CHIASMA, INC
Form 424B4
July 16, 2015
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Registration Number 333-204949
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PROSPECTUS

6,365,000 Shares

Common Stock

This is the initial public offering of shares of common stock of Chiasma, Inc. We are offering 6,365,000 shares of our common stock. Prior to this offering, there has been no public market for our common stock. Our common stock has been approved for listing on The NASDAQ Global Select Market under the trading symbol CHMA.

We are an emerging growth company under applicable Securities and Exchange Commission rules and will be subject to reduced public company reporting requirements for this prospectus and future filings. See Prospectus Summary Implications of Being an Emerging Growth Company.

Investing in our common stock involves a high degree of risk. See *Risk Factors* *beginning on page 11.*

	Per Share	Total
Initial public offering price	$ 16.00	$ 101,840,000
Underwriting discounts and commissions[(1)]	$ 1.12	$ 7,128,800
Proceeds to us, before expenses	$ 14.88	$ 94,711,200

(1) See Underwriting for additional disclosure regarding underwriting discounts, commissions and estimated expenses.

Certain of our existing stockholders, including certain affiliates of our directors, are purchasing an aggregate of 1,681,250 shares of our common stock in this offering at the initial public offering price.

We have granted the underwriters an option to purchase up to an additional 954,750 shares of common stock from us at the initial price to the public less the underwriting discount.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed on the adequacy or accuracy of this prospectus. Any representation to the contrary is a criminal offense.

The underwriters expect to deliver the shares against payment in New York, New York on July 21, 2015.

Barclays **Cowen and Company**

William Blair **Oppenheimer & Co.**

Prospectus dated July 15, 2015

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We are responsible for the information contained in this prospectus and in any free-writing prospectus we prepare or authorize. We have not, and the underwriters have not, authorized anyone to provide you with different information, and we take no responsibility for any other information others may give you. We are not, and the underwriters are not, making an offer to sell these securities in any jurisdiction where the offer or sale is not permitted. You should not assume that the information contained in this prospectus is accurate as of any date other than the date on the cover page of this prospectus. Our business, financial condition, results of operations and prospects may have changed since that date.

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PROSPECTUS SUMMARY

This summary highlights information contained elsewhere in this prospectus and does not contain all of the information that you should consider in making your investment decision. Before investing in our common stock, you should carefully read this entire prospectus, including our financial statements and the related notes thereto and the information set forth under the sections titled Risk Factors and Management s Discussion and Analysis of Financial Condition and Results of Operations, in each case included in this prospectus. Unless the context otherwise requires, we use the terms Chiasma, the company, we, us, our and similar designations in this prospectus to refer to Chiasma, Inc. and its wholly owned subsidiary.

Company Overview

We are a late-stage biopharmaceutical company focused on improving the lives of patients suffering from orphan diseases by developing and commercializing novel oral forms of therapies that are available today only by injection. Using our proprietary Transient Permeability Enhancer, or TPE, technology platform, we seek to develop oral therapies that eliminate the significant limitations and burdens generally associated with existing injectable therapies. We have completed a multinational Phase 3 clinical trial of our most advanced TPE platform-based product candidate, oral octreotide, for the treatment of acromegaly, a condition that results in the body s production of excess growth hormone. Octreotide is an analog of somatostatin, a natural inhibitor of growth hormone secretion. We believe that our lead product candidate, if approved by regulatory authorities, will be the first somatostatin analog available for oral administration. Our oral octreotide product candidate has been granted orphan designation in the United States and the European Union for the treatment of acromegaly. We submitted a new drug application, or NDA, to the U.S. Food and Drug Administration, or FDA, on June 15, 2015, seeking approval for the marketing and sale of oral octreotide for the maintenance therapy of adult patients with acromegaly. The FDA has 60 days after receipt of the NDA to preliminarily review and determine if the application is sufficiently complete to permit a substantive review and meets the threshold for filing. In light of our clinical data and feedback from patients and healthcare providers, we believe that oral octreotide, if approved, could become a new standard of care in acromegaly.

Acromegaly is a condition caused by a benign tumor of the pituitary gland that releases excess growth hormone, or GH, which in turn elevates insulin-like growth factor 1, or IGF-1. These elevated hormone levels result in a number of painful and disfiguring symptoms and, if not treated promptly, acromegaly can lead to serious illness and is associated with premature death, primarily due to cardiovascular disease. According to data published by the Mayo Clinic in 2013, the mortality rate of people afflicted by acromegaly who go untreated is two to three times higher than that of the general population. Recent data from a published study presented at the Endocrine Society s Annual Meeting in 2015 suggest that the global prevalence of acromegaly may be between 85 and 118 cases per million people.

The current standard of care for patients diagnosed with acromegaly consists of lifelong, once-monthly injections of an extended release somatostatin analog, primarily octreotide or lanreotide. These products contain a viscous formulation and are typically administered by a healthcare professional with large-gauge needles into the muscle or deep subcutaneously, that is, deeply under the skin. While injectable somatostatin analogs are generally effective at reducing GH and IGF-1 levels and therefore providing disease control, the injections are associated with significant limitations and patient burdens, including suboptimal symptom control, pain, injection-site reactions and other injection-related side effects, inconvenience, lost work days and emotional issues. The worldwide market for injectable somatostatin analogs is approximately $2.0 billion annually, of which approximately $730 million represents annual sales for the treatment of acromegaly.

Our lead product candidate, oral octreotide, is a novel formulation of octreotide designed to achieve biochemical disease control, that is, reduced levels of GH and IGF-1, and improved symptom control while addressing the

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pain and treatment burdens commonly experienced with current injectable therapies. We are developing oral octreotide as a pill, liquid-filled solid gelatin capsule formulation, intended to be taken twice a day. We expect that patients who are prescribed oral octreotide, if approved, by their physicians will receive a 28-day supply of pills, which may be stored at room temperature. Oral octreotide is the first somatostatin analog formulated for oral administration to complete a Phase 3 clinical trial and demonstrate clinical proof of concept in treating patients with acromegaly.

In our Phase 3 clinical trial, we observed that oral octreotide maintained biochemical disease control and improved symptom control. In this 155-patient Phase 3 clinical trial designed to evaluate oral octreotide in acromegaly patients already controlled on injectable somatostatin analogs, 65% of patients receiving oral octreotide twice a day for up to seven months achieved the primary endpoint, maintenance of biochemical disease control. This biochemical disease control was durable and 86% of patients who completed the seven-month core treatment period of the trial elected to continue on oral therapy during the six-month extension phase, for up to a total of 13 months of treatment after first dosing, rather than switch back to injections. In the majority of patients in our trial, oral octreotide achieved comparable biochemical disease control and reduced incidence and severity of acromegaly symptoms relative to injectable somatostatin analogs currently used to treat this disease. The adverse events observed for oral octreotide were similar to those previously reported for injectable somatostatin analogs, but without injection-site reactions.

Based in part on the data from our Phase 3 clinical trial, we submitted an NDA on June 15, 2015 seeking approval for the marketing and sale of oral octreotide for the maintenance therapy of adult patients with acromegaly. Assuming the FDA reviews and responds to our NDA in accordance with the goals and policies agreed to by the FDA under the Prescription Drug User Fee Act, or PDUFA, and subject to the FDA s acceptance of the NDA for filing, we anticipate a regulatory decision on marketing approval in April 2016. To support approval by the European Medicines Agency, or the EMA, and subject to final agreement with the EMA on the protocol for the trial, we intend to initiate an additional Phase 3 clinical trial of oral octreotide in acromegaly in the second half of 2015 in the United States and internationally to show parallel comparative safety and effectiveness as required by the EMA. Assuming we receive favorable results from this second Phase 3 clinical trial, we expect to submit a marketing authorization application, or MAA, to the EMA in late 2017 or early 2018. In addition, if we receive regulatory approval of oral octreotide in acromegaly, we expect to initiate a Phase 2 clinical trial of oral octreotide in the second half of 2016 for the symptomatic control of neuroendocrine tumors, or NET, which are currently treated predominantly by injectable somatostatin analogs.

We have applied for regulatory approval of oral octreotide for the maintenance therapy of acromegaly in the United States utilizing the FDA s 505(b)(2) regulatory pathway and we will apply for regulatory approval in Europe utilizing the hybrid application pathway, which is analogous to the 505(b)(2) regulatory pathway. The 505(b)(2) pathway enables a potentially shorter development timeline compared to the development time for drugs that are new chemical entities by allowing us to rely, in part, on the FDA s prior findings of safety and efficacy for a previously approved product, or published literature, in support of our NDA. In the case of oral octreotide in acromegaly, the approved product to which our NDA submission refers is the short-acting subcutaneous injectable formulation of octreotide previously approved by the FDA. Since this formulation of octreotide has been approved by the FDA in generic form and is therefore no longer proprietary, we are not aware of any third party from which we would be required to obtain any license or acquire any rights to commercialize oral octreotide, if approved.

Oral octreotide is currently protected by issued patents lasting until at least 2029 in the United States, United Kingdom and Japan, and pending patent applications in additional jurisdictions which will last until 2029, if granted.

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Commercialization Strategy

We retain worldwide rights to develop and commercialize oral octreotide with no royalty obligations to third parties. Due to the well-identified and largely concentrated physician base in acromegaly, we intend to commercialize oral octreotide ourselves in the United States through a focused in-house sales and marketing organization.

Approximately 40% of people with acromegaly undergoing treatment in the United States are treated by endocrinologists at a small number of academic institutions with pituitary experts, which we refer to as pituitary centers. The remaining people with acromegaly undergoing treatment are generally treated by community endocrinologists. We believe we will be able to market oral octreotide, if approved, directly to these pituitary centers that treat high volumes of patients with acromegaly through our own small, targeted sales force. We also intend to direct our sales and marketing efforts towards the larger number of community endocrinologists. Finally, we intend to continue to engage in direct patient outreach efforts. We believe that the clinical benefits and preferences of patients and healthcare professionals for an oral product together with our patient-centric approach could enable oral octreotide, if approved, to become a new standard of care in acromegaly.

Our Proprietary TPE Technology Platform

In contrast to conventional small molecule drugs, the oral absorption of larger molecules, such as peptides and other protein molecules, is limited due to low intestinal permeability and digestion in the stomach and intestine. Our TPE technology is a proprietary platform, developed internally by our scientists, that transiently enhances intestine permeability, allowing peptides and other drugs that are otherwise poorly absorbed when administered orally to pass through the intestine and reach therapeutic levels in the blood. We believe our TPE platform is particularly well suited to therapies used in chronic indications for which injections are required and for which the active agent can be administered orally without adverse safety implications. While our technology will not be appropriate for all drugs that cannot currently be administered orally, based on our nonclinical proof of concept data we believe that we can administer a number of peptide-based drugs orally using our TPE technology and achieve therapeutic levels in the blood. We intend to use our TPE platform to develop a new line of oral medications, beyond oral octreotide, to help improve the lives of patients suffering from other debilitating diseases that are currently being treated with injectable therapies. We intend to select at least one new product candidate in late 2016 and initiate nonclinical development of another product candidate in 2017.

As we consider new peptide-based drugs to develop using our TPE platform, to reduce the development time and expenses and overall level of investment required, we intend to focus our efforts on drugs for which we may utilize the FDA s 505(b)(2) regulatory pathway in the United States and the hybrid application pathway in Europe. With oral octreotide, we brought a TPE-based product candidate from concept to the first clinical trial within 18 months and then on to clinical proof of concept within an additional 12 months.

Our Senior Leadership Team and Investors

We have assembled an experienced team with extensive drug discovery, development and commercialization capabilities. Our President and Chief Executive Officer, Mark Leuchtenberger, has extensive experience in commercial operations, business development and preparing biopharmaceutical companies for product approval and commercialization. During his time at Biogen Inc., he managed the late-stage development, registration, marketing and North American launch of the company s first commercial product, Avonex, a $3.0 billion product. Our Chief Development Officer, Roni Mamluk, Ph.D., led the development of oral octreotide and is one of the primary inventors of our TPE platform. Our Chief Financial Officer, Mark J. Fitzpatrick, has more than 20 years of financial management experience in both public and private companies, having most recently served as chief financial officer at

Aegerion Pharmaceuticals, Inc., Proteon Therapeutics, Inc. and RenaMed Biologics, Inc. In addition, our Senior Medical Advisor, Gary Patou, M.D., brings over 20 years of extensive experience in clinical and regulatory affairs to the organization, having taken several drugs through development and FDA approval, including Exparel, which is marketed by Pacira Pharmaceuticals, Inc.

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Our investors include funds affiliated with MPM Capital, Fidelity Securities, Abingworth, 7 Med Health Ventures, F2 Capital, ARCH Venture Partners, Sofinnova Ventures and Rock Springs Capital.

Strategy

Our goal is to become a leading patient-focused biopharmaceutical company by developing and commercializing oral octreotide for acromegaly and other orphan indications, and leveraging our TPE platform to develop and commercialize novel oral products for other debilitating diseases currently treated only by injectable therapies. Our strategy to pursue this goal includes the following elements:

- Obtain U.S. regulatory approval of oral octreotide for the treatment of acromegaly.
- Independently commercialize oral octreotide in the United States.
- Obtain European regulatory approval of oral octreotide for the treatment of acromegaly.
- Explore collaboration opportunities in Europe and the rest of the world for oral octreotide in acromegaly and other indications.
- Pursue the development of oral octreotide in additional indications currently treated by injectable therapies, such as NET.
- Leverage our proprietary TPE platform to develop a pipeline of new high-value oral therapeutics.

Competitive Strengths

We believe we are well positioned to achieve our corporate and strategic goals based on the following key strengths:

- Based on our clinical data and feedback from patients and healthcare providers, we believe oral octreotide has the potential to become a standard of care in the treatment of acromegaly.
- Oral octreotide is the only somatostatin analog formulated for oral administration to complete a Phase 3 clinical trial.
- Treatment of acromegaly is a well-characterized market that we believe we can address with a focused and differentiated commercial infrastructure.

Our business model and regulatory strategy utilizing the FDA s 505(b)(2) regulatory pathway target shorter development timelines and lower associated expenses.

We believe that we have the ability to leverage our proprietary TPE platform to develop additional high-value oral therapeutics.

Our leadership team has significant drug development and commercial experience and possesses important intellectual capital.

Risks Affecting Us

Our business is subject to a number of risks and uncertainties, including those highlighted in the section titled Risk Factors immediately following this prospectus summary. Some of these risks are:

We are heavily dependent on the regulatory approval of oral octreotide for the treatment of acromegaly in the United States and Europe, and subsequent commercial success of oral octreotide, both of which may never occur. The FDA may determine that our NDA for oral octreotide for the treatment of acromegaly is not sufficiently complete to permit a substantive review.

Even if we receive regulatory approval of oral octreotide, we may still face future development and regulatory challenges.

We face substantial competition from larger companies with considerable resources that already have somatostatin analogs available in the market, and they or others may also discover, develop or commercialize additional products before or more successfully than we do.

Even if we receive regulatory approval of oral octreotide, it may not achieve an adequate level of acceptance by physicians, healthcare payors and patients, and we may not generate sufficient revenue or be able to achieve or sustain profitability.

We currently have no sales and marketing organization and, as a company, have not commercialized any products. If we are unable to establish effective sales and marketing capabilities in the United States and access them in Europe and other international markets, we may not succeed in commercializing oral octreotide.

Oral octreotide and other products we may develop may not be commercially viable if we fail to obtain coverage and an adequate level of reimbursement for these products from governmental payors, including Medicare and Medicaid programs, private insurers, and other third-party payors. The market for oral octreotide and other products we may develop may also be limited by the indications for which their use may be reimbursed.

We are, and expect to be for the foreseeable future, dependent on a limited number of third parties to manufacture oral octreotide, and our commercialization of oral octreotide could be halted, delayed or made less profitable if those third parties fail to pass inspections by the FDA or comparable foreign regulatory authorities, fail to provide us with sufficient quantities of oral octreotide or fail to do so at acceptable quality levels or prices or on a timely basis.

Clinical drug development involves a lengthy and expensive process with an uncertain outcome, results of earlier studies and trials may not be predictive of future trial results, and approval in one jurisdiction may not be predictive of approval in other jurisdictions.

The longer term growth of our business depends on our efforts to leverage our TPE platform to expand our portfolio of product candidates, which may require substantial financial resources and may ultimately be unsuccessful.

A key element of our strategy is to enter into licensing or collaboration agreements with respect to oral octreotide and future product candidates in certain territories. We may not be able to identify suitable collaborators and, even if we do, our dependence on such relationships may adversely affect our business.

We have incurred significant losses since our inception and anticipate that we will incur continued losses for the next several years and thus may never achieve or maintain profitability.

We may need additional capital to support our growth, which may be difficult to obtain and restrict our operations and would result in additional dilution to our stockholders.

If we are unable to protect our intellectual property rights or if our intellectual property rights are inadequate to protect our technology and product candidates, our competitors could develop and commercialize technology and drugs similar to ours, and our competitive position could be harmed.

Corporate Information

We were incorporated under the laws of the State of Delaware and commenced business operations in 2001. Our principal executive offices are located at 60 Wells Avenue, Suite 102, Newton, MA 02459 and our telephone

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number is (866) 637-9703. Our website address is www.chiasmapharma.com. The information contained on our website, or that can be accessed through our website, is not a part of this prospectus and is not incorporated by reference into this prospectus. You should not rely on any such information in deciding whether to purchase our common stock.

We own various U.S. federal trademark registrations and applications, and unregistered trademarks and service marks, including Chiasma, TPE and our corporate logo. All trademarks or trade names referred to in this prospectus are the property of their respective owners. Solely for convenience, the trademarks and trade names in this prospectus may be referred to without the ® and symbols, but such references should not be construed as any indicator that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto. We do not intend our use or display other companies trademarks and trade names to imply a relationship with, or endorsement or sponsorship of us by, any other companies.

Implications of Being an Emerging Growth Company

As a company with less than $1.0 billion in revenue during our most recently completed fiscal year, we qualify as an emerging growth company as defined in Section 2(a) of the Securities Act of 1933, as amended, or the Securities Act, as modified by the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. As an emerging growth company, we may take advantage of specified reduced disclosure and other requirements that are otherwise applicable, in general, to public companies that are not emerging growth companies. These provisions include:

- reduced disclosure about our executive compensation arrangements;
- exemption from the non-binding stockholder advisory votes on executive compensation or golden parachute arrangements;
- exemption from the auditor attestation requirement in the assessment of our internal control over financial reporting; and
- reduced disclosure of financial information in this prospectus, such as being permitted to include only two years of audited financial information and two years of selected financial information in addition to any required unaudited interim financial statements, with correspondingly reduced Management s Discussion and Analysis of Financial Condition and Results of Operations disclosure.

We may take advantage of these exemptions for up to five years or such earlier time that we are no longer an emerging growth company. We would cease to be an emerging growth company if we have more than $1.0 billion in annual revenues as of the end of a fiscal year, have more than $700 million in market value of our capital stock held by non-affiliates as of any December 31 before that time or if we issue more than $1.0 billion of non-convertible debt over a three-year-period. We may choose to take advantage of some, but not all, of the available exemptions. We have taken advantage of some reduced reporting burdens in this prospectus. Accordingly, the information contained herein may be different than the information you receive from other public companies in which you hold stock.

The JOBS Act permits an emerging growth company to take advantage of an extended transition period to comply with new or revised accounting standards applicable to public 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 non-emerging growth companies.

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THE OFFERING

Common stock offered by us	6,365,000 shares
Common stock to be outstanding immediately after this offering	22,974,642 shares
Underwriters option to purchase additional shares	We have granted a 30-day option to the underwriters to purchase up to an aggregate of 954,750 additional shares of common stock.
Use of proceeds	We estimate that the net proceeds from the issuance of our common stock in this offering will be approximately $92.2 million, or approximately $106.4 million if the underwriters exercise their option to purchase additional shares in full, based upon the initial public offering price of $16.00 per share, after deducting underwriting discounts and commissions and estimated offering expenses payable by us. We intend to use the net proceeds from this offering to build out our infrastructure to support the commercial launch of oral octreotide in the United States for the treatment of acromegaly; initiate an additional Phase 3 clinical trial of oral octreotide to support regulatory approval in Europe for the treatment of acromegaly; initiate a Phase 2 clinical trial of oral octreotide for the treatment of neuroendocrine tumors; continued research and development on our product pipeline using our TPE platform; and for working capital and other general corporate purposes. See Use of Proceeds for additional information.
Risk factors	See Risk Factors and the other information included in this prospectus for a discussion of factors you should carefully consider before deciding to invest in our common stock.
NASDAQ Global Select Market symbol	CHMA

Certain of our existing stockholders, including certain affiliates of our directors, are purchasing an aggregate of 1,681,250 shares of our common stock in this offering at the initial public offering price.

The number of shares of our common stock to be outstanding after this offering is based on 16,609,642 shares of our common stock outstanding as of June 30, 2015 and excludes:

3,632,210 shares of common stock issuable upon the exercise of stock options outstanding as of June 30, 2015 at a weighted-average exercise price of $4.56 per share;

3,624,012 shares of common stock issuable upon the exercise of warrants outstanding as of June 30, 2015 at a weighted-average exercise price of $4.85 per share;

2,602,283 shares of common stock reserved for future issuance under our 2015 Stock Option and Incentive Plan, or the 2015 Plan; and

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260,000 shares of common stock reserved for the future issuance under our 2015 Employee Stock Purchase Plan.

Unless otherwise indicated, all information in this prospectus reflects or assumes the following:

a 1-for-9.132 reverse stock split of our common stock effected on June 30, 2015;

the conversion of all 149,792,472 of our outstanding shares of our preferred stock into 16,403,011 shares of common stock, which will occur immediately prior to the closing of this offering;

no issuance or exercise of stock options or warrants on or after June 30, 2015; and

no exercise by the underwriters of their option to purchase up to an additional 954,750 shares of common stock in this offering.

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SUMMARY CONSOLIDATED FINANCIAL DATA

The following summary consolidated financial data for the years ended December 31, 2013 and 2014 and the balance sheet data as of December 31, 2014 are derived from our audited consolidated financial statements included elsewhere in this prospectus. The summary consolidated financial data as of March 31, 2015 and for the three months ended March 31, 2014 and 2015 have been derived from our unaudited condensed consolidated financial statements included elsewhere in this prospectus. In the opinion of management, the unaudited condensed consolidated financial statements have been prepared on a basis consistent with our audited consolidated financial statements and contain all adjustments, consisting of only normal recurring adjustments, that management considers necessary for the fair presentation of the financial information set forth in those statements. You should read this data together with our consolidated financial statements and related notes included elsewhere in this prospectus and the information under the section titled Management s Discussion and Analysis of Financial Condition and Results of Operations. Our historical results for any prior period are not necessarily indicative of results to be expected in any future period and our operating results for the three-month period ended March 31, 2015 are not necessarily indicative of the results that may be expected for the full year ending December 31, 2015 or any other interim periods or any future year or period.

