OFFICER
PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Hunter Smith, certify that:

1. I have reviewed this quarterly report on Form 10-Q of Rhythm Pharmaceuticals, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) for the registrant and have:

(a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

(b) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

(c) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

(a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

(b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: May 14, 2018

/s/ Hunter Smith
Name: Hunter Smith
Title: Chief Financial Officer and Treasurer
(Principal Financial And Accounting Officer)

Exhibit 32.1

CERTIFICATION OF CHIEF EXECUTIVE OFFICER
PURSUANT TO 18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

I, Keith M. Gottesdiener, certify pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that, to my knowledge, the Quarterly Report on Form 10-Q of Rhythm Pharmaceuticals, Inc. for the fiscal quarter ended March 31, 2018 fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934 and the information contained in such Form 10-Q fairly presents, in all material respects, the financial condition and results of operations of Rhythm Pharmaceuticals, Inc.

/s/ Keith M. Gottesdiener
Name: Keith M. Gottesdiener
Title: Chief Executive Officer, President and Director
(Principal Executive Officer)

May 14, 2018

Exhibit 32.2

CERTIFICATION OF CHIEF FINANCIAL OFFICER
PURSUANT TO 18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

I, Hunter Smith, certify pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that, to my knowledge, the Quarterly Report on Form 10-Q of Rhythm Pharmaceuticals, Inc. for the fiscal quarter ended March 31, 2018 fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934 and the information contained in such Form 10-Q fairly presents, in all material respects, the financial condition and results of operations of Rhythm Pharmaceuticals Inc.

/s/ Hunter Smith
Name: Hunter Smith
Title: Chief Financial Officer and Director
(Principal Financial and Accounting Officer)

May 14, 2018