	Year Ended December 31,		Three Months Ended March 31,	
	2013	2014	2014	2015
	(audited)		(unaudited)	
	(in thousands, except share and per share data)			
Consolidated Statement of Operations Data				
Revenue from license agreement	$ 73,134	$ 13,166	$ 4,573	$
Operating expenses:				
Research and development	26,455	11,527	1,650	2,219
Marketing, general and administrative	8,065	3,469	954	1,931
Total operating expenses	34,520	14,996	2,604	4,150
Income (loss) from operations	38,614	(1,830)	1,969	(4,150)
Other expenses, net	1,208	4	25	89
Income (loss) before provision for income taxes	37,406	(1,834)	1,944	(4,239)
Provision for income taxes	1,224	176	(129)	5
Net income (loss)	36,182	(2,010)	2,073	(4,244)
Accretion of deemed liquidation related to Series D redeemable convertible preferred stock	(38,504)			
Accretion of redeemable convertible preferred stock	(3,034)	(904)	(340)	(98)
Net (loss) income attributable to common stockholders	$ (5,356)	$ (2,914)	$ 1,733	$ (4,342)

Net (loss) income per share attributable to common stockholders, basic	$ (125.29)	$ (66.21)	$ 39.82	$ (59.73)
Weighted average common shares outstanding, basic	42,760	44,017	43,558	72,693
Net (loss) income per share attributable to common stockholders, diluted	$ (125.29)	$ (66.21)	$ 0.19	$ (59.73)
Weighted average common shares outstanding, diluted	42,760	44,017	11,130,865	72,693
Pro forma net loss per share attributable to common stockholders, basic and diluted (unaudited)[1]				$ (0.30)
Pro forma weighted average common shares outstanding, basic and diluted (unaudited)[1]				13,982,593

(1) See Note 3 to our audited consolidated financial statements and Note 2 of our unaudited condensed consolidated financial statements appearing elsewhere in this prospectus for an explanation of the method used to calculate the historical and pro forma net loss per share, basic and diluted, and the number of shares used in the computation of the per share amounts.

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	March 31, 2015		
	Actual	Pro Forma(1)	Pro Forma As Adjusted(2)
Consolidated Balance Sheet Data		(in thousands)	
Cash	$ 70,872	$ 70,872	$ 163,141
Working capital	67,541	67,541	159,810
Total assets	72,638	72,638	164,907
Long-term liabilities	4,724	4,724	4,724
Redeemable convertible preferred stock	138,796		
Accumulated deficit	(85,752)	(85,752)	(85,752)
Total stockholders (deficit) equity	(74,658)	64,138	156,343

(1) The pro forma column reflects the automatic conversion of all outstanding shares of our preferred stock into 16,403,011 shares of our common stock, which will occur immediately prior to the closing of this offering.

(2) The pro forma as adjusted column reflects the pro forma adjustments described in (1) above, and further reflects the sale of shares of our common stock offered in this offering, based upon the initial public offering price of $16.00 per share, after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

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RISK FACTORS

Investing in our common stock involves a high degree of risk. You should carefully consider the risks and uncertainties described below together with all of the other information contained in this prospectus, including our financial statements and the related notes appearing at the end of this prospectus, before deciding to invest in our common stock. If any of the following risks actually occur, our business, prospects, operating results and financial condition could suffer materially, the trading price of our common stock could decline and you could lose all or part of your investment. The risks and uncertainties described below are not the only ones we face. Additional risks and uncertainties not presently known to us or that we currently believe to be immaterial may also adversely affect our business.

Risks Related to Development, Regulatory Approval and Commercialization of Oral Octreotide and any Future Product Candidates

We are heavily dependent on the regulatory approval of oral octreotide for the treatment of acromegaly in the United States and Europe, and subsequent commercial success of oral octreotide, both of which may never occur.

We are a biopharmaceutical company with no products approved by regulatory authorities or available for commercial sale. As a result, our future success is currently dependent upon the regulatory approval and commercial success of oral octreotide for the treatment of acromegaly in the United States, Europe and other countries. Our ability to generate revenues in the near term will depend on our ability to obtain regulatory approval and successfully commercialize oral octreotide on our own in the United States, the first country in which we intend to make oral octreotide available for sale. We may experience delays in obtaining regulatory approval in the United States for oral octreotide, if it is approved at all, and our stock price may be negatively impacted. Even if we receive regulatory approval, the timing of the commercial launch of oral octreotide in the United States is dependent upon a number of factors, including, but not limited to, hiring sales and marketing personnel, pricing and reimbursement timelines, the production of sufficient quantities of commercial drug product and implementation of marketing and distribution infrastructure, and we do not anticipate commercial sales of oral octreotide until mid-2016, at the earliest.

In addition, we have incurred and expect to continue to incur significant expenses and to utilize a substantial portion of our effort and financial resources as we continue to pursue the approval of oral octreotide in the United States, Europe and elsewhere, prepare for the commercial launch of oral octreotide and continue to grow our operational capabilities. This represents a significant investment in the clinical, commercial and regulatory success of oral octreotide, which is uncertain. The success of oral octreotide, if approved, will depend on several factors, including:

- execution of an effective sales and marketing strategy for the commercialization of oral octreotide;
- acceptance by patients, the medical community and third-party payors;
- the incidence and prevalence of acromegaly in those markets in which oral octreotide is approved;
- the prevalence and severity of side effects, if any, experienced with oral octreotide;

the availability, perceived advantages, cost, safety and efficacy of alternative treatments;

our success in educating physicians and patients about the benefits, administration and use of oral octreotide;

successful implementation of our manufacturing processes that are included in our new drug application, or NDA, and production of sufficient quantities of commercial drug product;

maintaining compliance with regulatory requirements, including current good manufacturing practices, or cGMPs; and

obtaining and maintaining patent, trademark and trade secret protection and regulatory exclusivity and otherwise protecting our rights in our intellectual property portfolio.

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We may also fail to develop future product candidates. If this were to occur, we would continue to be dependent on the regulatory approval and successful commercialization of oral octreotide, our development costs may increase and our ability to generate revenue or profits, or to raise additional capital could be impaired.

If we are not able to obtain required regulatory approvals for oral octreotide, we will not be able to commercialize the product candidate and our ability to generate revenue or profits or to raise future capital could be limited.

On June 15, 2015, we submitted an NDA to the U.S. Food and Drug Administration, or the FDA, for oral octreotide for the maintenance therapy of acromegaly. The FDA has 60 days after receipt of the NDA to preliminarily review and determine if the application is sufficiently complete to permit a substantive review and meets the threshold for filing. In addition, we intend to initiate an additional Phase 3 clinical trial of oral octreotide in acromegaly in the second half of 2015 to show comparative effectiveness as required by the European Medicines Agency, or the EMA, to support approval. Initiation of this planned Phase 3 clinical trial is subject to our final agreement with the EMA on the protocol for this trial, which could be delayed. The FDA may not approve our NDA and our planned Phase 3 clinical trial may not be successful and therefore we may never receive approval to market oral octreotide in the United States, Europe or elsewhere.

The research, testing, manufacturing, labeling, packaging, storage, approval, sale, marketing, advertising and promotion, pricing, export, import and distribution of drug products are subject to extensive regulation by the FDA and other regulatory authorities in the United States and other countries, which regulations differ from country to country and change over time. We are not permitted to market oral octreotide in the United States until we receive approval of an NDA from the FDA, or in any foreign countries until we receive the requisite approvals in such countries. In the United States, the FDA generally requires the completion of nonclinical testing and clinical trials of each drug to establish its safety and efficacy and extensive pharmaceutical development to ensure its quality and other factors before an NDA is approved. Regulatory authorities in other jurisdictions impose similar requirements. Of the large number of drugs in development, only a small percentage result in the submission of an NDA to the FDA and even fewer are approved for commercialization.

Even if regulatory approval is obtained, subsequent safety, efficacy, quality or other issues can result in a product approval being suspended or withdrawn. Other than the submission of our NDA for oral octreotide in acromegaly to the FDA, we have not yet submitted comparable applications to other regulatory authorities. If our development efforts for oral octreotide, including regulatory approval, are not successful for its planned indications or are delayed, or if adequate demand for oral octreotide is not generated, our business will be harmed.

The success of oral octreotide will depend on the receipt and maintenance of regulatory approval and the issuance and maintenance of such approvals is uncertain and subject to a number of risks, including the following:

- the FDA or comparable foreign regulatory authorities, institutional review boards, or IRBs, or ethics committees may disagree with the design or conduct of our clinical trials;
- we may not be able to provide acceptable evidence of oral octreotide s safety and efficacy;
- the results of our clinical trials may not meet the level of statistical or clinical significance required by the FDA, the EMA or other regulatory agencies for marketing approval;

the dosing of oral octreotide in a particular clinical trial may not be at an optimal level;

patients in our clinical trials may suffer adverse effects for reasons that may or may not be related to oral octreotide;

the data collected from clinical trials may not be sufficient to support the submission of an NDA or other submission or to obtain regulatory approval in the United States or elsewhere;

the FDA or comparable foreign regulatory authorities may fail to approve the manufacturing processes or facilities of third-party manufacturers with which we contract for clinical and commercial supplies or may later suspend or withdraw such approval;

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- the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval; and

- even if we obtain marketing approval in one or more countries, future safety or other issues could result in the suspension or withdrawal of regulatory approval in such countries.

In particular, we cannot guarantee that regulators will agree with our assessment of the results of the clinical trials we have conducted to date or that any future trials will be successful. For example, the FDA may not agree that the data from our completed Phase 3 trial and other data and information in our NDA demonstrate sufficient efficacy or clinical benefit of oral octreotide. The FDA has advised us that the interpretability of the efficacy findings from our Phase 3 clinical trial will be a review issue, in particular whether the response rate evidenced in our Phase 3 clinical trial is sufficient to warrant approval. The agency also advised us that the population for the primary analysis should be all enrolled and treated patients at baseline and that analyses based on the modified intent to treat, per protocol and fixed dose, populations will be regarded as supportive. The FDA, EMA and other regulators have substantial discretion in the approval process and may refuse to accept any application or may decide that our data are insufficient for approval and require additional clinical trials, or nonclinical or other studies.

In addition, varying interpretations of the data obtained from nonclinical and clinical testing or manufacturing could delay, limit or prevent regulatory approval of oral octreotide or other product candidates we may develop in the future. Of note, in July 2014, F. Hoffmann-La Roche Ltd. and Hoffmann-La Roche Inc., collectively Roche, elected to terminate our license agreement for oral octreotide after reviewing the data from the seven-month core treatment period of our Phase 3 clinical trial and after a May 2014 pre-NDA meeting with the FDA. Roche cited no reason for its decision in its formal notice of termination, but stated publicly at the time that it had elected to make this decision after receiving additional information about our Phase 3 clinical trial and after further consultation with regulatory authorities. Subsequent to this decision, we independently met with the FDA to discuss the clinical development of oral octreotide, including the Phase 3 clinical results from the six-month extension phase of the clinical trial. At this meeting, the FDA advised us that it had not identified an issue that would preclude us from submitting an NDA for review. However, there can be no assurance that the FDA will determine that the data package included in the NDA, in particular the results from our Phase 3 clinical trial, will be sufficient to warrant approval of the NDA. The FDA has advised us that interpreting efficacy from a voluntary long-term extension study is subject to limitations and therefore the data at the seven-month time point in our Phase 3 clinical trial will carry more weight in the efficacy evaluation than the extension data. The FDA has also informed us that, in its view, a single-arm study is not as informative as a controlled study such as an active control trial using a non-inferiority design, and that the interpretability of the efficacy findings we submit from our single-arm study, and whether these findings are robust enough to warrant approval, will be review issues as the agency evaluates our NDA. The FDA may ultimately determine that our data are insufficient for approval. The FDA may require that we conduct additional clinical trials, or nonclinical or other studies, before oral octreotide can be approved.

We have only limited experience in filing the applications necessary to gain regulatory approvals and expect to rely on consultants and third-party contract research organizations, or CROs, with expertise in this area to assist us in this process. Securing FDA approval requires the submission of extensive nonclinical and clinical data, information about product manufacturing processes and inspection of facilities and supporting information to the FDA for each therapeutic indication to establish a product candidate s safety and efficacy for each indication and manufacturing quality. Oral octreotide or any future product candidates we may develop may prove to have undesirable or unintended side effects, toxicities or other characteristics that may preclude our obtaining regulatory approval or prevent or limit commercial use with respect to one or all intended indications.

The process of obtaining regulatory approvals is expensive, often takes many years, if approval is obtained at all, and can vary substantially based upon, among other things, the type, complexity and novelty of the product candidates involved, the jurisdiction in which regulatory approval is sought and the substantial discretion of the regulatory authorities. Changes in the regulatory approval policy during the development period, changes in or

the enactment of additional statutes or regulations, or changes in regulatory review for a submitted product

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application may cause delays in the approval or rejection of an application or may result in future withdrawal of approval. Regulatory approval obtained in one jurisdiction does not necessarily mean that a product candidate will receive regulatory approval in all jurisdictions in which we may seek approval, but the failure to obtain approval in one jurisdiction may negatively impact our ability to seek approval in a different jurisdiction. Failure to obtain regulatory marketing approval of oral octreotide in any indication will prevent us from commercializing the product candidate, and our ability to generate revenue will be impaired.

The FDA may determine that our NDA for oral octreotide for the maintenance therapy of acromegaly is not sufficiently complete to permit a substantive review.

On June 15, 2015, we submitted to the FDA an NDA for oral octreotide for the maintenance therapy of acromegaly. Within 60 days of the agency s receipt of our NDA, the FDA will make a threshold determination of whether the NDA is sufficiently complete to permit a substantive review. This 60-day review period is referred to as the filing review. If the NDA is sufficiently complete, the FDA will file the NDA. If the agency refuses to file the NDA, it will notify us and state the reason(s) for the refusal. The FDA may refuse to file our NDA for various reasons, including but not limited to, if:

- the NDA is incomplete because it does not on its face contain the information required under the Federal Food, Drug, and Cosmetic Act, or FDCA, or the FDA s regulations;
- the NDA does not contain a statement that each nonclinical laboratory study was conducted in compliance with the Good Laboratory Practices, or GLP, requirements, or for each study not so conducted, a brief statement of the reason for the noncompliance;
- the NDA does not contain a statement that each clinical trial was conducted in compliance with the IRB regulations or was not subject to those regulations, and the agency s informed consent regulations or a brief statement of the reason for noncompliance; or
- the drug is a duplicate of a listed drug approved before receipt of the NDA and is eligible for approval under an abbreviated new drug application, or ANDA, for generic drugs.

In its procedures, the FDA has stated that it could find a Section 505(b)(2) NDA, the U.S. regulatory pathway we are pursuing with oral octreotide in acromegaly, incomplete and refuse to file it if the NDA:

- fails to include appropriate literature or a listed drug citation to support the safety or efficacy of the drug product;
- fails to include data necessary to support any aspects of the proposed drug that represent modifications to the listed drug(s) relied upon;

fails to provide a bridge, e.g., via comparative bioavailability data, between the proposed drug product and the listed drug product to demonstrate that such reliance is scientifically justified;

uses an unapproved drug as a reference product for a bioequivalence study; or

fails to provide a patent certification or statement as required by the FDA s regulations where the 505(b)(2) NDA relies on one or more listed drugs.

Additionally, the FDA will refuse to file our NDA if an approved drug with the same active moiety is entitled to five years of exclusivity, unless the exclusivity period has elapsed or unless four years of the five-year period have elapsed and our NDA contains a certification of patent invalidity or non-infringement.

If the FDA refuses to file our NDA, we may amend the NDA and resubmit it. In such a case, the FDA will again review the NDA and determine whether it may be filed. There can be no assurance that the FDA will file our NDA. If the agency refuses to file our NDA, we will need to address the deficiencies cited by the FDA, which could substantially delay the review process.

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Our development, regulatory and commercialization strategy for oral octreotide depends, in part, on published scientific literature and the FDA s prior findings regarding the safety and efficacy of approved products containing octreotide.

The Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Act, added Section 505(b)(2) to the Federal Food, Drug, and Cosmetic Act, or Section 505(b)(2). Section 505(b)(2) permits the submission of an NDA where at least some of the information required for approval comes from investigations that were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted. The FDA interprets Section 505(b)(2) to permit the applicant to rely, in part, upon published literature or the FDA s previous findings of safety and efficacy for an approved product. The FDA also requires companies to perform additional clinical trials or measurements to support any difference from the previously approved product. The FDA may then approve the new product candidate for all or some of the label indications for which the listed drug has been approved, as well as for any new indication(s) sought by the Section 505(b)(2) applicant as supported by additional data. The label, however, may require all or some of the limitations, contraindications, warnings or precautions included in the listed drug s label, including a black box warning, or may require additional limitations, contraindications, warnings or precautions.

We have designed our clinical programs to advance oral octreotide for registration filing in the United States using the FDA s 505(b)(2) regulatory pathway and the hybrid application pathway, which is analogous to the 505(b)(2) regulatory pathway, in Europe. As such, our NDA in the United States relies, and our marketing authorization application, or MAA, in Europe will rely, in part, on previous findings of safety and efficacy for an approved immediate-release injectable octreotide product and published scientific literature for which we have not received a right of reference. Even though we expect to be able to take advantage of Section 505(b)(2) and the hybrid application pathway to support potential regulatory approval of oral octreotide in the United States and Europe, the relevant regulatory authorities may require us to perform additional clinical trials or measurements to support approval over and above the clinical trials that we have already completed and the additional clinical trials we currently plan to commence with respect to indications other than acromegaly. The relevant regulatory authorities also may determine that we have not provided sufficient data to justify reliance on prior investigations involving the approved immediate-release injectable octreotide product.

In addition, notwithstanding the approval of many products by the FDA pursuant to Section 505(b)(2), in the past some pharmaceutical companies and others have objected to the FDA s interpretation of Section 505(b)(2). For example, parties have filed citizen petitions objecting to the FDA approving a Section 505(b)(2) NDA on both scientific and legal and regulatory grounds. Scientific arguments have included the assertions that for the FDA to determine the similarity of the drug in the 505(b)(2) NDA to the listed drug, the agency would need to reference proprietary manufacturing information or trade secrets in the listed drug s NDA; that it would be scientifically inappropriate for the FDA to rely on public or nonpublic information about the listed drug because it differs in various ways from the drug in the 505(b)(2) NDA; or that differences between the listed drug and the drug in the 505(b)(2) NDA may impair the latter s safety and effectiveness. Legal and regulatory arguments have included the assertion that Section 505(b)(2) NDAs must contain a full report of investigations conducted on the drug proposed for approval, and that approving a drug through the 505(b)(2) regulatory pathway would lower the approval standards. In addition, citizen petitions have made patent-based challenges against 505(b)(2) NDAs. For example, petitioners have asserted that the FDA should refuse to file a 505(b)(2) NDA unless it references a specific NDA as the listed drug, because it is most similar to the proposed drug, and provides appropriate patent certification to all patents listed for that NDA; or that when a 505(b)(2) NDA is pending before the agency, but before it is approved, where the FDA approves an NDA for a drug that is pharmaceutically equivalent to the drug that is the subject of the 505(b)(2) NDA, then the FDA should require that the 505(b)(2) NDA be resubmitted referencing the approved NDA as the listed drug and certifying to the listed patents for that approved drug. In the case of oral octreotide, we expect that we will be able to provide an

appropriate patent certification for all applicable patents listed in our oral octreotide NDA, because octreotide has previously been approved by the FDA in generic form. However, if the FDA or EMA changes its interpretation of

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Section 505(b)(2) or the hybrid application pathway, or if the FDA s or EMA s interpretation is successfully challenged in court, this could delay or even prevent the FDA or EMA, as applicable, from approving any Section 505(b)(2) NDAs or hybrid application pathway MAAs that we submit. Such a result could require us to conduct additional testing and costly clinical trials, which could substantially delay or prevent the approval and launch of oral octreotide for the treatment of acromegaly or any future product candidates we may develop.

Clinical drug development involves a lengthy and expensive process with an uncertain outcome, results of earlier studies and trials may not be predictive of future trial results, and approval in one jurisdiction may not be predictive of approval in other jurisdictions.

We intend to initiate a second Phase 3 clinical trial of oral octreotide in acromegaly to support approval by the EMA, and Phase 2 clinical trials of oral octreotide in indications other than acromegaly, such as neuroendocrine tumors, or NETs. Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain, and we will continue to be subject to these risks. Failure can occur at any time during the clinical trial process and results of future trials can adversely affect regulatory approvals previously received. The results of nonclinical studies and prior clinical trials may not be predictive of the results of future clinical trials. For example, the positive results generated in our completed clinical trials for oral octreotide in acromegaly do not ensure that future clinical trials, including the additional Phase 3 trial required to support EMA approval or other trials required by the FDA, or clinical trials for other indications, will also generate positive results. We cannot assure you that the FDA or EMA will view the results as we do or that any future trials of oral octreotide, including our planned second Phase 3 clinical trial in acromegaly or clinical trials for other indications, such as NET, will achieve positive results. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy traits despite having progressed through nonclinical studies and prior clinical trials. A number of companies in the biopharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy or adverse safety profiles, notwithstanding promising results in prior trials.

Despite the results reported in earlier nonclinical studies and clinical trials for oral octreotide for the treatment of acromegaly, any future clinical trial results of oral octreotide may not be successful in any particular indication. A number of factors could contribute to a lack of favorable safety and efficacy results for oral octreotide for other indications. For example, such trials could result in increased variability due to varying site characteristics, such as local standards of care, differences in evaluation period, and due to varying patient characteristics including demographic factors and health status. If later-stage clinical trials do not produce favorable results, our ability to achieve regulatory approval of oral octreotide for the treatment of acromegaly or other indications, and any other product candidates we may develop, may be adversely impacted.

Further, our NDA relies upon the FDA s 505(b)(2) regulatory pathway for oral octreotide in acromegaly in the United States. There can be no assurance that our clinical trials, or the clinical trials conducted by third parties, will demonstrate sufficient safety and efficacy for the FDA to approve oral octreotide for the treatment of acromegaly or any other indication that may be specified in future NDA submissions. Even if we do obtain approval from the FDA for oral octreotide for the treatment of acromegaly in the United States, we may not be successful in obtaining approval from the EMA or other regulatory authorities.

Any negative clinical results from, termination or suspension of, or delays in the commencement or completion of, any necessary future trials of oral octreotide for the treatment of acromegaly or for any additional indications, in the United States or other countries, or future clinical trials of product candidates we may develop could result in increased costs to us, delay or limit our ability to generate revenue and negatively impact our commercial prospects.

Delays in the commencement or completion of the Phase 3 clinical trial we intend to initiate prior to applying for marketing approval with the EMA in Europe, the Phase 2 clinical trials of oral octreotide for NETs and other indications, or any future clinical trials we intend to conduct for other product candidates we may develop, or negative findings in those trials, could significantly affect our product development costs or our ability to commercialize oral octreotide. We do not know whether such trials will begin, will be completed on schedule, if

at all, or will be successful. The commencement and completion of these clinical trials can be delayed for a number of reasons, including delays related to:

- the FDA, the EMA or any other relevant regulatory authority failing to grant permission to proceed and placing the clinical trial on hold;

- delays in patient enrollment and variability in the number and types of patients available for clinical trials, which is particularly challenging for orphan indications;

- a facility manufacturing oral octreotide or any other product candidate we may develop being ordered by the FDA, EMA or other government or regulatory authorities to temporarily or permanently shut down due to violations of cGMP requirements or other applicable requirements, or cross-contaminations of product candidates in the manufacturing process;

- any changes to our manufacturing process that may be necessary or desired;

- patients choosing an alternative treatment for any of the indications for which we are developing oral octreotide or potential product candidates, or participating in competing clinical trials;

- difficulty in maintaining contact with patients after treatment, resulting in incomplete data;

- patients experiencing drug-related adverse effects;

- reports from clinical testing on similar technologies and products raising safety and/or efficacy concerns;

- third-party clinical investigators losing their license or permits necessary to perform our clinical trials, not performing our clinical trials on our anticipated schedule or employing methods consistent with the clinical trial protocol, good clinical practice, or GCP, requirements, or other third parties not performing data collection and analysis in a timely or accurate manner;

- inspections of clinical trial sites by the FDA, EMA or other regulatory authorities finding regulatory violations that require us to undertake corrective action, result in suspension or termination of one or more sites or the imposition of a clinical hold on the entire trial, or that prohibit us from using some or all of the data in support of our marketing applications;

third-party contractors becoming debarred or suspended or otherwise penalized by the FDA or other government or regulatory authorities for violations of regulatory requirements, in which case we may need to find a substitute contractor, and we may not be able to use some or any of the data produced by such contractors in support of our marketing applications;

one or more institutional review boards, or IRBs, or ethics committees refusing to approve, suspending or terminating the study at an investigational site, precluding enrollment of additional patients, or withdrawing its approval of the trial;

reaching agreement on acceptable terms with prospective 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;

deviations of the clinical sites from trial protocols or dropping out of a trial;

delays in adding new clinical trial sites;

the inability of the CRO to execute any clinical trials for any reason; or

government or regulatory delays or clinical holds requiring suspension or termination of a trial.

Product development costs for oral octreotide in acromegaly, NET or any other future indications we may pursue or for product candidates we may develop in the future will increase if we have delays in testing or approval, or if we need to perform more or larger clinical studies than planned. If we experience delays in completion of, or if we, the FDA, other regulatory authorities, IRBs or other reviewing entities, or any of our clinical trial sites suspend or terminate any of our clinical trials of oral octreotide for any indication, its commercial prospects may be harmed and our ability to generate product revenues will be delayed. Any delays in completing our clinical

trials will increase our costs, slow down our development and approval process and jeopardize our ability to commence product sales and generate revenues. Any of these occurrences may harm our business, financial condition and prospects significantly. In addition, many of the factors that cause, or lead to, termination or suspension of, or a delay in the commencement or completion of, clinical trials may also ultimately lead to the denial or even withdrawal of regulatory approval of oral octreotide for any indication. In addition, if one or more clinical trials are delayed, our competitors may be able to bring products to market before we do, and the commercial viability of oral octreotide could be significantly reduced.

Changes in regulatory requirements and guidance may also occur and we may need to amend clinical trial protocols submitted to applicable regulatory authorities to reflect these changes. Amendments may require us to resubmit clinical trial protocols to IRBs or ethics committees for re-examination, which may impact the costs, timing or successful completion of a clinical trial.

The FDA s and other regulatory authorities policies may change, and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of oral octreotide and any future product candidates we may develop. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained, and we may not achieve or sustain profitability, which would harm our business, prospects, financial condition and results of operations.

If we are required to conduct additional clinical trials or other studies with respect to oral octreotide or any future product candidates we may develop beyond those that we currently contemplate, or if we are unable to successfully complete our clinical trials or other studies, we may be delayed in obtaining regulatory approval of oral octreotide and any future product candidates we may develop, we may not be able to obtain regulatory approval at all or we may obtain approval of indications that are not as broad as intended. Our product development costs will also increase if we experience delays in testing or approvals, and we may not have sufficient funding to complete the testing and approval process for oral octreotide or any future product candidates we may develop. Significant clinical trial delays could allow our competitors to bring products to market before we do and impair our ability to commercialize our products if and when approved. If any of this occurs, our business would be harmed.

We may find it difficult to enroll patients in our clinical trials, in particular with respect to oral octreotide and any other product candidates that we may pursue, which could delay or prevent clinical trials of oral octreotide and any future product candidates we may develop and potentially harm our business.

Identifying and qualifying patients to participate in clinical trials of oral octreotide and any future product candidates we may develop is critical to our success. The timing of our clinical trials depends on the speed at which we can recruit patients to participate in testing oral octreotide and any future product candidates we may develop as well as completion of required follow-up periods. If patients are unwilling to participate in our clinical trials for any reason, including if patients choose to enroll in competitive clinical trials for similar patient populations, the timeline for recruiting patients, conducting studies and obtaining regulatory approval of oral octreotide and any future product candidates we may develop may be delayed. These delays could result in increased costs, delays in advancing oral octreotide or any of our future product candidates, delays in testing the effectiveness of our product candidates or termination of the clinical trials altogether.

We may not be able to identify, recruit and enroll a sufficient number of patients, or those with required or desired characteristics to achieve diversity in a trial, to complete our clinical trials in a timely manner. In particular, the conditions for which we currently plan to evaluate oral octreotide are orphan diseases with limited patient pools from

which to draw for clinical trials. The eligibility criteria of our clinical trials will further limit the pool of available trial participants.

Patient enrollment is affected by factors including:

- severity of the disease under investigation;

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- design of the clinical trial protocol;
- size and nature of the patient population;
- eligibility criteria for the trial in question;
- perceived risks and benefits of the product candidate under trial;
- proximity and availability of clinical trial sites for prospective patients;
- availability of competing therapies and clinical trials;
- perceptions of patients and healthcare providers as to the potential advantages of the drug being studied in relation to other available therapies, including any new drugs that may be approved for the indications we are investigating;
- efforts to facilitate timely enrollment of patients in clinical trials;
- patient referral practices of physicians; and
- our ability to monitor patients adequately during and after treatment.

If we have difficulty enrolling a sufficient number of patients to conduct our clinical trials as planned, we may be forced to delay, limit or terminate ongoing or planned clinical trials, any of which would have an adverse effect on our business. We could encounter delays if physicians encounter unresolved ethical issues associated with enrolling patients in clinical trials of oral octreotide and any future product candidates we may develop in lieu of prescribing existing treatments that have established safety and efficacy profiles. We plan to seek initial marketing approval of oral octreotide in the United States and Europe. We may not be able to initiate or continue clinical trials if we cannot enroll a sufficient number of eligible patients to participate in the clinical trials required by the FDA, the EMA or other regulatory authorities. Our ability to successfully initiate, enroll and complete a clinical trial in any foreign country is subject to numerous risks unique to conducting business in foreign countries, including:

- difficulty in establishing or managing relationships with CROs and physicians;
- different requirements and standards for conducting clinical trials;

our inability to locate qualified local consultants, physicians and partners; and

the potential burden of complying with a variety of foreign laws, medical standards and regulatory requirements, including the regulation of pharmaceutical and biotechnology products and treatments.

Even if we receive regulatory approval of oral octreotide, we may still face future development and regulatory challenges.

Even if we obtain regulatory approval of oral octreotide for the treatment of acromegaly, NET and other indications we may pursue, or any other product candidates we may develop, they will be subject to ongoing requirements by the FDA and comparable foreign regulatory authorities governing manufacturing, quality control, further development, labeling, packaging, storage, distribution, safety surveillance, import, export, advertising, promotion, recordkeeping and reporting of safety and other post-market information. The safety profile of oral octreotide and any future product candidates we may develop will continue to be closely monitored by the FDA and comparable foreign regulatory authorities after approval. If new safety information becomes available after approval of oral octreotide and any future product candidates we may develop, the FDA or comparable foreign regulatory authorities may require labeling changes or establishment of a Risk Evaluation and Mitigation Strategy, or REMS, or similar strategy, impose significant restrictions on our product candidates, indicated uses or marketing, or impose ongoing requirements for potentially costly post-approval studies or post-market surveillance. For example, the label ultimately approved for oral octreotide, if it achieves marketing approval, may include restrictions on use, which could limit the marketability of oral octreotide and impair our ability to have oral octreotide gain market acceptance.

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In addition, manufacturers of drug products and their facilities are subject to continual review and periodic inspections by the FDA and other regulatory authorities for compliance with cGMP and other regulations. If we or a regulatory authority discover previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured, we may recall or withdraw the product from the market or a regulatory authority may impose restrictions on that product, the manufacturing facility or us, including requiring suspension of manufacturing. If we, our products or the manufacturing facilities for our products fail to comply with applicable regulatory requirements, a regulatory authority may:

- issue warning letters or untitled letters;
- mandate modifications to promotional materials or require us to provide corrective information to healthcare practitioners;
- require us to enter into a consent decree, which can include imposition of various fines, reimbursements for inspection costs, required due dates for specific actions and penalties for noncompliance;
- seek an injunction or impose civil or criminal penalties or monetary fines;
- suspend or withdraw regulatory approval;
- suspend any ongoing clinical trials;
- refuse to approve pending applications or supplements to applications filed by us;
- suspend or impose restrictions on operations, including costly new manufacturing requirements; or
- seize or detain products, refuse to permit the import or export of products, or request that we initiate a product recall.

The occurrence of any event or penalty described above may inhibit or preclude our ability to commercialize oral octreotide and any future product candidates we may develop and generate revenue.

We face substantial competition from larger companies with considerable resources that already have somatostatin analogs available in the market, and they or others may also discover, develop or commercialize additional products before or more successfully than we do.

Our industry is highly competitive and subject to rapid and significant technological change as researchers learn more about diseases and develop new technologies and treatments. Our potential competitors include primarily large pharmaceutical, biotechnology and specialty pharmaceutical companies. In attempting to achieve the widespread

commercialization of oral octreotide, we will face competition from established drugs and major brand names and also generic versions of these products. In addition, new products developed by others could emerge as competitors to our future products. Key competitive factors affecting the commercial success of oral octreotide and any other product candidates we may develop are likely to be efficacy, safety and tolerability profile, reliability, convenience of administration, price and reimbursement. For example, physicians may choose not to prescribe oral octreotide, if approved, because a lower percentage of patients respond to it than to some currently available injectable somatostatin analogs. Competition could also force us to lower prices or could result in reduced sales.

The current treatment options for patients suffering from acromegaly all involve injectable therapies marketed by large companies with substantial resources and well-established presence in the endocrinology market. Novartis AG, or Novartis, markets octreotide LAR, which is administered monthly and intramuscularly using a large-gauge needle. Ipsen SA markets lanreotide, another long-acting analog of somatostatin, like octreotide, which is administered monthly using a deep subcutaneous injection. For patients not controlled on these somatostatin analogs, Pfizer, Inc. markets pegvisomant daily injections and Novartis also markets pasireotide LAR, which is another somatostatin analog administered via intramuscular injection. We are aware of other companies involved in early-stage nonclinical and clinical studies of similar somatostatin analogs, but we believe all involve administration via injection.

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Many of our existing or potential competitors have substantially greater financial, technical and human resources than we do and significantly greater experience in the discovery and development of product candidates, obtaining FDA and other regulatory approvals of products and the commercialization of those products. These companies also have long-established relationships within the medical and patient community, including patients, physicians, nurses and commercial third-party payors and government payors. Our ability to compete successfully will depend largely on our ability to:

- discover and develop product candidates that are superior to other products in the market;
- obtain required regulatory approvals;
- adequately communicate the benefits of oral octreotide, if approved;
- attract and retain qualified personnel;
- obtain and maintain patent and/or other proprietary protection for oral octreotide and any future product candidates we may develop; and
- obtain collaboration arrangements to commercialize oral octreotide and any future product candidates we may develop.

Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a small number of our competitors. Accordingly, our competitors may be more successful than we may be in obtaining FDA approval of drugs and achieving widespread market acceptance. Our competitors drugs may be more effective, or more effectively marketed and sold, than any drug we may commercialize and may render oral octreotide or any future product candidates we may develop obsolete or non-competitive before we can recover the expenses of developing and commercializing oral octreotide or any future product candidates we may develop. Our competitors may also obtain FDA or other regulatory approval of their products more rapidly than we may obtain approval of ours. We anticipate that we will face intense and increasing competition as new drugs enter the market and more advanced technologies become available. For example, a competitor could develop another oral formulation of a somatostatin analog or other technology that could make administration of peptide-based therapies more convenient. If we are unable to compete effectively, our opportunity to generate revenue from the sale of oral octreotide or any future product candidates we may develop, if approved, could be impaired.

The number of patients suffering from acromegaly is small, and has not been established with precision. Our assumptions and estimates regarding prevalence may be wrong. If our oral octreotide product candidate is approved for sale, and the actual number of patients in the applicable market is smaller than we estimate, our revenue could be adversely affected, possibly materially.

There is no patient registry or other method of establishing with precision the actual number of patients with acromegaly in any geography.

There are an estimated 62,300 individuals with acromegaly worldwide, of which an estimated 35,100 receive lifelong injections. The U.S. National Institutes of Health, or NIH, estimates that there are roughly 20,000 individuals with acromegaly in the United States, based on its published prevalence of an estimated 60 cases per million. However, recent data presented at the Endocrine Society s Annual Meeting in 2015 suggest that pituitary tumors may be more prevalent than previously thought, and that the global prevalence of acromegaly may be higher, between 85 and 118 cases per million people. NIH also cites an annual incidence of three to four new cases per million each year. However, there is no guarantee that these estimates are correct. The number of patients with acromegaly, in particular the number of patients for whom our oral octreotide product, if approved, is approved for use, could actually be significantly lower than these estimates.

We believe that the actual size of the total addressable acromegaly market in those markets in which our oral octreotide product is approved, if at all, will be determined only after we have substantial history as a commercial

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company. If the total addressable market for our products is smaller than we expect, our revenue could be adversely affected, possibly materially.

Even if we receive regulatory approval of oral octreotide, it may not achieve an adequate level of acceptance by physicians, patients and third-party payors and government payors, and we may not generate sufficient revenue or be able to achieve or sustain profitability.

The commercial success of oral octreotide will depend in large part on the willingness of physicians to prescribe these products to their patients. Oral octreotide will compete against products that have achieved broad recognition and acceptance among medical professionals. In order to achieve an acceptable level of prescriptions for oral octreotide, we must be able to meet the needs of both the medical community and patients with respect to cost, efficacy and other factors. The degree of market acceptance of oral octreotide will depend on a number of factors, including:

- the clinical safety, efficacy, tolerability and other factors regarding oral octreotide relative to injectable somatostatin analogs;
- relative convenience, the number of capsules that need to be taken, the requirement to fast before and after each dose of oral octreotide, and other factors affecting the ease of administration;
- the prevalence and severity of any adverse effects;
- the willingness of physicians to prescribe oral octreotide and of the target patient population to try new therapies;
- the introduction of any new products that may in the future become available to treat indications for which oral octreotide may be approved;
- changes in the clinical or economic profiles of alternative treatments;
- new procedures or methods of treatment that may reduce the incidences of any of the indications in which oral octreotide may show utility;
- pricing and cost-effectiveness;
- the effectiveness of our or any future collaborators sales and marketing programs;
- limitations or warnings contained in FDA-approved labeling;

our ability to obtain and maintain sufficient third-party coverage and adequate reimbursement from government health care programs, including Medicare and Medicaid, private health insurers and other third-party payors;

the willingness of patients to pay out-of-pocket in the absence of third-party coverage or reimbursement;

competitor activities; and

our ability to reliably manufacture and supply oral octreotide.

In addition, even if we obtain regulatory approvals, the timing or scope of any approvals may prohibit or reduce our ability to commercialize oral octreotide successfully. For example, if the approval process takes too long, we may miss market opportunities and give other companies the ability to develop competing products or establish market dominance. Any regulatory approval we ultimately obtain may be limited or subject to restrictions or post-approval commitments that render oral octreotide not commercially viable. For example, regulatory authorities may approve oral octreotide for fewer or more limited indications than we request, may grant approval contingent on the performance of costly post-marketing clinical trials, or may approve oral octreotide with a label that does not include the labeling claims necessary or desirable for the successful commercialization of that indication. Any of the foregoing scenarios could harm the commercial prospects for oral octreotide.

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Even if oral octreotide is approved, it may not achieve an adequate level of acceptance by physicians, healthcare payors and patients, and we may not generate sufficient revenue or be able to achieve or sustain profitability. Our revenue and profitability may also be delayed during the period of time when commercial third-party payors and government payors are becoming familiar with oral octreotide and patients are transitioning from injected alternatives to oral octreotide. Our efforts to educate the medical community, patients and third-party payors on the benefits of oral octreotide may require significant resources and may never be successful. Even if we are able to demonstrate and maintain a competitive advantage over our competitors, if the market for octreotide decreases, we may not generate sufficient revenue.

We currently have no sales and marketing organization and, as a company, have not commercialized any products. If we are unable to establish effective sales and marketing capabilities in the United States and access them in Europe and other international markets, we may not succeed in commercializing oral octreotide.

At present, we have no sales personnel and a limited number of marketing personnel. We intend to use a portion of the proceeds from this offering to build our sales and marketing infrastructure to support commercial launch in the United States, assuming our NDA is approved. Therefore, since we expect to receive a response from the FDA with respect to our NDA in April 2016, then assuming the NDA is approved at that time, our sales and marketing team will have worked together for only a limited period prior to our anticipated commercial launch of oral octreotide. We cannot guarantee that we will be successful in marketing oral octreotide in the United States.

We may not be able to establish a direct sales force in a cost-effective manner or realize a positive return on this investment. In addition, we will have to compete with other pharmaceutical and biotechnology companies to recruit, hire, train and retain sales and marketing personnel. Factors that may inhibit our efforts to commercialize oral octreotide in the United States without strategic partners or licensees include:

- our inability to recruit and retain adequate numbers of effective sales and marketing personnel;
- the inability of our relatively small sales force to obtain access to or inform adequate numbers of physicians, particularly the pituitary centers and the significantly larger number of community endocrinologists, about the potential benefits of oral octreotide;
- the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines;
- the inability of market-access personnel to obtain sufficient levels of pricing and reimbursement in each jurisdiction; and
- unforeseen costs, expenses and delays associated with creating a commercial organization.

If we are not successful in timely recruiting of sales and marketing personnel or in building a sales and marketing infrastructure or if we do not successfully enter into appropriate collaboration arrangements, we will have difficulty commercializing oral octreotide, which could harm our business, operating results and financial condition.

Expansion of our business into the European Union and other international markets will require significant management attention and additional financial resources. We currently intend to explore commercializing oral octreotide in Europe and other international markets by entering into collaboration agreements with other biopharmaceutical companies, and we may not be successful in entering into these collaboration agreements. In the event that we do enter into such agreements, we may have limited or no control over the sales, marketing and distribution activities of these third parties. Additional factors and risks that may inhibit our efforts to commercialize oral octreotide in foreign markets include:

- our inability to directly control commercial activities because we are relying on third parties, should we enter into third-party collaborations;

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varying pricing in different foreign markets, which could adversely affect pricing in the United States or other countries;

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 collection times for accounts receivable;

longer lead times for shipping;

language barriers for technical training;

reduced protection of intellectual property rights in some foreign countries, and related prevalence of generic alternatives to therapeutics;

foreign currency exchange rate fluctuations;

our customers ability to obtain adequate reimbursement for oral octreotide in foreign markets at all, either at all or at prices that exceed our costs; and

the interpretation of contractual provisions governed by foreign laws in the event of a contract dispute.

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

Our future revenues may depend heavily on the success of the efforts of these third parties. We may not be able to establish a commercial operation in a cost-effective manner or realize a positive return on this investment, even with the assistance of one or more third-party collaborators, should we choose to enter into such an arrangement. In addition, we will have to compete with other pharmaceutical and biotechnology companies to recruit, hire, train and retain sales and marketing personnel.

If we or third-party collaborators are not successful in recruiting sales and marketing personnel or in building a sales and marketing infrastructure or if we do not successfully enter into additional collaboration arrangements with third parties, we may not be able to successfully commercialize oral octreotide and any future product candidates we may develop in foreign markets, which could impair our business, operating results and financial condition.

Even with the potential assistance of third-party collaborators, we may not be successful in establishing a commercial operation in foreign markets for numerous reasons, including, but not limited to, failing to attract, retain and motivate the necessary skilled personnel and failing to develop a successful marketing strategy. Failure to establish a commercial operation in foreign markets will have a negative outcome on our ability to commercialize oral octreotide and generate revenue.

Additionally, if approved for marketing in one or more countries, we and/or our potential third-party collaborators may encounter unexpected or unforeseen delays in establishing our commercial operations that delay the commercial launch in these countries. These delays may increase the cost of and the resources required for successful commercialization of oral octreotide internationally. We do not have any experience in a commercial launch in Europe or elsewhere.

We will need to grow the size of our organization in order to establish our sales and marketing infrastructure, which is vital to our ability to successfully commercialize oral octreotide, and we may experience difficulties in managing this growth.

We anticipate that in the near term our ability to generate revenues will depend solely on our ability to successfully commercialize oral octreotide, if approved, in the United States. A commercial launch is a

significant undertaking that requires substantial financial and managerial resources. As of March 31, 2015, we had 13 employees. As our development and commercialization plans and strategies evolve, we will need to expand the size of our employee base for managerial, operational, sales, marketing, financial and other resources. The recruitment and hiring of these personnel will take time and could delay the commercialization of oral octreotide. Future growth would impose significant added responsibilities on members of management, including the need to identify, recruit, maintain, motivate and integrate additional employees. Also, our management may have to divert a disproportionate amount of its attention away from our day-to-day activities and devote a substantial amount of time to managing these growth activities. Our future financial performance and our ability to commercialize oral octreotide and other product candidates we may develop and to compete effectively will depend, in part, on our ability to effectively manage any future growth and related costs. We may not be able to effectively manage a rapid pace of growth and timely implement improvements to our management infrastructure and control systems.

Even if we obtain marketing approval of oral octreotide or any future product candidates we may develop, we will be subject to ongoing obligations and continued regulatory review with respect to the advertising and promotion of any product candidate that obtains approval.

Advertising and promotion of any product candidate that obtains approval in the United States will be heavily scrutinized by, among others, the FDA, the Department of Justice, or DOJ, the Office of Inspector General of the Department of Health and Human Services, or HHS, state attorneys general, members of Congress and the public, as well as by foreign regulatory authorities in the countries in which we commercialize oral octreotide. Even if oral octreotide is being marketed, the manufacture and marketing of oral octreotide will be subject to ongoing regulation, including compliance with cGMPs, adverse event reporting requirements and general prohibitions against promoting products for unapproved or off-label uses. Violations of these ongoing regulations are subject to enforcement letters, inquiries and investigations, and civil and criminal sanctions by the FDA or other government agencies. Additionally, advertising and promotion of any product candidate that obtains approval outside of the United States will be heavily scrutinized by comparable foreign regulatory authorities.

In the United States, engaging in impermissible promotion of our drug products for off-label uses can also subject us to false claims litigation under federal and state statutes, and other litigation and/or investigation, which can lead to significant administrative civil and criminal penalties and fines and agreements that materially restrict the manner in which we promote or distribute our drug products. These false claims statutes include the federal False Claims Act, which allows any individual to bring a lawsuit against a pharmaceutical company on behalf of the federal government alleging submission of false or fraudulent claims, or causing to present such false or fraudulent claims, for payment by a federal program such as Medicare or Medicaid. If the government decides to intervene and prevails in the lawsuit, the individual will share in any fines or settlement funds. Since 2004, these False Claims Act lawsuits against pharmaceutical companies have increased significantly in volume and breadth, leading to substantial civil and criminal settlements based on certain sales practices promoting off-label drug uses. This increasing focus and scrutiny has increased the risk that a pharmaceutical company will have to defend a false claim action, pay settlement fines or restitution, agree to comply with burdensome reporting and compliance obligations, and be excluded from the Medicare, Medicaid and other federal and state healthcare programs, among other penalties. If we do not lawfully promote our approved products, we may become subject to such litigation and/or investigation and, if we are not successful in defending against such actions, those actions could compromise our ability to become profitable.

The manufacture and packaging of pharmaceutical products such as oral octreotide are subject to FDA requirements and those of similar foreign regulatory bodies. If we or our third-party manufacturers fail to satisfy these requirements, our product development and commercialization efforts may be harmed.

The manufacture and packaging of pharmaceutical products, such as oral octreotide, if approved, are regulated by the FDA and similar foreign regulatory bodies and must be conducted in accordance with the FDA s cGMP and comparable requirements of foreign regulatory bodies. There are a limited number of manufacturers that operate

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under these cGMP regulations who are both capable of manufacturing oral octreotide and willing to do so. Failure by us or our third-party manufacturers to comply with applicable regulations or requirements could result in sanctions being imposed on us, including fines, injunctions, civil penalties, failure of regulatory authorities to grant marketing approval of our products, delays, suspension or withdrawal of approvals, seizures or voluntary recalls of product, operating restrictions and criminal prosecutions, any of which could harm our business. The same requirements and risks are applicable to the suppliers of the key raw material used to manufacture the active pharmaceutical ingredient, or API, for oral octreotide.

Changes in the manufacturing process or procedure, including a change in the location where the product is manufactured or a change of a third-party manufacturer, may require prior FDA review and approval of the manufacturing process and procedures in accordance with the FDA s cGMPs. Any new facility is subject to a pre-approval inspection by the FDA and would again require us to demonstrate product comparability to the FDA. There are comparable foreign requirements. This review may be costly and time consuming and could delay or prevent the launch of a product.

Furthermore, in order to obtain approval of our product candidates, including oral octreotide, by the FDA and foreign regulatory agencies, we will be required to consistently produce the API, and the finished product in commercial quantities and of specified quality on a repeated basis and document our ability to do so. This requirement is referred to as process validation. Each of our potential API suppliers will likely use a different method to manufacture API, which has the potential to increase the risk to us that our manufacturers will fail to meet applicable regulatory requirements. We also need to complete process validation on the finished product in the packaging we propose for commercial sales. This includes testing of stability, measurement of impurities and testing of other product specifications by validated test methods. If the FDA does not consider the result of the process validation or required testing to be satisfactory, we may not obtain approval to launch the product or approval, launch or commercial supply after launch may be delayed.

The FDA and similar foreign regulatory bodies may also implement new requirements, or change their interpretation and enforcement of existing requirements, for manufacture, packaging or testing of products at any time. If we are unable to comply, we may be subject to regulatory, civil actions or penalties which could harm our business.

If we do not achieve our projected development and commercialization goals in the timeframes we announce and expect, the commercialization of oral octreotide and any future product candidates we may develop may be delayed, and our business will be harmed.

We estimate for planning purposes the timing of the accomplishment of various scientific, clinical, regulatory and other product development objectives. These milestones may include our expectations regarding the commencement or completion of scientific studies, clinical trials, the submission of regulatory filings, or commercialization objectives. From time to time, we may publicly announce the expected timing of some of these milestones, such as the completion of an ongoing clinical trial, the initiation of other clinical programs, receipt of marketing approval, or a commercial launch of a product. The achievement of many of these milestones may be outside of our control. All of these milestones are based on a variety of assumptions which may cause the timing of achievement of the milestones to vary considerably from our estimates, including:

- our available capital resources or capital constraints we experience;

the rate of progress, costs and results of our clinical trials and research and development activities, including the extent of scheduling conflicts with participating clinicians and collaborators, and our ability to identify and enroll patients who meet clinical trial eligibility criteria;

our receipt of approvals by the FDA and other regulatory agencies and the timing thereof; other actions, decisions or rules issued by regulators;

our ability to access sufficient, reliable and affordable supplies of compounds used in the manufacture of oral octreotide and any future product candidates we may develop;

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the efforts of our collaborators and the success of our own efforts with respect to the commercialization of our products; and

the securing of, costs related to, and timing issues associated with, product manufacturing as well as sales and marketing activities.

If we fail to achieve announced milestones in the timeframes we announce and expect, the commercialization of oral octreotide and any future product candidates we may develop may be delayed and our business and results of operations may be harmed.

Oral octreotide and other products we may develop may not be commercially viable if we fail to obtain coverage and an adequate level of reimbursement for these products from governmental payors, including Medicare and Medicaid programs, private insurers, and other third-party payors. The market for oral octreotide and other products we may develop may also be limited by the indications for which their use may be reimbursed.

The availability of coverage and adequate levels of reimbursement by governmental and other third-party payors will affect the market for oral octreotide, if approved, and other products that we may develop. These third-party payors continually attempt to contain or reduce the costs of health care by challenging the prices charged for medical products and services and by applying value assessments to clinical outcomes using different safety and efficacy standards than used for marketing approval by the FDA and the EMA.

In the United States, in the event that oral octreotide is approved, we will seek to obtain reimbursement for oral octreotide from third-party payors. In recent years, through legislative and regulatory actions, the federal government has made substantial changes to various payment systems under the Medicare program. Comprehensive reforms to the U.S. healthcare system were recently enacted. These reforms could significantly reduce payments from Medicare and Medicaid over the next 10 years. Reforms or other changes to these payment systems, including modifications to the conditions on qualification for payment, bundling of payments or the imposition of enrollment limitations on new providers, may change the availability, methods and rates of reimbursements from governmental payors, private insurers and other third-party payors for oral octreotide and our other potential products. Some of these changes and proposed changes could result in reduced reimbursement rates for oral octreotide and our other potential products, which would adversely affect our business strategy, operations and financial results.

In the United States, no uniform policy of coverage and reimbursement for products exists among third-party payors. As a result, obtaining coverage and reimbursement approval of a product from a governmental or other third-party payor is a time-consuming and costly process that could require us to provide to each payor supporting scientific, clinical and cost-effectiveness data for the use of our products on a payor-by-payor basis, with no assurance that coverage and adequate reimbursement will be obtained. Even if we obtain coverage for a given product, the resulting reimbursement payment rates might not be adequate for us to achieve or sustain profitability or may require co-payments that patients find unacceptably high.

We expect that private insurers will consider the efficacy, cost effectiveness and safety of oral octreotide, if approved, in determining whether to provide reimbursement for oral octreotide and at what level. Obtaining these additional approvals for reimbursement can be a time-consuming and expensive process. Even if we receive regulatory approval to market oral octreotide, our business would be harmed if we do not receive approval of reimbursement of oral octreotide from third-party payors on a timely or satisfactory basis. Medicare does not cover particular drugs if it determines that they are not reasonable and necessary for its beneficiaries. Limitations on coverage could also be imposed at the local Medicare carrier level or by fiscal intermediaries. Our business could be harmed if Medicare, local Medicare carriers or fiscal intermediaries were to make such a determination and deny or limit the

reimbursement of oral octreotide.

Our business could also be harmed if governments, private insurers, Medicare, Medicaid or other reimbursing bodies or payors limit the indications for which oral octreotide will be reimbursed to a smaller set than we

believe it is safe and effective in treating, or establish a limitation on the frequency with which oral octreotide may be administered that is less often than we believe would be safe and effective, or establish a limitation on dose that is lower than we believe would be safe and effective.

We expect to experience pricing pressures in connection with the sale of oral octreotide and any future product candidates we may develop due to healthcare reforms, as well as the trend toward programs aimed at reducing health care costs, the increasing influence of health maintenance organizations, additional legislative proposals, and the economic health of companies. If coverage and reimbursement for our products are unavailable, or are limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be harmed.

In Europe and many other foreign countries, the pricing of prescription pharmaceuticals is subject to governmental control, and each country has a different reviewing body that evaluates reimbursement dossiers submitted by holders of marketing authorizations for new drugs. That governing body then makes recommendations as to whether or not the drug should be reimbursed. In these countries, pricing negotiations with governmental authorities can take 12 months or longer after the receipt of regulatory approval. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidate, such as oral octreotide, to other available therapies.

The longer term growth of our business depends on our efforts to leverage our TPE platform to expand our portfolio of product candidates, which may require substantial financial resources and may ultimately be unsuccessful.

The longer term growth of our business depends upon our ability to utilize our proprietary Transient Permeability Enhancer, or TPE, technology platform to develop and commercialize oral forms of therapies that are currently only available in injectable or other non-absorbable forms. In addition to the development and commercialization of oral octreotide, we intend to pursue development of other product candidates. We may never be able to identify other peptide drugs or poorly absorbed small-molecule drugs that we can successfully develop into product candidates utilizing our TPE platform, let alone receive regulatory approval of such product candidates.

A significant portion of the research that we are conducting involves new technologies. Research programs to identify new disease targets and product candidates require substantial technical, financial and human resources whether or not we ultimately identify any product candidates. Our research programs may initially show promise in identifying potential product candidates, yet fail to yield product candidates for clinical development for a number of reasons, including:

- the research methodology used may not be successful in identifying potential product candidates; or
- potential product candidates may on further study be shown to have harmful side effects or other characteristics that indicate they are unlikely to be effective drugs.

There are a number of FDA requirements that we must satisfy before we can commence a clinical trial. If we are able to identify additional potential product candidates, satisfaction of these regulatory requirements will entail substantial time, effort and financial resources. We may never satisfy these requirements. Any time, effort and financial resources we expend on development of other product candidates may impair our ability to continue development and commercialization of oral octreotide for the treatment of acromegaly and other indications, and we may never commence clinical trials of such development programs despite expending significant resources in pursuit of their

development. If we do commence clinical trials of other product candidates, these product candidates may never demonstrate sufficient safety and efficacy to be approved by the FDA or other regulatory authorities. If any of these events occur, we may be forced to abandon our development efforts for such program or programs, which would harm our business.

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Our ability to develop a viable pipeline of potential future products may require us to enter into license agreements with third parties, and we may not be successful in negotiating the necessary agreements.

Although we are currently seeking to develop our pipeline of future potential products through internal research programs, we may also consider expanding the scope of our pipeline by licensing injectable or poorly absorbed drugs from third parties, with the goal of converting these drugs into novel oral forms of therapies using our TPE platform.

We may, however, be unable to license or acquire suitable product candidates from third parties, for a number of reasons. In particular, the licensing and acquisition of pharmaceutical products is a competitive area. Several more established companies are also pursuing strategies to license or acquire products in the somatostatin analog field. These established companies may have a competitive advantage over us due to their size, cash resources and greater clinical development and commercialization capabilities. Other factors that may prevent us from licensing or otherwise acquiring suitable product candidates include the following:

- we may be unable to license or acquire the relevant technology on terms that would allow us to make an appropriate return from the product;
- companies that perceive us to be their competitors may be unwilling to assign or license their product rights to us; or
- we may be unable to identify suitable products or product candidates within our areas of expertise.

Additionally, we may not have sufficient human and financial resources to develop suitable potential product candidates both through internal research programs and by obtaining rights from third parties, thereby limiting our ability to develop a diverse product portfolio. If we are unable to develop such a portfolio, our business may suffer.

We may be unable to obtain orphan drug designation or exclusivity for future product candidates we may develop. If our competitors are able to obtain orphan drug exclusivity for their products that are the same as our product candidates, we may not be able to have competing products approved by the applicable regulatory authority for a significant period of time.

Our oral octreotide product candidate has been granted orphan designation in the United States and the European Union for the oral treatment of acromegaly. Regulatory authorities in some jurisdictions, including the United States and the European Union, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act of 1983, the FDA may designate a product candidate as an orphan drug if it is intended to treat a rare disease or condition, which is generally defined as having a patient population of fewer than 200,000 individuals diagnosed annually 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. In the European Union, the European Commission, after reviewing the opinion of the EMA s Committee for Orphan Medicinal Products, or COMP, grants orphan drug designation to promote the development of products that are intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition affecting not more than five in 10,000 persons in the European Union. Additionally, designation is granted for products intended for the diagnosis, prevention or treatment of a life-threatening, seriously debilitating or serious and chronic condition when, without incentives, it is unlikely that sales of the drug in the European Union would be sufficient to justify the necessary investment in developing the product candidate. Even if we request orphan drug designation for

any future product candidates we may develop, there can be no assurances that the FDA or the European Commission will grant any of these product candidates such designation. Additionally, the designation by the FDA of any of our product candidates as an orphan drug does not guarantee that the FDA will accelerate regulatory review of or ultimately approve that product candidate.

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

the United States and 10 years in Europe. The European exclusivity period can be reduced to six years if a product no longer meets the criteria for orphan drug designation or if the product is sufficiently profitable so that market exclusivity is no longer justified. Orphan drug exclusivity may be lost if the FDA or EMA 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.

Even though we have obtained orphan drug exclusivity for oral octreotide in acromegaly and may obtain orphan drug exclusivity for oral octreotide in other indications or for future product candidates we may develop, that exclusivity may not effectively protect the product candidate from competition because different drugs can be approved for the same condition and the same drugs can be approved for different indications and might then be used off-label in our approved indication. In the United States, even after an orphan drug is approved, the FDA can subsequently approve another drug for the same condition if the FDA concludes that the later drug is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care. In addition, if one of our product candidates that receives an orphan drug designation is approved for a particular indication or use within the rare disease or condition, the FDA may later approve the same drug for additional indications or uses within that rare disease or condition that are not protected by our exclusive approval. As a result, if our product is approved and receives orphan drug status, the FDA can still approve other drugs for use in treating the same indication or disease covered by our product, which could create a more competitive market for us.

Our relationships with customers and third-party payors will be subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.

Healthcare providers, physicians and third-party payors will play a primary role in the recommendation and prescription of oral octreotide and any future product candidates we may develop for which we obtain marketing approval. Our arrangements with third-party payors and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may affect the business or financial arrangements and relationships through which we would market, sell and distribute our products. Even though we do not and will not control referrals of healthcare services or bill directly to Medicare, Medicaid or other third-party payors, federal and state healthcare laws and regulations pertaining to fraud and abuse and patients rights are and will be applicable to our business. Restrictions under applicable federal and state healthcare laws and regulations that may affect our operations and expose us to areas of risk including the following:

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

- federal civil and criminal false claims laws and civil monetary penalty laws, which impose criminal and civil penalties, including through civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, including the Medicare and Medicaid programs, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government;

the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program and also created federal criminal laws that prohibit knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statements in connection with the delivery of or payment for healthcare benefits, items or services;

HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, which also imposes obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;

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The Patient Protection and Affordable Care Act, or the Affordable Care Act, which requires certain manufacturers of drugs, devices, biologics and medical supplies that are reimbursable under Medicare, Medicaid or Children s Health Insurance Program to report annually to Centers for Medicare and Medicaid Services, or CMS, information related to payments and other transfers of value to physicians and teaching hospitals, and ownership and investment interests held by physicians and their immediate family members and applicable group purchasing organizations; and

analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, which may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers; some state laws require pharmaceutical companies to comply with the pharmaceutical industry s voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government and may require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures; and state and foreign laws govern the privacy and security of health information in specified circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Efforts to ensure that our business arrangements with third parties are compliant with applicable healthcare laws and regulations will involve the expenditure of appropriate, and possibly significant, resources. Nonetheless, it is possible that governmental authorities will conclude that our business practices may 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 are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, disgorgement, imprisonment, exclusion from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations. If any physicians or other healthcare providers or entities with whom we expect to do business are found to not be in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

Legislative or regulatory reform of the health care system in the United States and foreign jurisdictions may adversely impact our business, operations or financial results.

Our industry is highly regulated and changes in law may adversely impact our business, operations or financial results. In particular, in March 2010, the Affordable Care Act and a related reconciliation bill were signed into law. This legislation changes the current system of healthcare insurance and benefits intended to broaden coverage and control costs. The law also contains provisions that will affect companies in the pharmaceutical industry and other healthcare related industries by imposing additional costs and changes to business practices. Provisions affecting pharmaceutical companies include the following:

mandatory rebates for drugs sold into the Medicaid program have been increased, and the rebate requirement has been extended to drugs used in risk-based Medicaid managed care plans.

the definition of average manufacturer price was revised for reporting purposes, which could increase the amount of Medicaid drug rebates by state.

the 340B Drug Pricing Program under the Public Health Service Act has been extended to require mandatory discounts for drug products sold to certain critical access hospitals, cancer hospitals and other covered entities.

pharmaceutical companies are required to offer discounts on brand-name drugs to patients who fall within the Medicare Part D coverage gap, commonly referred to as the donut hole.

pharmaceutical companies are required to pay an annual non-tax deductible fee to the federal government based on each company s market share of prior year total sales of branded products to certain federal healthcare programs. The aggregated industry-wide fee is expected to total $28 billion through 2019. Since we expect our branded pharmaceutical sales to constitute a small portion of the

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total federal health program pharmaceutical market, we do not expect this annual assessment to have a material impact on our financial condition.

Despite initiatives to invalidate the Affordable Care Act, the U.S. Supreme Court has upheld certain key aspects of the legislation, including the requirement that all individuals maintain health insurance coverage or pay a penalty, referred to as the individual mandate, and a key provision of the Affordable Care Act, which provides federal premium tax credits to individuals purchasing coverage through health insurance exchanges. Additionally, there are legal challenges to the Affordable Care Act in lower courts on other grounds. We will not know the full effects of the Affordable Care Act until applicable federal and state agencies issue regulations or guidance under the law. Although it is too early to determine the effect of the Affordable Care Act, the law appears likely to continue the pressure on pharmaceutical pricing, especially under the Medicare program, and may also increase our regulatory burdens and operating costs.

The full effects of the U.S. healthcare reform legislation cannot be known until the new law is fully implemented through regulations or guidance issued by CMS and other federal and state healthcare agencies. The financial impact of the U.S. healthcare reform legislation over the next few years will depend on a number of factors including but not limited to the policies reflected in implementing regulations and guidance and changes in sales volumes for products affected by the new system of rebates, discounts and fees.

In addition, other legislative changes have been proposed and adopted in the United States since the Affordable Care Act was enacted. On August 2, 2011, the Budget Control Act of 2011 among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation s automatic reduction to several government programs. This includes aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, starting in 2013, which will remain in effect until 2024 unless additional congressional action is taken. On January 2, 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, increased the statute of limitations period for the government to recover overpayments to providers from three to five years. We expect that additional 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, and in turn could significantly reduce the projected value of certain development projects and reduce our profitability.

In addition, in September 2007, the Food and Drug Administration Amendments Act of 2007 was enacted giving the FDA enhanced post-marketing authority including the authority to require post-marketing studies and clinical trials, labeling changes based on new safety information and compliance with risk evaluations and mitigation strategies approved by the FDA. The FDA s exercise of this authority could result in delays or increased costs during product development, clinical trials and regulatory review, increased costs to ensure compliance with post-approval regulatory requirements and potential restrictions on the sale and/or distribution of approved products. Other legislative and regulatory initiatives have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. For example, the Drug Supply Chain Security Act of 2013 imposes new obligations on manufacturers of certain pharmaceutical products related to product tracking and tracing. We do not know whether additional legislative changes will be enacted, or whether the FDA regulations, guidance documents or interpretations will be changed, or what the impact of such changes on the marketing approvals of oral octreotide, if any, may be. In addition, increased scrutiny by Congress of the FDA s approval process may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post-marketing testing and other requirements.

Further, in some foreign jurisdictions, including the European Union and Canada, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental

authorities can take 12 months or longer after the receipt of regulatory approval and product launch. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that

compares the cost-effectiveness of oral octreotide and any future product candidate we may develop to other available therapies. Our business could be harmed if reimbursement of our products is unavailable or limited in scope or amount or if pricing is set at unsatisfactory levels.

Moreover, we cannot predict what healthcare reform initiatives may be adopted in the future. Further, federal and state legislative and regulatory developments are likely, and we expect ongoing initiatives in the United States to increase pressure on drug pricing. Such reforms could have an adverse effect on anticipated revenues from oral octreotide and any other product candidates that we may successfully develop and for which we may obtain regulatory approval and may affect our overall financial condition and ability to develop product candidates.

We may not be able to maintain our current product liability coverage, and, even if we do, our coverage may not be adequate to cover any or all liabilities that we may incur, which could decrease our cash and harm our business.

We currently have $10.0 million in product liability insurance coverage in the aggregate, which may not be adequate to cover any or all liabilities that we may incur. Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise. We intend to expand our product liability insurance coverage to include the sale of commercial products if we obtain marketing approval of oral octreotide and any future product candidates we may develop, but we may be unable to obtain commercially reasonable product liability insurance for our product candidates, if approved for marketing. Large judgments have been awarded in class action lawsuits based on drugs that had unanticipated side effects. A successful product liability claim or series of claims brought against us, particularly if judgments exceed our insurance coverage, could decrease our cash and harm our business. In addition, we may not be able to maintain sufficient insurance coverage at an acceptable cost or otherwise to protect against potential product liability claims, which could prevent or inhibit the commercial production and sale of our products.

Additionally, if any claims are brought against us, even if we are fully covered by insurance, we may suffer harm such as adverse publicity. We also could suffer diversion of attention of technical and management personnel and incur substantial costs in resolving disputes, including litigation, with our insurance provider regarding coverage.

Risks Related to Our Reliance on Third Parties

We are, and expect to be for the foreseeable future, dependent on a limited number of third parties to manufacture oral octreotide, and our commercialization of oral octreotide could be halted, delayed or made less profitable if those third parties fail to pass inspections by the FDA or comparable foreign regulatory authorities, fail to provide us with sufficient quantities of oral octreotide or fail to do so at acceptable quality levels or prices or on a timely basis.

We do not currently have, nor do we plan to acquire, the capability or infrastructure to manufacture the API in oral octreotide for use in our clinical trials or for commercial product, if regulatory approvals are obtained. We have qualified Novetide Ltd., a subsidiary of Teva Pharmaceuticals Industries Ltd., in Israel, and Bachem Americas Inc., in the United States, as suppliers of the generic API, octreotide acetate. All excipients, or substances formulated together with the API, used in manufacture of oral octreotide are readily available. The octreotide API is formulated with our TPE technology and filled into capsules and enteric-coated by Lyophilization Services of New England Inc. in Bedford, NH and Encap Drug Delivery, a division of Capsugel, or Encap, in Livingston, Scotland.

The facilities used by our contract manufacturers to manufacture oral octreotide must be evaluated by the FDA pursuant to inspections that will be conducted following acceptance of our NDA by the FDA for filing. We do not control the manufacturing process of, and are completely dependent on, our contract manufacturing partners for

compliance with cGMPs for manufacture of both active drug substances and finished drug products. These cGMP regulations cover all aspects of the manufacturing, testing, quality control and record keeping relating to

oral octreotide. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or others, we will not be able to secure and/or maintain regulatory approval of our product candidate being manufactured at their manufacturing facilities. If the FDA or a comparable foreign regulatory authority finds deficiencies at these facilities and does not approve our NDA for oral octreotide or if it withdraws any such approval in the future, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory approval of or market oral octreotide, if approved.

Our contract manufacturers will be subject to ongoing periodic unannounced inspections by the FDA and corresponding state and foreign agencies for compliance with cGMPs and similar regulatory requirements. We do not have control over our contract manufacturers compliance with these regulations and requirements. Failure by any of our contract manufacturers to comply with applicable regulations could result in sanctions being imposed on us, including fines, injunctions, civil penalties, failure to grant approval to market oral octreotide, delays, suspensions or withdrawals of approvals, operating restrictions and criminal prosecutions, any of which could harm our business. In addition, we have no control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. Failure by our contract manufacturers to comply with or maintain any of these requirements could impair our ability to develop, obtain regulatory approval of or market oral octreotide.

If, for any reason, these third parties are unable or unwilling to perform, we may not be able to terminate our agreements with them, and we may not be able to locate alternative manufacturers or formulators or enter into favorable agreements with them and we cannot be certain that any such third parties will have the manufacturing capacity to meet future requirements. If these manufacturers or any alternate manufacturer of finished drug product experiences any significant difficulties in its respective manufacturing processes for our API or finished oral octreotide product or should cease doing business with us, we could experience significant interruptions in the supply of oral octreotide or may not be able to create a supply of oral octreotide at all. Were we to encounter manufacturing issues, our ability to produce a sufficient supply of oral octreotide might be negatively affected. Our inability to coordinate the efforts of our third-party manufacturing partners, or the lack of capacity available at our third-party manufacturing partners, could impair our ability to supply oral octreotide at required levels. Because of the significant regulatory requirements that we would need to satisfy in order to qualify a new bulk or finished product manufacturer, if we face these or other difficulties with our current manufacturing partners, we could experience significant interruptions in the supply of oral octreotide if we decided to transfer the manufacture of oral octreotide to one or more alternative manufacturers in an effort to deal with the difficulties.

Any manufacturing problem or the loss of a contract manufacturer could be disruptive to our operations and result in lost sales. Additionally, we rely on third parties to supply the raw materials needed to manufacture our potential products. Any reliance on suppliers may involve several risks, including a potential inability to obtain critical materials and reduced control over production costs, delivery schedules, reliability and quality. Any unanticipated disruption to future contract manufactures caused by problems at suppliers could delay shipment of oral octreotide, increase our cost of goods sold and result in lost sales.

We cannot guarantee that our current manufacturing and supply partners or any alternative service providers will be able to reduce the costs of commercial scale manufacturing of oral octreotide over time. If the manufacturing costs of oral octreotide remain at current levels, these costs may significantly impact our operating results. In order to reduce costs, we may need to develop and implement process improvements. However, in order to do so, we will need, from time to time, to notify or make submissions with regulatory authorities, and the improvements may be subject to approval by such regulatory authorities. We cannot be sure that we will receive these necessary approvals or that these approvals will be granted in a timely fashion. We also cannot guarantee that we will be able to enhance and optimize output in our commercial manufacturing process. If we cannot enhance and optimize output, we may not be able to

reduce our costs over time.

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If our third-party manufacturers use hazardous and biological materials in a manner that causes injury or violates applicable law, we may be liable for damages.

Our research and development activities involve the controlled use of potentially hazardous substances, including chemical and biological materials by our third-party manufacturers. Our manufacturers are subject to federal, state and local laws and regulations in the United States governing medical, radioactive and hazardous materials. Although we believe that our manufacturers procedures for using, handling, storing and disposing of these materials comply with legally prescribed requirements, we cannot completely eliminate the risk of contamination or injury resulting from such materials. As a result of any such contamination or injury we may incur liability or local, city, state or federal authorities may curtail the use of these materials, interrupting our business operations. In the event of an accident, we could be held liable for damages or penalized with fines, and the liability could exceed our resources. Compliance with applicable environmental laws and regulations is expensive, and current or future environmental regulations may impair our research, development and production efforts, which could harm our business, prospects, financial condition or results of operations.

A key element of our strategy is to enter into licensing or collaboration agreements with respect to oral octreotide and future product candidates in certain territories. We may not be able to identify suitable collaborators and, even if we do, our dependence on such relationships may adversely affect our business.

Because we have limited resources, we may seek to enter into collaboration agreements with other pharmaceutical or biotechnology companies. Our strategy for commercializing oral octreotide and any future product candidates we may develop outside of the United States may depend on our ability to enter into agreements with collaborators to obtain assistance and funding for the development and potential commercialization of our product candidates in the territories in which we may seek to partner. Despite our efforts, we may be unable to secure collaborative licensing or other arrangements that are necessary for us to further develop and commercialize our product candidates. Supporting diligence activities conducted by potential collaborators and negotiating the financial and other terms of a collaboration agreement are long and complex processes with uncertain results. Even if we are successful in entering into one or more collaboration agreements, collaborations may involve greater uncertainty for us, as we have less control over certain aspects of our collaborative programs than we do over our proprietary development and commercialization programs.

Any failure by our partners to perform their obligations or any decision by our partners to terminate these agreements could negatively impact our ability to successfully develop, obtain regulatory approvals for and commercialize our product candidates. In the event we grant exclusive rights to such partners, we could be precluded from potential commercialization of our product candidates within the territories in which we have a partner. In addition, any termination of our collaboration agreements will terminate any funding we may receive under the relevant collaboration agreement and may impair our ability to fund further development efforts and our progress in our development programs. For example, in July 2014, Roche elected to terminate a license agreement with us for oral octreotide. As a result, we assumed responsibility for the further development and commercialization of oral octreotide and will receive no additional funding from Roche for this purpose.

Further, our potential future collaborators may develop alternative products or pursue alternative technologies either on their own or in collaboration with others, including our competitors, and the priorities or focus of our collaborators may shift such that our product candidates receive less attention or resources than we would like, or they may be terminated altogether. Any such actions by our potential future collaborators may harm our business prospects and ability to earn revenues. In addition, we could have disputes with our potential future collaborators, such as the interpretation of terms in our agreements. Any such disagreements could lead to delays in the development or commercialization of our product candidates or could result in time-consuming and expensive litigation or arbitration,

which may not be resolved in our favor.

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We rely, and will rely in the future, on third parties to conduct our nonclinical studies and clinical trials. If these third parties do not appropriately carry out their contractual duties, fail to conduct high-quality studies or meet expected deadlines, regulatory approval and commercialization of oral octreotide or any future candidates we may develop could be delayed or not obtained at all.

We do not have the ability to conduct all of our clinical trials independently. We will continue to rely on third parties, including clinical investigators, third-party CROs and consultants, to monitor, manage data for, and execute our ongoing nonclinical and planned clinical programs for oral octreotide and other potential product candidates, and we control only some aspects of their activities. Because we rely on third parties, our internal capacity to perform these functions is limited. We currently have a small number of employees, which limits the internal resources we have available to identify and monitor our third-party providers. Nevertheless, we are responsible for ensuring that each of our nonclinical studies and clinical trials are conducted in accordance with the applicable protocol and legal, regulatory and scientific requirements and standards, including, for example, Good Laboratory Practices, or GLPs, the Animal Welfare Act and Good Clinical Practices, or GCPs. Our reliance on third parties does not relieve us of our regulatory responsibilities. Regulatory authorities enforce GCPs through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any of these third parties fail to comply with applicable GCPs, the clinical data generated in our clinical trials may be deemed unreliable and the relevant regulatory authorities may require us to perform additional clinical trials in support of our marketing applications. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials comply with GCP requirements. Failure to comply with these regulations may require us to repeat nonclinical studies and clinical trials, which would delay the regulatory approval process.

The third parties conducting our nonclinical studies and clinical trials are not our employees, and, we cannot control whether or not they devote sufficient time and resources to our ongoing clinical and nonclinical programs. To the extent we are unable to identify and successfully manage the performance of third-party service providers in the future, our business may be adversely affected. If these third parties do not successfully carry out their contractual duties or obligations or meet expected deadlines, or if the quality or accuracy of the data they obtain is compromised due to the failure to adhere to our protocols, regulatory requirements or for other reasons, our nonclinical studies and clinical trials may be extended, delayed or terminated and we may not be able to obtain regulatory approval of or successfully commercialize oral octreotide and any future product candidates we may develop. As a result, our results of operations and the commercial prospects for our product candidates could be harmed, our costs could increase and our ability to generate revenues could be delayed.

Risks Related to Our Financial Position and Capital Resources

We have incurred significant losses since our inception and anticipate that we will incur continued losses for the next several years and thus may never achieve or maintain profitability.

Since inception, we have incurred significant operating losses. Our net loss was $2.0 million for the year ended December 31, 2014 and $4.2 million for the three months ended March 31, 2015. We had net income of $36.2 million for the year ended December 31, 2013 and $2.1 million for the three months ended March 31, 2014, primarily the result of revenue recognized under the license agreement with Roche. As of March 31, 2015, we had an accumulated deficit of $85.8 million. We have no products approved for commercialization and have never generated any product revenue. We expect to incur increasing operating losses over the next several years. Past operating losses, combined with expected future operating losses, have had and will continue to have an adverse effect on our cash resources, stockholders equity and working capital. If we obtain regulatory approval of oral octreotide or any future product candidates, we may incur significant sales, marketing, in-licensing and outsourced manufacturing expenses, as well as continued research and development expenses. In addition, we expect our research and development expenses to

significantly increase in connection with our proposed Phase 3 clinical trial for oral octreotide for the treatment of acromegaly, and Phase 2 clinical trials for oral octreotide for the treatment of NETs and other indications, and as we explore additional product candidates for our drug pipeline. As a result, we expect to continue to incur significant and increasing operating losses for the foreseeable future. Because of the

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numerous risks and uncertainties associated with developing and commercializing 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 achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable could depress the value of our stock and impair our ability to raise capital, expand our business, maintain our development efforts, obtain regulatory approvals, diversify our product pipeline or continue our operations. A decline in the value of our company could also cause you to lose all or part of your investment.

We have not generated any revenue from any commercial products and may never be profitable.

Our ability to become profitable depends upon our ability to generate revenue. Unless and until marketing approval is obtained from either the FDA or EMA for oral octreotide or any future product candidates we may develop, we may not be able to generate sufficient revenue to attain profitability. In addition, our ability to generate profits after any FDA or EMA approval of our product candidates is subject to our ability to contract for the manufacture of commercial quantities of our product candidates at acceptable cost levels and establish sales and marketing capabilities or identify and enter into one or more strategic collaborations to effectively market and sell any approved product candidate.

Even if oral octreotide or any future product candidates is approved for commercial sale, any approved product candidate may not gain market acceptance or achieve commercial success. In addition, we would anticipate incurring significant costs associated with commercializing any approved product. We may not achieve profitability soon after generating product sales, if ever. If we are unable to generate product revenues, we will not become profitable and may be unable to continue operations without continued funding.

We have a limited operating history and no history of commercializing drugs, which may make it difficult for you to evaluate the success of our business to date and to assess our future viability.

Although we commenced operations in 2001, our operations to date have been largely focused on raising capital and developing oral octreotide, including undertaking nonclinical studies and conducting clinical trials. Oral octreotide is our only current product candidate for which we have conducted clinical trials and for oral octreotide we have completed only a single later-stage clinical trial to date. We have not yet demonstrated our ability to successfully complete additional later-stage clinical trials, obtain regulatory approvals, manufacture a commercial-scale drug or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful commercialization. Consequently, any predictions you make about our future success or viability may not be as accurate as they could be if we had a longer operating history or a history of successfully developing and commercializing drugs.

We may encounter unforeseen expenses, difficulties, complications, delays and other known or unknown factors in achieving our business objectives. We will need to transition at some point from a company with a development focus to a company capable of supporting commercial activities. We may not be successful in such a transition.

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We may need additional capital to support our growth, which may be difficult to obtain and restrict our operations and would result in additional dilution to our stockholders.

Our business will require additional capital that we have not yet secured. We expect that the net proceeds from this offering and our cash as of March 31, 2015 will fund our operating expenses and capital expenditure requirements through at least the end of 2016. During this period, we expect to seek regulatory approval of oral octreotide in the United States and, if this is granted, launch oral octreotide in the United States, initiate an additional Phase 3 clinical trial of oral octreotide to treat acromegaly required for European regulatory approval, continue clinical development plans for the use of oral octreotide in other indications, and conduct additional nonclinical studies to expand our product pipeline. However, the actual amount of funds that we will need will be determined by many factors, some of which are beyond our control, and we may need funds sooner than currently anticipated. These factors include but are not limited to:

- the status of our NDA for oral octreotide in acromegaly;
- the amount of our future operating losses;
- expenses relating to the commercialization of oral octreotide, if approved;
- if oral octreotide is approved, the level of success of its initial commercial launch in the United States;
- the timing of approvals, if any, of oral octreotide in additional jurisdictions; the need and cost of conducting additional clinical trials for oral octreotide and our other drug candidates;
- the amount of our research and development, marketing and general and administrative expenses;
- the extent to which we enter into, maintain, and derive revenues from licensing agreements, including agreements to out-license oral octreotide, research and other collaborations, joint ventures and other business arrangements;
- our success in integrating, technologies or companies that we may acquire; and
- regulatory changes and technological developments in our markets.

General market conditions or the market price of our common stock may not support capital-raising transactions, such as an additional public or private offering of our common stock or other securities. In addition, our ability to raise additional capital may be dependent upon our stock being quoted on The NASDAQ Global Select Market or upon obtaining stockholder approval. There can be no assurance that we will be able to satisfy the criteria for continued listing on The NASDAQ Global Select Market or that we will be able to obtain stockholder approval if it is necessary.

If we are unable to obtain additional funds on a timely basis or on terms favorable to us, even if our NDA for oral octreotide is approved, we may be required to cease or reduce further commercialization, to cease or reduce certain research and development projects, to sell some or all of our technology or assets or business units or to merge all or a portion of our business with another entity. In the event additional financing is needed or advisable, we may seek to fund our operations through the sale of equity securities, additional debt financing and strategic collaboration agreements. We cannot be sure that additional financing from any of these sources will be available when needed or that, if available, the additional financing will be obtained on terms favorable to us or our stockholders especially in light of the current difficult financial environment. If we raise additional funds by selling shares of our capital stock, the ownership interest of our current stockholders will be diluted. If we attempt to raise additional funds through strategic collaboration agreements, we may not be successful in obtaining collaboration agreements, or in receiving milestone or royalty payments under those agreements, or the terms of the debt may involve significant cash payment obligations as well as covenants and specific financial ratios that may restrict our ability to commercialize oral octreotide or any future product candidates or operate our business.

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 and collaboration, strategic and licensing arrangements. To the extent that we raise additional capital through the sale

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of equity or convertible debt securities, your ownership interest will be diluted, and the terms may include liquidation or other preferences that adversely affect your rights as a stockholder. Debt financing, if available, 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 alliance and licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies or product candidates, or grant licenses on terms that are not favorable to us.

Risks Related to Our Business and Industry

We depend on the knowledge and skill of our senior management and other key employees, and if we are unable to retain or if we fail to recruit additional highly skilled personnel, our business will be harmed.

Our ability to compete in the highly competitive pharmaceuticals industry depends in large part upon our ability to attract and retain highly qualified managerial, commercial, scientific and medical personnel. We are highly dependent on our management, commercial, scientific and medical personnel. In order to induce valuable employees to remain with us, we have provided employees with stock options that vest over time. The value to employees of stock options that vest over time is significantly affected by movements in our stock price that we cannot control and, together with our other compensation programs and benefits, may at any time be insufficient to counteract more lucrative offers from other companies.

We are highly dependent upon the principal members of our management team, including Mark Leuchtenberger, our Chief Executive Officer, Roni Mamluk, our Chief Development Officer, and Mark J. Fitzpatrick, our Chief Financial Officer. These executives have significant research and development, endocrine, regulatory industry, sales and marketing, operational, and/or corporate finance experience. The loss of any executive or other principal member of our management team would impair our ability to identify, develop and market new products and conduct successful operations.

In addition, our growth will require us to hire a significant number of qualified technical, commercial and administrative personnel. There is intense competition from other companies and research and academic institutions for qualified personnel in the areas of our activities. Other biopharmaceutical companies with which we compete for qualified personnel may have greater financial and other resources, different risk profiles, and a longer history in the industry than we do. They also may provide more diverse opportunities and better chances for career advancement. Some of these characteristics may be more appealing to high-quality candidates than what we have to offer. If we are unable to continue to attract and retain high-quality personnel, the rate and success at which we can develop and commercialize oral octreotide and any future product candidates we may develop would be impaired and could adversely affect our growth and financial performance.

We may acquire additional businesses or form strategic alliances in the future, and we may not realize the benefits of such acquisitions or alliances.

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 have difficulty in developing, manufacturing and marketing the products of a newly acquired company that enhances the performance of our combined businesses or product lines to realize value from expected synergies. We cannot assure that, following an acquisition, we will achieve the revenues or specific net income that justifies the acquisition.

Potential technological changes in our field of business create considerable uncertainty.

We are engaged in the biopharmaceutical field, which is characterized by extensive research efforts and rapid technological progress. New developments in research are expected to continue at a rapid pace in both industry

and academia. We cannot assure you that research and discoveries by others will not render some or all of our programs or product candidates uncompetitive or obsolete. The longer-term success of our business depends upon our ability to utilize our TPE platform to develop and commercialize oral forms of therapies that are currently only available in injectable or other non-absorbable forms. We cannot assure you that unforeseen problems will not develop with our TPE technology or applications or that any commercially feasible products will ultimately be developed by us.

Our employees, independent contractors, consultants, commercial partners, principal investigators, CROs and vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements, which could cause significant liability for us and harm our reputation.

We are exposed to the risk that our employees, independent contractors, consultants, commercial partners, principal investigators, CROs and vendors may engage in fraudulent conduct or other misconduct, including intentional failures to comply with FDA regulations or similar regulations of comparable foreign regulatory authorities, to provide accurate information to the FDA or comparable foreign regulatory authorities, to comply with manufacturing standards we have established, to comply with federal and state healthcare fraud and abuse laws and regulations and similar laws and regulations established and enforced by comparable foreign regulatory authorities, and to report financial information or data accurately or disclose unauthorized activities to us. The misconduct of our employees and contractors could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. Upon the consummation of this offering, we will have implemented a code of conduct and ethics for our directors, officers and employees, but it is not always possible to identify and deter such misconduct, and the precautions we take to detect and prevent this activity may not be effective 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 be in compliance with such 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 and results of operations, including the imposition of significant fines or other sanctions.

Our business and operations would suffer in the event of computer system failures, cyber-attacks on our systems or deficiency in our cyber security.

Despite the implementation of security measures, our internal computer systems, and those of third parties on which we rely, are vulnerable to damage from computer viruses, unauthorized access, malware, natural disasters, fire, terrorism, war and telecommunication, electrical failures, cyber-attacks or cyber-intrusions over the Internet, attachments to emails, persons inside our organization, or persons with access to systems inside our organization. The risk of a security breach or disruption, particularly through cyber-attacks or cyber intrusion, including by computer hackers, foreign governments, and cyber terrorists, has generally increased as the number, intensity and sophistication of attempted attacks and intrusions from around the world have increased. In addition, our systems safeguard important confidential personal data regarding patients enrolled in our clinical trials. If a disruption event were to occur and cause interruptions in our operations, it could result in a disruption of our drug development programs. For example, the loss of clinical trial data from completed, ongoing or planned clinical trials 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 inappropriate disclosure of confidential or proprietary information, we could incur liability and the further development oral octreotide and any future product candidates we may develop could be delayed.

Business disruptions could seriously harm our future revenues and financial condition and increase our costs and expenses.

Our operations could be subject to earthquakes, power shortages, telecommunications failures, water shortages, floods, hurricanes, typhoons, fires, extreme weather conditions, medical epidemics, military conflicts, acts of terrorism and other natural or man-made disasters or business interruptions. Some of our operations are in Israel, which has a history of certain conflicts. The occurrence of any business disruptions could seriously harm our

operations and financial condition and increase our costs and expenses. We rely on third-party manufacturers to produce oral octreotide. Our ability to obtain clinical supplies of oral octreotide could be disrupted if the operations of these suppliers are affected by a man-made or natural disaster or other business interruption, as we do not carry insurance to cover such risks.

Laws and regulations governing conduct of international operations may negatively impact our development, manufacture and sale of products outside of the United States and require us to develop and implement costly compliance programs.

As we have substantial operations in Israel and may seek to further expand our operations outside of the United States, we must comply with numerous laws and regulations in Israel and each other jurisdiction in which we plan to operate. The creation and implementation of international business practices compliance programs is costly and such programs are difficult to enforce, particularly where we must rely on third parties.

The Foreign Corrupt Practices Act, or FCPA, prohibits any U.S. individual or business from paying, offering, authorizing payment or offering of anything of value, directly or indirectly, to any foreign official, political party or candidate for the purpose of influencing any act or decision of the foreign entity 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 such companies to maintain books and records that accurately and fairly reflect all transactions of the corporation, including international subsidiaries, and to devise and maintain an adequate system of internal accounting controls for international operations. The anti-bribery provisions of the FCPA are enforced primarily by the DOJ. The Securities and Exchange Commission, or SEC, is involved with enforcement of the books and records provisions of the FCPA.

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 foreign nationals, of information classified for national security purposes, as well as certain products and technical data relating to those products. Our expanding presence outside of the United States will require us to dedicate additional resources to comply with these laws, and these laws may preclude us from developing, manufacturing, or selling oral octreotide and any future product candidates we may develop 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 penalties, including suspension or debarment from government contracting. Violation of the FCPA can result in significant civil and criminal penalties. Indictment alone under the FCPA can lead to suspension of the right to do business with the U.S. government until the pending claims are resolved. Conviction of a violation of the FCPA can result in long-term disqualification as a government contractor. The termination of a government contract or relationship as a result of our failure to satisfy any of our obligations under laws governing international business practices would have a negative impact on our operations and harm our reputation and ability to procure government contracts. Additionally, the SEC also may suspend or bar issuers from trading securities on U.S. exchanges for violations of the FCPA s accounting provisions.

Exchange rate fluctuations between the U.S. dollar and non-U.S. currencies may negatively affect our results of operations.

The U.S. dollar is our functional and reporting currency, however, a portion of our operations are currently conducted in Israel and most of the Israeli expenses are currently paid in New Israeli Shekels, or NIS. We also

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contract with CROs internationally, primarily for the execution of clinical trials and manufacturing activities. A portion of these transactions are settled in Euros or Great British Pounds, or GBPs. As a result, we are exposed to the risk that the NIS, Euro or GBP may appreciate relative to the U.S. dollar, or, if the NIS, Euro or GBP instead devalue relative to the U.S. dollar, that the relative inflation rate may exceed such rate of devaluation, or that the timing of such devaluation may lag behind the relative inflation. In any such event, the U.S. dollar cost of our operations in Israel and transactions with certain CROs would increase and our U.S. dollar-denominated results of operations would be adversely affected. To date, we have not engaged in hedging transactions. In the future, we may enter into currency hedging transactions to decrease the risk of financial exposure from fluctuations in the exchange rates of our principal operating currencies. These measures, however, may not adequately protect us from the material adverse effects of such fluctuations. If the U.S. dollar cost of our operations increases, our U.S. dollar-measured results of operations will be adversely affected. See Management s Discussion and Analysis of Financial Condition and Results of Operations Quantitative and Qualitative Disclosure About Market Risk.

Risks Related to Our Intellectual Property

If we are unable to protect our intellectual property rights or if our intellectual property rights are inadequate to protect our technology and product candidates, our competitors could develop and commercialize technology and drugs similar to ours, and our competitive position could be harmed.

Our commercial success will depend in large part on our ability to obtain and maintain patent and other intellectual property protection in the United States and other countries with respect to our proprietary technology and products. We rely on trade secret, patent, copyright and trademark laws, and confidentiality and other agreements with employees and third parties, all of which offer only limited protection. Our strategy is to seek patent protection for our product candidates and compositions, their methods of use and processes for their manufacture, and any other aspects of inventions that are commercially important to the development of our business.

The patent prosecution process is expensive and time-consuming, and we and any future licensors and licensees may not be able to apply for or prosecute patents on certain aspects of our product candidates or delivery technologies at a reasonable cost, in a timely fashion, or at all. We may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the rights to patents licensed to third parties. Therefore, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business. It is also possible that we or any future licensors or licensees, will fail to identify patentable aspects of inventions made in the course of development and commercialization activities before it is too late to obtain patent protection on them. Therefore, our patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business. It is possible that defects of form in the preparation or filing of our patents or patent applications may exist, or may arise in the future, such as with respect to proper priority claims, inventorship, claim scope or patent term adjustments. If any future licensors or licensees, are not fully cooperative or disagree with us as to the prosecution, maintenance, or enforcement of any patent rights, such patent rights could be compromised and we might not be able to prevent third parties from making, using, and selling competing products. If there are material defects in the form or preparation of our patents or patent applications, such patents or applications may be invalid or unenforceable. Moreover, our competitors may independently develop equivalent knowledge, methods, and know-how. Any of these outcomes could impair our ability to prevent competition from third parties, which may have an adverse impact on our business, financial condition, and operating results.

The patent positions of biotechnology and pharmaceutical companies generally are highly uncertain, involve complex legal and factual questions and have in recent years been the subject of much litigation. As a result, the issuance, scope, validity, enforceability and commercial value of any patents that issue, are highly uncertain. The steps we have taken to protect our proprietary rights may not be adequate to preclude misappropriation of our proprietary

information or infringement of our intellectual property rights, both inside and outside the United States. Further, the examination process may require us to narrow the claims of pending patent applications,

which may limit the scope of patent protection that may be obtained if these applications issue. The rights that may be granted under future issued patents may not provide us with the proprietary protection or competitive advantages we are seeking. If we are unable to obtain and maintain patent protection for our technology and products, or if the scope of the patent protection obtained is not sufficient, our competitors could develop and commercialize technology and products similar or superior to ours, and our ability to successfully commercialize our technology and products may be impaired.

With respect to patent rights, we do not know whether any of our patent applications will result in issued patents or, if any of our patent applications do issue, whether such patents will protect our technology and drugs, in whole or in part, or whether such patents will effectively prevent others from commercializing competitive technologies and products. There is no guarantee that any of our issued or granted patents will not later be found invalid or unenforceable. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing or in some cases not at all, until they are issued as a patent. Therefore we cannot be certain that we were the first to make the inventions claimed in our pending patent applications, that we were the first to file for patent protection of such inventions, or that we have found all of the potentially relevant prior art relating to our patents and patent applications that could invalidate one or more of our patents or prevent one or more of our patent applications from issuing. Even if patents do successfully issue and even if such patents cover our product candidates, third parties may initiate oppositions, interferences, re-examinations, post-grant reviews, *inter partes* reviews, nullification or derivation actions in court or before patent offices or similar proceedings challenging the validity, enforceability, or scope of such patents, which may result in the patent claims being narrowed or invalidated. Furthermore, even if they are unchallenged, our patents and patent applications may not adequately protect our intellectual property, provide exclusivity for our product candidates, or prevent others from designing around our claims. Any of these outcomes could impair our ability to prevent competition from third parties.

Furthermore, the issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our owned and licensed patents may be challenged in the courts or patent offices in the United States and abroad. Such challenges may result in loss of exclusivity or freedom to operate or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical technology and drugs, or limit the duration of the patent protection of our technology and drugs. Given the amount of time required for the development, testing and regulatory review of new drug candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing drugs similar or identical to ours.

We may become 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. In a patent litigation in the United States, defendant counterclaims alleging invalidity or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, for example, lack of novelty, obviousness or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO, or made a misleading statement, during prosecution. The outcome following legal assertions of invalidity and unenforceability during patent litigation is unpredictable. A court may decide that a patent of ours or our licensors is not valid or is unenforceable, 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. With respect to the validity question, for example, we cannot be certain that

no invalidating prior art exists. An adverse result in any litigation or defense proceedings could put one or more of our patents at risk of being invalidated, found unenforceable, or interpreted narrowly, and it could put our patent applications at risk of not issuing. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee

resources from our business. If a defendant were to prevail on a legal assertion of invalidity or unenforceability, we would lose at least part, and perhaps all, of the patent protection on one or more of our products or certain aspects of our platform technology. Such a loss of patent protection could have an adverse impact on our business.

Interference proceedings brought by the USPTO may be necessary to determine the priority of inventions with respect to our patents and patent applications or those of our collaborators or licensors. An unfavorable outcome could require us to cease using the technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if a prevailing party does not offer us a license on terms that are acceptable to us. Litigation or interference proceedings may fail and, even if successful, may result in substantial costs and distraction of our management and other employees. We may not be able to prevent, alone or with our licensors, misappropriation of our proprietary 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. In addition, there could 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 substantial adverse effect on the price of our common stock.

Moreover, we may be subject to a third-party pre-issuance submission of prior art to the USPTO or other foreign patent offices, or become involved in opposition, derivation, reexamination, *inter partes* review, post-grant review or interference proceedings challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or drugs and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize drugs without infringing third-party patent rights. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop, or commercialize current or future product candidates.

We may not be able to protect our intellectual property rights throughout the world.

Filing, prosecuting and defending patents on oral octreotide and our TPE platform throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States may be less extensive than those in the United States. In addition, the laws and practices of some foreign countries do not protect intellectual property rights, especially those relating to life sciences, to the same extent as federal and state laws in the United States. For example, novel formulations of existing drugs and manufacturing processes may not be patentable in certain jurisdictions, and the requirements for patentability may differ in certain countries, particularly developing countries. Also, some foreign countries, including European Union countries, India, Japan and China, have compulsory licensing laws under which a patent owner may be compelled under certain circumstances to grant licenses to third parties. Consequently, we may have limited remedies if patents are infringed or if we are compelled to grant a license to a third party, and 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 into or within the United States or other jurisdictions. This could limit our potential revenue opportunities. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products, and may export otherwise infringing products to territories where we have patent protection, but where enforcement is not as strong as that in the United States. These products may compete with our products in jurisdictions where we do not have any issued patents and our patent claims or other intellectual property rights may not be effective or sufficient to prevent them from competing with us in these jurisdictions. Accordingly, our efforts to enforce intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from our intellectual property. We may not prevail in any lawsuits that we initiate in these foreign countries and the damages or other remedies awarded, if any, may not be commercially meaningful.

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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.

Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on patents and applications are required to be paid to the USPTO and various governmental patent agencies outside of the United States in several stages over the lifetime of the patents and applications. The USPTO and various non-U.S. governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process and after a patent has issued. There are situations in which non-compliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction.

Third parties may initiate legal proceedings alleging that we are infringing their intellectual property rights, the outcome of which could be uncertain and could harm our business.

While our product candidates are in nonclinical studies and clinical trials, we believe that the use of our product candidates in these nonclinical studies and clinical trials falls within the scope of the exemptions provided by 35 U.S.C. Section 271(e) in the United States, which exempts from patent infringement liability activities reasonably related to the development and submission of information to the FDA. As our product candidates progress toward commercialization, the possibility of a patent infringement claim against us increases. There can be no assurance that our product candidates do not infringe other parties patents or other proprietary rights, however, and competitors or other parties may assert that we infringe their proprietary rights in any event. We may become party to, or threatened with, future adversarial proceedings or litigation regarding intellectual property rights with respect to our product candidates, including interference or derivation proceedings before the USPTO. Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future. If we are found to infringe a third party s intellectual property rights, we could be required to obtain a license from such third party to continue commercializing our product candidates. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if a license can be obtained on acceptable terms, the rights may be non-exclusive, which could give our competitors access to the same technology or intellectual property rights licensed to us. If we fail to obtain a required license, we may be unable to effectively market product candidates based on our technology, which could limit our ability to generate revenue or achieve profitability and possibly prevent us from generating revenue sufficient to sustain our operations. Alternatively, we may need to redesign our infringing products, which may be impossible or require substantial time and monetary expenditure. Under certain circumstances, we could be forced, including by court order, to cease commercializing our product candidates. In addition, in any such proceeding or litigation, we could be found liable for substantial monetary damages, potentially including treble damages and attorneys fees, if we are found to have willfully infringed. A finding of infringement could prevent us from commercializing our product candidates or force us to cease some of our business operations, which could harm our business. Any claims by third parties that we have misappropriated their confidential information or trade secrets could have a similar negative impact on our business.

The cost to us in defending or initiating any litigation or other proceeding relating to patent or other proprietary rights, even if resolved in our favor, could be substantial, and litigation would divert our management s attention. Some of our competitors may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could delay our research and development efforts and limit our ability to continue our operations.

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Oral octreotide or any future products we may develop may infringe the intellectual property rights of others, which could increase our costs and delay or prevent our development and commercialization efforts.

Our success depends in part on avoiding infringement of the proprietary technologies of others. The pharmaceutical industry has been characterized by frequent litigation regarding patent and other intellectual property rights. Identification of third-party patent rights that may be relevant to our proprietary technology is difficult because patent searching is imperfect due to differences in terminology among patents, incomplete databases and the difficulty in assessing the meaning of patent claims. Additionally, because patent applications are maintained in secrecy until the application is published, we may be unaware of third-party patents that may be infringed by commercialization of oral octreotide or any future product candidate. There may be certain issued patents and patent applications claiming subject matter that we may be required to license in order to research, develop, or commercialize oral octreotide, and we do not know if such patents and patent applications would be available to license on commercially reasonable terms, or at all. Any claims of patent infringement asserted by third parties would be time-consuming and may:

result in costly litigation;

divert the time and attention of our technical personnel and management;

cause product development or commercialization delays;

prevent us from commercializing a product until the asserted patent expires or is held finally invalid or not infringed in a court of law;

require us to cease or modify our use of the technology and/or develop non-infringing technology; or

require us to enter into royalty or licensing agreements.

Although no third party has asserted a claim of infringement against us, others may hold proprietary rights that could prevent oral octreotide from being marketed. Any patent-related legal action against our collaborators or us claiming damages and seeking to enjoin commercial activities relating to oral octreotide or our processes could subject us to potential liability for damages and require us to obtain a license to continue to manufacture or market oral octreotide or any future product candidates. We cannot predict whether we would prevail in any such actions or that any license required under any of these patents would be made available on commercially acceptable terms, if at all. In addition, we cannot be sure that we could redesign oral octreotide or any future product candidates or processes to avoid infringement, if necessary. Accordingly, an adverse determination in a judicial or administrative proceeding, or the failure to obtain necessary licenses, could prevent us from developing and commercializing oral octreotide or a future product candidate, which could harm our business, financial condition and operating results.

A number of companies, including several major pharmaceutical companies, have conducted research on pharmaceutical uses of somatostatin analogs, which resulted in the filing of many patent applications related to this research. If we were to challenge the validity of these or any issued U.S. patent in court, we would need to overcome a statutory presumption of validity that attaches to every U.S. patent. This means that, in order to prevail, we would

have to present clear and convincing evidence as to the invalidity of the patent s claims. If we were to challenge the validity of these or any issued U.S. patent in an administrative trial before the Patent Trial and Appeal Board in the USPTO, we would have to prove that the claims are unpatentable by a preponderance of the evidence. There is no assurance that a jury and/or court would find in our favor on questions of infringement, validity or enforceability.

Our competitors may be able to circumvent our patents by developing similar or alternative technologies or products in a non-infringing manner.

Our competitors may seek to market generic versions of any approved products by submitting abbreviated NDAs to the FDA in which our competitors claim that our patents are invalid, unenforceable or not infringed. Alternatively, our competitors may seek approval to market their own products that are the same as, similar to or

otherwise competitive with oral octreotide and any future product candidates we may develop. In these circumstances, we may need to defend or assert our patents, by means including filing lawsuits alleging patent infringement requiring us to engage in complex, lengthy and costly litigation or other proceedings. In any of these types of proceedings, a court or government agency with jurisdiction may find our patents invalid, unenforceable or not infringed. We may also fail to identify patentable aspects of our research and development before it is too late to obtain patent protection. Even if we have valid and enforceable patents, these patents still may not provide protection against competing products or processes sufficient to achieve our business objectives.

Changes in either U.S. or foreign patent law or interpretation of such laws could diminish the value of patents in general, thereby impairing our ability to protect our products.

As is the case with other biotechnology companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biotechnology industry involve both technological and legal complexity, and it therefore is costly, time-consuming and inherently uncertain. In addition, on September 16, 2011, the Leahy-Smith America Invents Act, or the AIA, was signed into law. The AIA includes a number of significant changes to U.S. patent law, including provisions that affect the way patent applications will be prosecuted and may also affect patent litigation.

An important change introduced by the AIA is that, as of March 16, 2013, the United States transitioned to a first-to-file system for deciding which party should be granted a patent when two or more patent applications are filed by different parties claiming the same invention. A third party that files a patent application in the USPTO after that date but before us could therefore be awarded a patent covering an invention of ours even if we had made the invention before it was made by the third party. This will require us to be cognizant going forward of the time from invention to filing of a patent application.

Among some of the other changes introduced by the AIA are changes that limit where a patentee may file a patent infringement suit and providing opportunities for third parties to challenge any issued patent in the USPTO. This applies to all of our U.S. patents, even those issued before March 16, 2013. Because of a lower evidentiary standard necessary to invalidate a patent claim in USPTO proceedings compared to the evidentiary standard in United States federal court, a third party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim invalid even though the same evidence would be insufficient to invalidate the claim if first presented in a district court action. Accordingly, a third party may attempt to use the USPTO procedures to invalidate our patent claims that would not have been invalidated if first challenged by the third party as a defendant in a district court action.

Depending on decisions by the United States Congress, the federal courts, the USPTO, or similar authorities in foreign jurisdictions, 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 and patents that we might obtain in the future.

If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed.

In addition to seeking patent protection for certain aspects of our product candidates and delivery technologies, we also consider trade secrets, including confidential and unpatented know-how important to the maintenance of our competitive position. We protect trade secrets and confidential and unpatented know-how, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to such knowledge, such as our employees, outside scientific collaborators, CROs, contract manufacturers, consultants, advisors and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and

consultants that obligate them to maintain confidentiality and assign their inventions to us. Despite these efforts, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming,

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and the outcome is unpredictable. In addition, some courts in the United States and certain foreign jurisdictions are less willing or unwilling to protect trade secrets. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent them from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor, our competitive position would be harmed.

If our trademarks are not adequately protected, then we may not be able to build name recognition in our markets of interest and our business may be adversely affected.

Our trademarks may be challenged, infringed, circumvented or declared generic or determined to be infringing on other marks. We may not be able to protect our rights to these trademarks or may be forced to stop using these names, which we need for name recognition by potential partners or customers in our markets of interest. If we are unable to establish name recognition based on our trademarks, we may not be able to compete effectively and our business may be adversely affected.

We may be subject to claims that our employees, consultants or independent contractors have wrongfully used or disclosed confidential information of third parties.

We have received confidential and proprietary information from third parties. In addition, we employ individuals who were previously employed at other companies and universities. We may be subject to claims that we or our employees, consultants or independent contractors have inadvertently or otherwise used or disclosed confidential information of these third parties or our employees former employers. Litigation may be necessary to defend against these claims. Even if we are successful in defending against these claims, litigation could result in substantial cost and be a distraction to our management and employees.

Risks Related to Our Operations in Israel

The tax benefits available to us under Israeli law require us to meet several conditions and may be terminated or reduced in the future, which would increase our costs and taxes.

We have generated income and are able to take advantage of tax exemptions and reductions resulting from the beneficiary enterprise status of our facilities in Israel. To remain eligible for these tax benefits, we must continue to meet certain conditions stipulated in the Israeli Law for the Encouragement of Capital Investments, 1959 and its regulations. If we fail to meet these conditions in the future, the tax benefits would be canceled and we could be required to refund any tax benefits we might already have received. These tax benefits may not be continued in the future at their current levels or at any level. In recent years, the Israeli government has reduced the benefits available and has indicated that it may further reduce or eliminate some of these benefits in the future. The termination or reduction of these tax benefits may increase our income taxes in the future. Additionally, if we increase our activities outside of Israel, for example, by future acquisitions, our increased activities generally will not be eligible for inclusion in Israeli tax benefit programs.

We may become subject to claims for remuneration or royalties for assigned service invention rights by our employees, which could result in litigation and harm our business.

A significant portion of our intellectual property has been developed by our employees in the course of their employment for us. Under the Israeli Patent Law, 5727-1967, or the Patent Law, and recent decisions by the Israeli Supreme Court and the Israeli Compensation and Royalties Committee, a body constituted under the Patent Law, employees may be entitled to remuneration for intellectual property that they develop for us unless they explicitly

waive any such rights. Although we enter into agreements with our employees pursuant to which they agree that any inventions created in the scope of their employment or engagement are owned exclusively by us, we may face claims demanding remuneration. As a consequence of such claims, we could be required to pay additional remuneration or royalties to our current and former employees, or be forced to litigate such claims, which could negatively affect our business.

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Our research and development and administrative facilities and one of our third-party manufacturers are located in Israel and, therefore, our business could be hurt by political and military instability in Israel.

Our research and development and administrative facilities and one of our third-party manufacturers facilities are located in Israel. Accordingly, political, economic and military conditions in Israel and the surrounding region may directly affect our business. Since the establishment of the State of Israel in 1948, a number of armed conflicts have taken place between Israel and its Arab neighbors, as well as certain political and military groups. Any hostilities involving Israel or the interruption or curtailment of trade within Israel or between Israel and its trading partners could materially and adversely affect our business, financial condition and results of operations and could make it more difficult for us to raise capital. In particular, an interruption of operations at the Tel Aviv airport related to the conflict in the Gaza Strip could prevent or delay shipments of our components or products. An extended interruption could materially and adversely affect our business, financial condition and results of operations. Recent political uprisings, social unrest and violence in various countries in the Middle East and North Africa, including Israel s neighbors Egypt and Syria, are affecting the political stability of those countries. This instability may lead to deterioration of the political relationships that exist between Israel and these countries and has raised concerns regarding security in the region and the potential for armed conflict. Our commercial insurance does not cover losses that may occur as a result of an event associated with the security situation in the Middle East. Any losses or damages incurred by us could have an adverse effect on our business. Any armed conflicts, terrorist activities or political instability in the region could materially and adversely affect our business, financial condition and results of operations.

Our operations may be disrupted as a result of the obligation of Israeli citizens to perform military service.

Many Israeli citizens are obligated to perform several days, and in some cases more, of annual military reserve duty each year until they reach the age of 40 (or older, for reservists who are military officers or have certain occupations) and, in the event of a military conflict, may be called to active duty. In response to increases in terrorist activity, there have been periods of significant call-ups of military reservists. It is possible that there will be military reserve duty call-ups in the future. Our operations could be disrupted by such call-ups, which may include the call-up of members of our management. Such disruption could harm our business, financial condition and results of operations.

Under current Israeli law, we may not be able to enforce our Israeli employees covenants not to compete and therefore may be unable to prevent our competitors from benefiting from the expertise of some of our former employees.

We generally enter into non-competition agreements with our key employees, in most cases within the framework of their employment agreements. These agreements prohibit our key employees, if they cease working for us, from competing directly with us or working for our competitors for a limited period. Under applicable Israeli law, we may be unable to enforce these agreements or any part thereof against our Israeli employees. If we cannot enforce our non-competition agreements against our Israeli employees, then we may be unable to prevent our competitors from benefiting from the expertise of these former employees, which could impair our business, results of operations and ability to capitalize on our proprietary information.

Risks Related to Our Common Stock and this Offering

We may not be able to utilize a significant portion of our net operating loss carryforwards, which could negatively impact our profitability.

At March 31, 2015, we had federal net operating loss, or NOL, carryforwards of $27.0 million. The federal NOL carryforwards expire at various dates through 2035. At March 31, 2015, we had NOL carryforwards in our Israeli

subsidiary of $0.3 million. The foreign NOLs may be carried forward indefinitely, but may not be used to offset future taxable income in the United States.

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Under Section 382 of the Internal Revenue Code of 1986, as amended, or Section 382, substantial changes in our ownership may limit the amount of federal NOL carryforwards that can be utilized annually in the future to offset our U.S. federal taxable income. Specifically, this limitation may arise in the event of a cumulative change in our ownership of more than 50% within any three-year period. Management has determined that we experienced an ownership change for purposes of Section 382 on August 16, 2005 and May 12, 2008. These ownership changes resulted in annual limitations to the amount of NOL carryforwards that can be utilized to offset future taxable income, if any, at the federal level. The annual limit is approximately $0.1 million for 2014 and each year thereafter. These annual limitations resulted in the loss of our ability to utilize approximately $8.9 million in federal NOL carryforwards, which resulted in a write-off of approximately $3.0 million of federal deferred tax assets prior to 2013. In addition, future changes in our stock ownership, which may be outside of our control, may trigger an ownership change, as may future equity acquisitions that have equity as a component and of the purchase price. If additional ownership changes occur in the future, our ability to utilize our net operating losses to offset income if we attain profitability may be limited.

Our directors, executive officers and principal stockholders exercise significant control over our company, which will limit your ability to influence corporate matters.

As of June 30, 2015, our executive officers, directors and principal stockholders collectively controlled 88.3% of our outstanding common stock, excluding any shares of common stock that such persons may have the right to acquire upon exercise of outstanding options or warrants. Certain of our existing stockholders, including certain affiliates of our directors, are purchasing an aggregate of 1,681,250 shares of our common stock in this offering at the initial public offering price. Accordingly, our executive officers, directors and principal stockholders will collectively control 67.5% of our outstanding common stock following this offering. As a result, these stockholders, if they act together, will be able to influence our management and affairs and all matters requiring stockholder approval, including the election of directors and approval of significant corporate transactions.

We will have broad discretion in how we use the proceeds of this offering and may use these proceeds in ways with which you do not agree and in ways that may not increase the value of your investment.

We will have considerable discretion in the application of the net proceeds of this offering. We intend to use the net proceeds from this offering to obtain marketing approval and prepare for the commercial launch in the United States of oral octreotide for the treatment of acromegaly, to initiate a second Phase 3 clinical trial of oral octreotide for the treatment of acromegaly, to initiate Phase 2 clinical trials of oral octreotide for the treatment of NETs and other indications, working capital and other general corporate purposes, which may include funding for the hiring of additional personnel, capital expenditures and the costs of operating as a public company. As a result, investors will be relying upon senior management s judgment with only limited information about our specific intentions for the use of the balance of the net proceeds of this offering. We may use the net proceeds for purposes that do not yield a significant return or any return at all for our stockholders. In addition, pending their use, we may invest the net proceeds from this offering in a manner that does not produce income or that loses value.

Provisions of Delaware law or our charter documents could delay or prevent an acquisition of our company, even if the acquisition would be beneficial to our stockholders, and could make it more difficult for you to change our current management.

Provisions of Delaware law and our amended and restated certificate of incorporation and amended and restated bylaws, which will be effective upon the completion of this offering, may discourage, delay or prevent a merger, acquisition or other change in control that stockholders may consider favorable, including transactions in which stockholders might otherwise receive a premium for their shares. These provisions may also prevent or delay attempts

by stockholders to replace or remove our current management or members of our board of directors. These provisions include:

a classified board of directors;

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limitations on the removal of directors;

advance notice requirements for stockholder proposals and nominations;

the inability of stockholders to act by written consent or to call special meetings;

the ability of our board of directors to make, alter or repeal our amended and restated bylaws; and

the authority of our board of directors to issue preferred stock with such terms as our board of directors may determine.

The affirmative vote of the holders of at least 75% of our shares of capital stock entitled to vote, and not less than 75% of the outstanding shares of each class entitled to vote thereon as a class, is necessary to amend or repeal the above provisions that are contained in our amended and restated certificate of incorporation. In addition, absent approval of our board of directors, our amended and restated bylaws may only be amended or repealed by the affirmative vote of the holders of at least 75% of our shares of capital stock entitled to vote.

In addition, upon the closing of this offering, we will be subject to the provisions of Section 203 of the Delaware General Corporation Law, which limits business combination transactions with stockholders of 15% or more of our outstanding voting stock that our board of directors has not approved. These provisions and other similar provisions make it more difficult for stockholders or potential acquirers to acquire us without negotiation. These provisions may apply even if some stockholders may consider the transaction beneficial to them.

As a result, these provisions could limit the price that investors are willing to pay in the future for shares of our common stock. These provisions might also discourage a potential acquisition proposal or tender offer, even if the acquisition proposal or tender offer is at a premium over the then current market price for our common stock.

Our amended and restated certificate of incorporation and amended and restated bylaws provide that the Court of Chancery of the State of Delaware is the exclusive forum for certain litigation that may be initiated by our stockholders, which could limit our stockholders ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.

Our amended and restated certificate of incorporation and amended and restated bylaws provide that the Court of Chancery of the State of Delaware is the exclusive forum for (i) any derivative action or proceeding brought on our behalf, (ii) any action asserting a claim for breach of a fiduciary duty owed by any of our directors, officers or other employee to us or our stockholders, (iii) any action asserting a claim arising pursuant to any provision of the Delaware General Corporation Law, our amended and restated certificate of incorporation or our amended and restated bylaws or (iv) any action asserting a claim governed by the internal affairs doctrine. The choice of forum provision may limit a stockholder s ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers or other employees, which may discourage such lawsuits against us and our directors, officers and other employees. Alternatively, if a court were to find the choice of forum provision contained in our amended and restated certificate of incorporation and amended and restated bylaws to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions.

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

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

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The trading price of our common stock may be volatile, and your investment in our common stock could decline in value and incur substantial losses.

Prior to this offering, there has been no public market for our common stock, and an active public market for our common stock may not develop or be sustained after this offering. The initial public offering price of our common stock was determined by negotiations between the representatives of the underwriters and us and may not be indicative of future market prices. The following factors were considered in determining the initial public offering price of our common stock:

- prevailing market conditions;
- estimates of our business potential and earnings prospects; and
- an assessment of our management.

If the market price of our common stock after this offering does not exceed the initial public offering price, you may not realize any return on your investment in us and may lose some or all of your investment. The market price for our common stock may be influenced by many factors, including:

- the commencement, enrollment or results of the planned clinical trials of oral octreotide or any future clinical trials we may conduct, or changes in the development status of oral octreotide or any other product candidates we may develop;
- any delay in our regulatory filings for oral octreotide or any other future product candidate and any adverse development or perceived adverse development with respect to the applicable regulatory authority s review of such filings, including without limitation the FDA s issuance of a refusal to file letter or a request for additional information;
- adverse results or delays in clinical trials;
- our decision to initiate a clinical trial, not to initiate a clinical trial or to terminate an existing clinical trial;
- adverse regulatory decisions, including failure to receive regulatory approval of oral octreotide;
- changes in laws or regulations applicable to oral octreotide or any other future product candidates, including clinical trial requirements for approvals;

adverse developments concerning our manufacturers;

our inability to obtain adequate supply for any approved drug or inability to do so at acceptable prices;

our inability to establish collaborations, if needed;

failure to commercialize oral octreotide or any other future product candidates;

our ability to obtain coverage and adequate reimbursement from third party payors for oral octreotide or any other future product candidates;

unanticipated serious safety concerns related to the use of oral octreotide or any other future product candidates;

our ability to effectively manage our growth;

the size and growth of our initial target markets;

actual or anticipated variations in our operating results;

changes in financial estimates by us or by any securities analysts who might cover our stock;

conditions or trends in our industry;

changes in the market valuations of similar companies;

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stock market price and volume fluctuations of comparable companies and, in particular, those that operate in the biopharmaceutical industry;

publication of research reports about us or our industry or positive or negative recommendations or withdrawal of research coverage by securities analysts;

announcements by us or our competitors of significant acquisitions, strategic partnerships or divestitures;

announcements of investigations or regulatory scrutiny of our operations or lawsuits filed against us;

capital commitments;

investors general perception of our company and our business;

recruitment or departure of key personnel;

sales of our common stock in the future, including sales by our directors and officers or specific stockholders;

overall performance of the equity markets;

trading volume of our common stock;

changes in accounting practices;

ineffectiveness of our internal controls;

disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;

significant lawsuits, including patent or stockholder litigation;

general political and economic conditions; and

other events or factors, many of which are beyond our control.

We may be subject to securities litigation, which is expensive and could divert our management s attention.

The market price of our securities may be volatile, and in the past companies that have experienced volatility in the market price of their securities have been subject to securities class action litigation. We may be the target of this type of litigation in the future. Securities litigation against us could result in substantial costs and divert our management s attention from other business concerns, which could seriously harm our business.

If you purchase shares of our common stock in this offering, you will suffer immediate dilution of your investment.

If you purchase common stock in this offering, you will pay more for your shares than the amounts paid by existing stockholders for their shares. You will incur, as of March 31, 2015, immediate and substantial dilution of $9.16 per share or $8.84 per share if the underwriters exercise in full their option to purchase additional shares, representing the difference between our pro forma net tangible book value per share after giving effect to this offering and based upon the initial public offering price of $16.00 per share. In the past, we issued restricted stock, options and warrants to acquire common stock at prices significantly below the initial public offering price. To the extent any outstanding options or warrants are ultimately exercised, you will sustain further dilution.

We are an emerging growth company and we intend to take advantage of reduced disclosure and governance requirements applicable to emerging growth companies, which could result in our securities being less attractive to investors.

We are an emerging growth company, as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. For as long as we continue to be an emerging growth company, we intend to take advantage of

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exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies, including not being required to comply with the auditor attestation requirements of Section 404(b) of the Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act, reduced disclosure obligations regarding executive compensation in this prospectus and our periodic reports and proxy statements and exemptions from the requirements of holding nonbinding advisory votes on executive compensation and stockholder approval of any golden parachute payments not previously approved. We could be an emerging growth company for up to five years following the year in which we complete this offering, although circumstances could cause us to lose that status earlier, including if the market value of our common stock held by non-affiliates exceeds $700 million as of June 30 in any year before that time or if we have total annual gross revenue of $1.0 billion or more during any fiscal year before that time, in which cases we would no longer be an emerging growth company as of the following December 31 or, if we issue more than $1.0 billion in non-convertible debt during any three-year period before that time, we would cease to be an emerging growth company immediately. Even after we no longer qualify as an emerging growth company, we may still qualify as a smaller reporting company which would allow us to take advantage of many of the same exemptions from disclosure requirements including not being required to comply with the auditor attestation requirements of Section 404(b) of the Sarbanes-Oxley Act and reduced disclosure obligations regarding executive compensation in this prospectus and our periodic reports and proxy statements. We cannot predict if investors will find our common stock less attractive because we may rely on these exemptions. If some investors find our securities less attractive as a result, there may be a less active trading market for our securities and the price of our securities may be more volatile.

Under the JOBS Act, emerging growth companies can also delay adopting new or revised accounting standards until such time as those standards apply to private companies. We have irrevocably elected not to avail ourselves of this exemption from new or revised accounting standards and, therefore, will be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies. As a result, changes in U.S. generally accepted accounting principles or their interpretation, the adoption of new guidance or the application of existing guidance to changes in our business could adversely affect our financial position and results of operations.

We have never paid dividends on our capital stock and we do not anticipate paying any dividends in the foreseeable future. Consequently, any gains from an investment in our common stock will likely depend on whether the price of our common stock increases, which may not occur.

We have not paid dividends on any of our classes of capital stock to date and we currently intend to retain our future earnings, if any, to fund the development and growth of our business. As a result, capital appreciation, if any, of our common stock will be your sole source of gain for the foreseeable future. Consequently, in the foreseeable future, you will likely only experience a gain from your investment in our common stock if the price of our common stock increases.

We incur significant increased costs as a result of operating as a public company, and our management is required to devote substantial time to new compliance initiatives and other activities associated with being a public company.

As a public company, we incur significant legal, accounting and other expenses that we did not incur as a private company. The Sarbanes-Oxley Act of 2002, as well as rules subsequently implemented by the SEC and The NASDAQ Stock Market, has imposed various new requirements on public companies, including requiring establishment and maintenance of effective disclosure and financial controls and changes in corporate governance practices. Our management and other personnel are required to devote a substantial amount of time to these new compliance initiatives. Moreover, these rules and regulations have substantially increased our legal and financial compliance costs and have made some activities more time consuming and costly. These rules and regulations may make it more difficult and more expensive for us to maintain our existing director and officer liability insurance or to obtain similar coverage from an alternative provider.

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The Sarbanes-Oxley Act requires, among other things, that we maintain effective internal controls for financial reporting and disclosure controls and procedures. In particular, pursuant to Section 404 of the Sarbanes-Oxley Act, we are required to perform system and process evaluation and testing of our internal controls over financial reporting to allow management to report on the effectiveness of our internal controls over financial reporting. Our testing, or the subsequent testing by our independent registered public accounting firm, may reveal deficiencies in our internal controls over financial reporting that are deemed to be material weaknesses. Our compliance with Section 404 will require us to continue to incur substantial accounting expense and expend significant management efforts. We currently do not have an internal audit group, and we may need to hire additional accounting and financial staff. Moreover, if we are not able to comply with the requirements of Section 404 in a timely manner or if we or our independent registered public accounting firm identifies deficiencies in our internal controls over financial reporting that are deemed to be material weaknesses, the market price of our stock could decline and we could be subject to sanctions or investigations by The NASDAQ Stock Market, the SEC or other regulatory authorities, which would require additional financial and management resources.

If we fail to maintain proper and effective internal controls, our ability to produce accurate financial statements on a timely basis could be impaired.

After the closing of this offering, we will be subject to the reporting requirements of the Securities Exchange Act of 1934, or the Exchange Act, the Sarbanes-Oxley Act and the rules and regulations of the stock market on which our common stock is listed. The Sarbanes-Oxley Act requires, among other things, that we maintain effective disclosure controls and procedures and internal control over financial reporting. Commencing with our fiscal year ending December 31, 2016, we must perform system and process evaluation and testing of our internal control over financial reporting to allow management to report on the effectiveness of our internal control over financial reporting in our Form 10-K filing for that year, as required by Section 404 of the Sarbanes-Oxley Act. This will require that we incur substantial additional professional fees and internal costs to expand our accounting and finance functions and that we expend significant management efforts. Prior to this offering, we have never been required to test our internal control within a specified period, and, as a result, we may experience difficulty in meeting these reporting requirements in a timely manner.

We may discover weaknesses in our system of internal financial and accounting controls and procedures that could result in a material misstatement of our financial statements. Our internal control over financial reporting will not prevent or detect all errors and all fraud. A control system, no matter how well designed and operated, can provide only reasonable, not absolute, assurance that the control system s objectives will be met. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that misstatements due to error or fraud will not occur or that all control issues and instances of fraud will be detected.

If we are not able to comply with the requirements of Section 404 of the Sarbanes-Oxley Act in a timely manner, or if we are unable to maintain proper and effective internal controls, we may not be able to produce timely and accurate financial statements. If that were to happen, the market price of our stock could decline and we could be subject to sanctions or investigations by the stock exchange on which our common stock is listed, the SEC or other regulatory authorities.

A significant portion of our total outstanding shares are restricted from immediate resale but may be sold into the market in the near future, which could cause the market price of our common stock to drop significantly, even if our business is otherwise doing well.

If our existing stockholders sell, or indicate an intent to sell, substantial amounts of our common stock in the public market after the 180-day contractual lock-up and other legal restrictions on resale discussed in this prospectus lapse,

the trading price of our common stock could decline significantly and could decline below the initial public offering price. Based on shares outstanding as of June 30, 2015, upon the completion of this

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offering, we will have 22,974,642 outstanding shares of common stock, assuming no exercise of outstanding options or warrants. Of these shares, assuming no shares were purchased in this offering by our existing stockholders, 6,365,000 shares of common stock, plus any shares sold pursuant to the underwriters option to purchase additional 954,750 shares, will be immediately freely tradable, without restriction, in the public market.

After the lock-up agreements pertaining to this offering expire and based on shares outstanding as of June 30, 2015, an additional 16,374,307 shares will be eligible for sale in the public market. In addition, the 3,632,210 shares subject to outstanding options under our stock option plans and the 2,602,283 shares reserved for future issuance under our stock option plans and 3,624,012 shares subject to outstanding warrants will become eligible for sale in the public market in the future, subject to certain legal and contractual limitations. Moreover, 180 days after the completion of this offering, holders of approximately 16,543,995 of our common stock will have the right to require us to register these shares under the Securities Act of 1933, as amended, or the Securities Act, pursuant to an investors rights agreement. If our existing stockholders sell substantial amounts of our common stock in the public market, or if the public perceives that such sales could occur, this could have an adverse impact on the market price of our common stock, even if there is no relationship between such sales and the performance of our business.

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

The trading market for our securities will depend in part on the research and reports that securities or industry analysts publish about us or our business. Securities and industry analysts do not currently, and may never, publish research on our company. If no securities or industry analysts commence coverage of our company, the trading price for our securities would likely be negatively impacted. In the event securities or industry analysts initiate coverage, if one or more of the analysts who cover us downgrade our stock or publish inaccurate or unfavorable research about our business, our trading price would likely decline. If one or more of these analysts cease coverage of our company or fail to publish reports on us regularly, demand for our stock could decrease, which might cause our trading price and trading volume to decline.

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CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus contains forward-looking statements. These statements include all matters that are not related to present facts or current conditions or that are not historical facts, including statements regarding our strategy, future operations, future financial position, future revenue, projected costs, prospects, plans, objectives of management and expected market growth. The words anticipate, believe, could, continue, should, predict, estimate, expect plan, potentially, will, may, would, or the negative of these terms or other similar expressions are intended to ide forward-looking statements, although not all forward-looking statements contain these identifying words. We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements.

We have based these forward-looking statements largely on our current expectations and projections about future events and financial trends that we believe may affect our financial condition, results of operations, business strategy and financial needs. These forward-looking statements are subject to a number of risks, uncertainties and assumptions described in the section titled Risk Factors and elsewhere in this prospectus, regarding, among other things:

- the acceptance of our NDA for oral octreotide, the regulatory review process generally and any regulatory approvals that may be issued or denied by the FDA, EMA or other regulatory agencies for oral octreotide in acromegaly or other indications;
- the therapeutic benefits, effectiveness and safety of oral octreotide;
- our estimates of the size and characteristics of the markets that may be addressed by oral octreotide;
- the commercial success and market acceptance of oral octreotide or any future product candidates that are approved for marketing in the United States or other countries;
- our ability to successfully commercialize oral octreotide with our small, targeted sales force;
- our ability to generate future revenue;
- the number, designs, results and timing of our clinical trials and nonclinical activities and the timing of the availability of data from these trials and activities;
- the safety and efficacy of therapeutics marketed by our competitors that are targeted to indications which oral octreotide has been developed to treat;

our ability to leverage our TPE platform to develop and commercialize novel oral product candidates incorporating peptides that are currently only available in injectable or other non-absorbable forms;

the possibility that competing products or technologies may make oral octreotide, other product candidates we may develop and successfully commercialize or our TPE technology obsolete;

our ability to manufacture sufficient amounts of oral octreotide for clinical trials and commercialization activities;

our ability to secure collaborators to license, manufacture, market and sell oral octreotide or any products for which we receive regulatory approval in the future outside of the United States;

our ability to protect our intellectual property and operate our business without infringing upon the intellectual property rights of others;

our expectations related to the use of proceeds, if any, from this offering; and

our estimates regarding our capital requirements and our need for additional financing.

These risks are not exhaustive. Other sections of this prospectus may include additional factors that could adversely impact our business and financial performance. Moreover, we operate in a very competitive and

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rapidly changing environment. New risk factors emerge from time to time, and it is not possible for our management to predict all risk factors nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in, or implied by, any forward-looking statements.

We have included important factors in the cautionary statements included in this prospectus, particularly in the Risk Factors section, that we believe could cause actual results or events to differ materially from the forward-looking statements that we make. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we may make. No forward-looking statement is a guarantee of future performance.

You should read this prospectus and the documents that we reference in this prospectus and have filed as exhibits to the registration statement of which this prospectus is a part completely and with the understanding that our actual future results may be materially different from what we expect. The forward-looking statements in this prospectus represent our views as of the date of this prospectus. We anticipate that subsequent events and developments will cause our views to change. However, while we may elect to update these forward-looking statements at some point in the future, we have no current intention of doing so except to the extent required by applicable law. You should, therefore, not rely on these forward-looking statements as representing our views as of any date subsequent to the date of this prospectus.

INDUSTRY AND MARKET DATA

This prospectus includes statistical and other industry and market data that we obtained from industry publications and research, surveys and studies conducted by us and third parties. The industry in which we operate is subject to a high degree of uncertainty and risks due to various factors, including those described in the section titled Risk Factors.

In addition, some of the information in this prospectus is derived by surveys conducted by us on people with acromegaly. Due to the limits on the number of patients surveyed, the voluntary nature of the data gathering process, and other limitations and uncertainties inherent in patient surveys, the information gathered in these surveys may not be indicative or reflective of all acromegaly patients if a broader survey were conducted.

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USE OF PROCEEDS

We estimate that the net proceeds from the sale of 6,365,000 shares of common stock in this offering will be approximately $92.2 million, based upon the initial public offering price of $16.00 per share, after deducting underwriting discounts and commissions and estimated offering expenses payable by us. If the underwriters exercise their option to purchase additional shares in full, we estimate that the net proceeds will be approximately $106.4 million after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

We intend to use the net proceeds from this offering as follows:

- approximately $32.0 million to build our corporate infrastructure, including our U.S. sales and marketing operations, to support the commercial launch of oral octreotide in the United States for the treatment of acromegaly;
- approximately $15.0 million to initiate an additional Phase 3 clinical trial of oral octreotide to support regulatory approval in Europe for the treatment of acromegaly; and
- approximately $3.0 million to initiate a Phase 2 clinical trial of oral octreotide for the treatment of neuroendocrine tumors.

We expect to use the remainder of any net proceeds from this offering to initiate clinical trials of oral octreotide in a new orphan indication, once selected, in late 2016 and for research and development on our TPE platform to enable us to develop additional product candidates targeting new indications and announce at least one new product candidate for clinical development in late 2016, and for working capital, capital expenditures and other general corporate purposes, including the costs of operating as a public company.

We believe that our intended use of proceeds as allocated above will be sufficient to accomplish our plans to build our corporate infrastructure, including our U.S. sales and marketing operations, to support our initial commercial launch of oral octreotide in the United States for the treatment of acromegaly, if it is approved. We also believe that our intended use of proceeds as allocated above will be sufficient to initiate our planned Phase 3 clinical trial of oral octreotide to support regulatory approval in Europe for the treatment of acromegaly and to initiate our planned Phase 2 clinical trial of oral octreotide for the treatment of neuroendocrine tumors.

However, our expected use of net proceeds from this offering represents our current intentions based upon our present plans and business conditions, which could change in the future as our plans and business conditions evolve. The amount and timing of our actual expenditures will depend upon numerous factors, including the timing of regulatory submissions and the feedback from regulatory authorities, the results of our research and development efforts and the timing and success of our nonclinical studies, current clinical studies or clinical studies we may commence in the future. As a result, our management will have broad discretion over the use of the net proceeds from this offering.

Although we may use a portion of the net proceeds of this offering for the acquisition or licensing, as the case may be, of additional technologies, other assets or businesses, or for other strategic investments or opportunities, we have no current understandings, agreements or commitments to do so.

Pending the use of the proceeds from this offering, we intend to invest the net proceeds in short-term, interest-bearing, investment-grade securities, certificates of deposit or government securities.

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DIVIDEND POLICY

We have never declared or paid any dividends on our capital stock. However, in March 2013, we utilized a portion of the proceeds from our now terminated license agreement with Roche to pay an aggregate of $55.0 million in cash as partial consideration for the redemption of certain shares of our preferred stock. We currently intend to retain all available funds and any future earnings, if any, to fund the development and expansion of our business and we do not anticipate paying any cash dividends in the foreseeable future. Any future determination to pay dividends will be made at the discretion of our board of directors. In addition, any future indebtedness that we may incur could preclude us from paying dividends. Investors should not purchase our common stock with the expectation of receiving cash dividends.

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CAPITALIZATION

The following table sets forth our cash and capitalization as of March 31, 2015 on:

- an actual basis;
- a pro forma basis to give effect to the automatic conversion of all 149,792,472 outstanding shares of our preferred stock into an aggregate of 16,403,011 shares of common stock immediately prior to the closing of this offering and the filing of our amended and restated certificate of incorporation immediately prior to the closing of this offering; and
- a pro forma as adjusted basis to give further effect to the sale of 6,365,000 shares of our common stock offered in this offering, based upon the initial public offering price of $16.00 per share, after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

You should read this information together with our financial statements and related notes appearing elsewhere in this prospectus and the information set forth in the sections titled Selected Consolidated Financial Data and Management s Discussion and Analysis of Financial Condition and Results of Operations.

	March 31, 2015		
	Actual	Pro Forma	Pro Forma As Adjusted
Cash	$ 70,871,768	$ 70,871,768	$ 163,141,215
Redeemable convertible preferred stock, $0.01 par value:			
Series B1 preferred, 1,134,997 shares authorized, issued and outstanding at March 31, 2015 actual; no shares issued and outstanding pro forma and pro forma as adjusted; (aggregate liquidation preference and redemption value of $7,218,438 at actual)	$ 9,143,823	$	$
Series C preferred, 40,719,409 shares authorized; 40,430,250 shares issued and outstanding at March 31, 2015 actual; no shares issued and outstanding pro forma and pro forma as adjusted; (aggregate liquidation preference and redemption value of $40,430,250 at actual)	40,430,250		
Series D preferred, 38,504,439 shares authorized, issued and outstanding at March 31, 2015 actual; no shares issued and outstanding pro forma and pro forma as adjusted; (aggregate liquidation preference and redemption value of $22,054,186 at actual)	22,054,186		
	67,168,201		

Series E preferred, 80,774,458 shares authorized; 69,722,786 shares issued and outstanding at March 31, 2015 actual; no shares issued and outstanding pro forma and pro forma as adjusted; (aggregate liquidation preference and redemption value of $69,722,786 at actual)			
Stockholders (deficit) equity:			
Undesignated preferred stock, $0.01 par value, no shares authorized, issued or outstanding actual; 5,000,000 shares authorized, no shares issued or outstanding pro forma and pro forma as adjusted			
Common stock, $0.01 par value, 250,000,000 shares authorized at March 31, 2015 actual, 81,870 shares issued and outstanding at March 31, 2015 actual; 250,000,000 shares authorized, 16,484,881 shares issued and outstanding pro forma; 125,000,000 shares authorized, 22,849,881 shares issued and outstanding pro forma as adjusted	818	164,848	228,498
Additional paid-in capital	11,093,496	149,725,926	241,866,342
Accumulated deficit	(85,752,282)	(85,752,282)	(85,752,282)
Total stockholders (deficit) equity	(74,657,968)	64,138,492	156,342,557
Total capitalization	$ 64,138,492	$ 64,138,492	$ 156,342,557

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The actual, pro forma and pro forma as adjusted information set forth in the table above excludes the following:

- 1,623,706 shares of common stock issuable upon the exercise of stock options outstanding as of March 31, 2015 at a weighted-average exercise price of $2.13 per share;
- 3,624,012 shares of common stock issuable upon the exercise of warrants outstanding as of March 31, 2015 at a weighted-average exercise price of $4.85 per share;
- 2,602,283 shares of common stock reserved for future issuance under our 2015 Stock Option and Incentive Plan, or the 2015 Plan; and
- 260,000 shares of common stock reserved for the future issuance under our 2015 Employee Stock Purchase Plan.

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DILUTION

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

We had a net tangible book value (deficit) of $(74.7) million, or $(911.91) per share of common stock, as of March 31, 2015. Our net tangible book value represents total tangible assets less total liabilities and redeemable convertible preferred stock. Our net tangible book value per share is our net tangible book value divided by the number of shares of our common stock outstanding as of March 31, 2015.

The pro forma net tangible book value of our common stock as of March 31, 2015 was $64.1 million, or $3.89 per share of our common stock. Pro forma net tangible book value represents the amount of our total tangible assets less our total liabilities, divided by the pro forma number of shares of our common stock outstanding after giving effect to the automatic conversion of our outstanding preferred stock into an aggregate of 16,403,011 shares of common stock upon the closing of this offering.

After giving further effect to the sale of 6,365,000 shares of common stock in this offering, after deducting underwriting discounts and commissions and estimated offering expenses payable by us, at the initial public offering price of $16.00 per share, our pro forma as adjusted net tangible book value as of March 31, 2015 would have been $156.3 million, or $6.84 per share of common stock. This represents an immediate increase in pro forma net tangible book value of $2.95 per share to our existing stockholders and an immediate dilution of $9.16 per share to investors participating in this offering. Dilution per share to new investors is determined by subtracting pro forma net tangible book value per share after this offering from the initial public offering price per share paid by new investors. The following table illustrates this dilution on a per share basis:

Initial public offering price per share		$ 16.00
Historical net tangible book value (deficit) per share as of March 31, 2015	$ (911.91)	
Pro forma increase in net tangible book value per share attributable to the conversion of preferred stock	915.80	
Pro forma net tangible book value per share as of March 31, 2015	3.89	
Pro forma increase in net tangible book value per share attributable to this offering	2.95	
Pro forma as adjusted net tangible book value per share, after giving effect to this offering		6.84
Dilution of pro forma as adjusted net tangible book value per share to new investors		$ 9.16

If the underwriters exercise their option to purchase additional shares in full, pro forma as adjusted net tangible book value will increase to $170.5 million, or $7.16 per share.

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The following table summarizes, on a pro forma as adjusted basis as of March 31, 2015, the number of shares of common stock purchased from us, the total consideration and the average price per share paid by existing stockholders (giving effect to the conversion of all outstanding shares of our preferred stock into 16,403,011 shares of common stock upon the completion of this offering) and by investors participating in this offering, before deducting underwriting discounts and commissions and estimated offering expenses, at the initial public offering price of $16.00 per share. As the table illustrates, new investors purchasing shares in this offering will pay an average price per share substantially higher than our existing stockholders paid.

	Shares purchased		Total consideration		Average price per share
	Number	Percent	Amount	Percent	
Existing stockholders(1)(2)	16,484,881	72.1%	$ 161,400,948	61.3%	$ 9.79
IPO investors	6,365,000	27.9	101,840,000	38.7	16.00
Total	22,849,881	100%	$ 263,240,948	100%	11.52

(1) Certain of our existing stockholders, including certain affiliates of our directors, are purchasing an aggregate of 1,681,250 shares of our common stock in this offering at the initial public offering price. The presentation in this table regarding ownership by existing stockholders does not give effect to any purchases in this offering by such stockholders.

(2) During 2013, we paid an aggregate of $55.0 million in cash as partial consideration for the redemption of certain shares of our redeemable preferred stock.

If the underwriters exercise their option to purchase additional shares in full, our existing stockholders would own 69.3% and our new investors would own 30.7% of the total number of shares of common stock outstanding after the closing of this offering.

The number of shares of common stock to be outstanding after this offering is based on 16,484,881 shares outstanding as of March 31, 2015 and excludes the following:

1,623,706 shares of common stock issuable upon the exercise of stock options outstanding as of March 31, 2015 at a weighted-average exercise price of $2.13 per share;

3,624,012 shares of common stock issuable upon the exercise of warrants outstanding as of March 31, 2015 at a weighted-average exercise price of $4.85 per share;

2,602,283 shares of common stock reserved for future issuance under our 2015 Stock Option and Incentive Plan, or the 2015 Plan; and

260,000 shares of common stock reserved for the future issuance under our 2015 Employee Stock Purchase Plan.

New investors will experience further dilution if any of our outstanding options are exercised, new options are issued and exercised under our equity incentive plans or we issue additional shares of common stock, other equity securities or convertible debt securities in the future.

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SELECTED CONSOLIDATED FINANCIAL DATA

The following selected consolidated statements of operations data for the years ended December 31, 2013 and 2014 and the consolidated balance sheet data as of December 31, 2013 and 2014 are derived from our audited consolidated financial statements appearing elsewhere in this prospectus. The selected consolidated statements of operations data for the three months ended March 31, 2014 and 2015 and the selected consolidated balance sheet data as of March 31, 2015 are derived from our unaudited condensed consolidated financial statements included elsewhere in this prospectus. In the opinion of management, the unaudited condensed consolidated financial statements have been prepared on a basis consistent with our audited consolidated financial statements and contain all adjustments, consisting of only normal recurring adjustments, that management considers necessary for the fair presentation of the financial information set forth in those statements. You should read this data together with our consolidated financial statements and related notes included elsewhere in this prospectus and the information under the section titled Management s Discussion and Analysis of Financial Condition and Results of Operations. Our historical results for any prior period are not necessarily indicative of results to be expected in any future period and the results of interim periods are not necessarily indicative of the results for the entire year.

	Year Ended December 31,		Three Months Ended March 31,	
	2013	2014	2014	2015
	(audited)		(unaudited)	
	(in thousands, except share and per share data)			
Consolidated Statement of Operations Data				
Revenue from license agreement	$ 73,134	$ 13,166	$ 4,573	$
Operating expenses:				
Research and development	26,455	11,527	1,650	2,219
Marketing, general and administrative	8,065	3,469	954	1,931
Total operating expenses	34,520	14,996	2,604	4,150
Income (loss) from operations	38,614	(1,830)	1,969	(4,150)
Other expenses, net	1,208	4	25	89
Income (loss) before provision for income taxes	37,406	(1,834)	1,944	(4,239)
Provision for income taxes	1,224	176	(129)	5
Net income (loss)	36,182	(2,010)	2,073	(4,244)
Accretion of deemed liquidation related to Series D redeemable convertible preferred stock	(38,504)			
Accretion of redeemable convertible preferred stock	(3,034)	(904)	(340)	(98)
Net (loss) income attributable to common stockholders	$ (5,356)	$ (2,914)	$ 1,733	$ (4,342)
	$ (125.29)	$ (66.21)	$ 39.82	$ (59.73)

Net (loss) income per share attributable to common stockholders, basic				
Weighted average common shares outstanding, basic	42,760	44,017	43,558	72,693
Net (loss) income per share attributable to common stockholders, diluted	$ (125.29)	$ (66.21)	$ 0.19	$ (59.73)
Weighted average common shares outstanding, diluted	42,760	44,017	11,130,865	72,693
Pro forma net loss per share attributable to common stockholders, basic and diluted (unaudited)[1]				$ (0.30)
Pro forma weighted average common shares outstanding, basic and diluted (unaudited)[1]				13,982,593

(1) See Note 3 to our audited consolidated financial statements and Note 2 of our unaudited condensed consolidated financial statements appearing elsewhere in this prospectus for an explanation of the method used to calculate the historical and pro forma net loss per share, basic and diluted, and the number of shares used in the computation of the per share amounts attributable to common stockholders.

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	December 31, 2013	2014	March 31, 2015 (unaudited)
Consolidated Balance Sheet Data		**(in thousands)**	
Cash	$ 12,850	$ 40,160	$ 70,872
Working capital (deficit)	(1,177)	36,153	67,541
Total assets	14,658	41,399	72,638
Deferred revenue and customer advances	2,883		
Long-term liabilities	97	4,612	4,724
Redeemable convertible preferred stock	70,732	104,486	138,796
Accumulated deficit	(79,498)	(81,508)	(85,752)
Total stockholders deficit	(70,635)	(72,018)	(74,658)

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

Overview

We are a late-stage biopharmaceutical company focused on improving the lives of patients suffering from orphan diseases by developing and commercializing novel oral forms of therapies that are available today only by injection. Using our proprietary Transient Permeability Enhancer, or TPE, technology platform, we seek to develop oral therapies that eliminate the significant limitations and burdens generally associated with existing injectable therapies. We have completed a multinational Phase 3 clinical trial of our most advanced TPE platform-based product candidate, oral octreotide, for the treatment of acromegaly. We believe oral octreotide, if approved by regulatory authorities, will be the first somatostatin analog available for oral administration. Our oral octreotide has been granted orphan designation in the United States and the European Union for the treatment of acromegaly. We submitted a new drug application, or NDA, to the U.S. Food and Drug Administration, or FDA, on June 15, 2015, seeking approval for the marketing and sale of oral octreotide for the maintenance therapy of adult patients with acromegaly. The FDA has 60 days after receipt of the NDA to preliminarily review and determine if the application is sufficiently complete to permit a substantive review and meets the threshold for filing. Assuming the FDA reviews and responds to our NDA in accordance with the goals and policies agreed to by the FDA under the Prescription Drug User Fee Act, or PDUFA, and subject to the FDA s acceptance of our NDA for filing, we anticipate a regulatory decision on marketing approval in April 2016. In light of our clinical data and feedback from patients and healthcare providers, we believe that oral octreotide, if approved, could become a new standard of care in acromegaly.

We retain worldwide rights to develop and commercialize oral octreotide with no royalty obligations to third parties. We intend to commercialize oral octreotide ourselves in the United States, and we plan to explore collaboration opportunities for commercializing oral octreotide in Europe and the rest of the world. Our goal is to become a leading patient-focused biopharmaceutical company by developing and commercializing oral octreotide for acromegaly and other orphan indications, and leveraging our TPE platform to develop and commercialize novel oral products for other debilitating diseases currently treated by injectable therapies.

We were incorporated in 2001 and commenced active operations in the same year. Our operations to date have been limited to organizing and staffing our company, business planning, raising capital, developing our TPE technology, identifying potential drug candidates, undertaking nonclinical studies and, beginning in 2010, conducting clinical trials and preparing for regulatory submissions. To date, we have financed our operations primarily through private placements, funding received from a licensing agreement, and a loan agreement. We have no products approved for sale and all of our revenue has been related to one license agreement, which has been terminated. Since our inception and through March 31, 2015, we have raised an aggregate of $259.7 million to fund our operations, of which $86.3 million was through our license agreement with F. Hoffmann-La Roche Ltd. and Hoffmann-La Roche Inc., collectively Roche, $161.4 million was from the issuance of private securities and $12.0 million was from borrowings under a loan agreement. In March 2013, using proceeds from the Roche license agreement, as described in more detail below, we repaid all outstanding borrowings under our loan agreement and paid an aggregate of $55.0 million in cash

as partial consideration for the redemption of certain shares of our redeemable preferred stock. As of March 31, 2015, our cash was $70.9 million, of which $1.3 million was held by Chiasma (Israel) Ltd., our wholly owned Israeli subsidiary.

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Since inception, we have incurred significant operating losses. Our net loss was $2.0 million for the year ended December 31, 2014. We had net income of $36.2 million for the year ended December 31, 2013, primarily the result of revenue recognized under the license agreement with Roche. Our net loss was $4.2 million for the three months ended March 31, 2015, as compared to net income of $2.1 million for the three months ended March 31, 2014. As of March 31, 2015, we had an accumulated deficit of $85.8 million. We expect to continue to incur significant expenses and operating losses for at least the next several years as we continue to incur substantial expenses related to preparing for and proceeding with the commercial launch of oral octreotide, if approved, additional clinical development of oral octreotide and the development of additional product candidates.

We expect to incur increasing operating losses over the next several years. These losses, combined with prior losses will continue to have an adverse effect on our cash resources, stockholders deficit and working capital. If we obtain regulatory approval of oral octreotide and any future product candidates we may develop, we may incur significant sales, marketing, in-licensing and outsourced manufacturing expenses, as well as continued research and development expenses. In addition, we expect our research and development expenses to significantly increase in connection with our planned additional Phase 3 clinical trial for oral octreotide for the treatment of acromegaly to support approval in the European Union, Phase 2 clinical trials for oral octreotide for the treatment of neuroendocrine tumors and other indications, and as we develop additional product candidates for our drug pipeline. Because of the numerous risks and uncertainties associated with developing and commercializing pharmaceutical products, we are unable to predict the extent of any future losses or when we will become profitable, if at all.

If approved, we anticipate commercial sales of oral octreotide in mid 2016 at the earliest. 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, as well as license and collaboration agreements with potential partners. We may be unable to raise capital when needed or on attractive terms, or to enter into collaborations agreements, which could force us to delay, limit, reduce or terminate our product development or future commercialization efforts. We will need to generate significant revenues to achieve profitability, which we may not be able to achieve.

The consolidated financial statements and following information include the accounts of Chiasma, Inc. and Chiasma (Israel) Ltd.

Roche License Agreement

In December 2012, we signed a license agreement with Roche, which went into effect on January 2013. Pursuant to the license agreement, we granted Roche an exclusive, non-transferable license to all intellectual property related to oral octreotide. Under the terms of the license, Roche obtained worldwide rights to research, develop, make, import, export, sell, market or distribute the commercial product. We retained certain responsibilities for research and development activities under a joint development plan. The agreement provided for an upfront payment to us of $65.0 million, future consideration of up to $530 million in development and commercial milestones and the right to receive tiered, double-digit royalties on net sales of oral octreotide.

During the year ended December 31, 2013, we received a total of $75.0 million from Roche related to the license agreement, which included the upfront payment of $65.0 million and the first milestone payment of $10.0 million. We received an additional $10.0 million during January 2014 related to the second milestone payment. The two milestones were achieved during the year ended December 31, 2013. During the year ended December 31, 2013, we recognized $73.1 million in revenue with $2.9 million recorded as deferred revenue and customer advances. During 2013, we also received a payment of $1.0 million for reimbursement of certain research and development expenses for which the related costs had not yet been incurred and for which we recorded the amount as customer advances.

In March 2013, using proceeds from the Roche license agreement, our board of directors approved the redemption of certain of our then outstanding shares of redeemable preferred stock. In consideration of this

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redemption, the holders of these shares received a cash payment of $55.0 million plus the issuance of newly authorized shares of preferred stock. See Note 9 to our audited consolidated financial statements as of and for the years ended December 31, 2013 and 2014, included elsewhere in this prospectus.

In April 2014, we entered into an additional agreement with Roche pursuant to which we were to receive an additional aggregate amount of $2.7 million, payable in three installments, covering certain development costs incurred by us. During 2014, we received the first installment of $1.3 million.

In July 2014, Roche terminated the license agreement and the April 2014 agreement. Upon termination, Roche returned all rights granted under the agreements. Subsequent to the termination, we purchased from Roche active pharmaceutical ingredients, or API, to continue the development and manufacturing of oral octreotide, together with Roche s proposed trade name for oral octreotide, for an aggregate amount of $5.1 million, payable in three annual installments of $1.7 million in January 2016, January 2017 and January 2018. Other than these payments, we have no further financial and operational obligations to Roche. During 2014, we recognized revenue of $13.2 million, including the first installment payment of $1.3 million under the April 2014 agreement. For the three months ended March 31, 2014, we recognized revenue of $4.6 million. We did not recognize any revenue during the three months ended March 31, 2015. Pursuant to the termination of the license agreement, we are not entitled to further payments from Roche, Roche has no remaining rights to oral octreotide and we retain all rights to oral octreotide and all related intellectual property.

Financial Overview

Revenue

Our revenue was derived from a license agreement with Roche, which included amounts recognized for research and development services provided and earned under the agreement. We do not expect to generate revenue from product sales for at least the next year. If we fail to complete the development of oral octreotide or any future product candidates in a timely manner or obtain regulatory approval for them, our ability to generate product sales, and our consolidated results of operations and financial position, would be adversely affected.

Research and Development

Research and development expenses consist of expenses incurred in performing research and development activities, including compensation and benefits for full-time research and development employees, an allocation of facilities expenses, overhead expenses, nonclinical pharmacology and toxicology studies, manufacturing process-development and scale-up activities, clinical trial and related clinical manufacturing expenses, fees paid to contract research organizations, or CROs, investigative sites, and other external expenses. In the early phases of development, our research and development costs include expanding our technology platform as well as early development of specific product candidates.

Our research and development costs consist of external costs and internal development costs, which are primarily compensation expenses for our full-time research and development employees and related expenses. As we expand the clinical development of oral octreotide and additional products, we expect the amount of research and development spending to continue to grow. We have incurred a total of $96.1 million in research and development expenses from inception through March 31, 2015, with a majority of the expenses being spent on the development of oral octreotide, our TPE platform and our early stage programs.

We expense research and development costs as incurred. Conducting a significant amount of research and development is central to our business model. Product candidates in late 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 late-stage clinical trials. We plan to increase our research and development expenses for the foreseeable future as we seek to obtain regulatory approval for oral octreotide outside the United States and to expand the indications for oral octreotide, and to further advance our nonclinical and earlier stage research and

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development projects into clinical stages. The successful development of oral octreotide and other product candidates we may develop is highly uncertain. At this time, we cannot reasonably estimate the nature, timing or costs of the efforts that will be necessary to complete the remainder of the development of oral octreotide, or any of our nonclinical programs or the period, if any, in which material net cash inflows from these product candidates may commence. Clinical development timelines, the probability of success and development costs can differ materially from expectations. For example, if the FDA or another regulatory authority were to require us to conduct clinical trials beyond those which we currently anticipate will be required for the completion of clinical development of a product candidate or if we experience significant delays in any of our clinical trials, we could be required to expend significant additional financial resources and time on the completion of clinical development.

Marketing, General and Administrative

Marketing expenses consist of professional fees related to preparation for the eventual commercialization of oral octreotide, if approved, as well as salaries and related benefits for marketing employees. As we accelerate our preparation for commercialization and, if it is approved, start to market oral octreotide and as we explore new collaborations to develop and commercialize oral octreotide and other products, we anticipate that these expenses will materially increase.

General and administrative expenses consist primarily of salaries and related benefits, including stock-based compensation, related to our executive, finance, business development, commercialization and support functions. Other general and administrative expenses include facility-related costs not otherwise allocated to research and development expenses, travel expenses for our general and administrative personnel and professional fees for auditing, tax, and corporate and intellectual property legal services. We anticipate that our general and administrative expenses will increase in future periods, reflecting an expanding infrastructure and increased professional fees associated with being a public company and potentially as a commercial-stage company.

Other Expense, Net

Other expense consists mainly of interest incurred on amounts borrowed under a loan agreement.

Change in Fair Value of Redeemable Convertible Preferred Stock Warrant Liability

Preferred stock warrant liability is associated with warrants to purchase Series C redeemable convertible preferred stock, or Series C preferred, issued to a lender under a loan agreement. Changes in the fair value of warrant liability generally consists of the calculated change in value based upon the fair value of the underlying security at the end of each reporting period as calculated using the Black-Scholes option-pricing model, or Black-Scholes. During 2013, the increase in the fair value of the warrant liability reflected an adjustment to increase the carrying value of the warrants to its fair value on the day of the exercise. There were no outstanding preferred stock warrants as of December 31, 2013 and 2014 and March 31, 2015.

Provision for Income Taxes

Our effective tax rate was 3.3% in 2013, (9.6%) in 2014, (6.6%) for the three months ended March 31, 2014 and (0.1%) for the three months ended March 31, 2015. We reported $1.2 million in provision for income taxes in 2013, which was mainly attributable to a federal alternative minimum tax liability resulting from our 2013 U.S. taxable income. In 2014, we reported $0.2 million of provision for income taxes. During the three months ended March 31, 2014 and 2015, we reported provision for income taxes of $(129,000) and $5,000, respectively.

Our deferred tax assets at December 31, 2013 and 2014 and March 31, 2015 were approximately $67,000, $40,000 and $67,000, respectively. Deferred tax assets were reported net of valuation allowances of $10.7 million, $11.3 million and $12.8 million at December 31, 2013, 2014 and March 31, 2015, respectively,

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primarily as a result of the recording of a full valuation allowance against net operating loss, or NOL, carryforwards, as we believe it is more likely than not that we will not be able to generate sufficient future taxable income to absorb them.

We file U.S. federal, various U.S. state and Israeli income tax returns. The associated tax filings remain subject to examination by applicable tax authorities for a certain length of time following the tax year to which those filings relate. In the United States and Israel, the 2011 and subsequent tax years remain subject to examination by the applicable taxing authorities as of March 31, 2015. However, U.S. NOL carryforward attributes that were generated prior to 2011 may still be adjusted upon examination by federal, state or local tax authorities if they either have been or will be used in a future period. As of December 31, 2013 and 2014, and March 31, 2015 we had provided a liability of $0.1 million, $0.2 million and $0.3 million, respectively, for uncertain tax positions related to various income tax matters that we do not expect to settle within the next 12 months. These uncertain tax positions would impact our effective tax rate, if recognized.

Critical Accounting Policies and Use of Estimates

Our management s discussion and analysis of financial condition and results of operations is based on our consolidated financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States, or GAAP. The preparation of these consolidated financial statements requires us to make estimates and assumptions that affect the reported amounts of assets, liabilities, revenues, and expenses, and the disclosure of contingent assets and liabilities as of and during the reporting periods. These items are monitored and analyzed by us for changes in facts and circumstances, and material changes in these estimates could occur in the future. 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 and the reported amount of revenues and expenses that are not readily apparent from other sources. Changes in estimates are reflected in reported results for the period in which they become known. Actual results may differ materially from these estimates under different assumptions or conditions.

While our significant accounting policies are described in more detail in the notes to our consolidated financial statements included elsewhere in this prospectus, we believe that the following accounting policies are critical to the process of making significant judgments and estimates in the preparation of our consolidated financial statements and understanding and evaluating our reported financial results.

Revenue Recognition

Revenue is recognized when the four basic criteria of revenue recognition are met: (1) persuasive evidence that an arrangement exists, (2) delivery has occurred or services have been rendered, (3) the fee is fixed or determinable and (4) collectability is reasonably assured. When one or more of the revenue recognition criteria are not met, we defer the recognition of revenue and records deferred revenue until such time that all criteria are met. For the years ending December 31, 2013 and 2014 and for the three months ended March 31, 2014, our revenue was derived primarily from our now terminated license agreement with Roche. The terms of the agreement included a non-refundable upfront fee; contingent development, commercial, and clinical milestone payments; reimbursement of certain research and development costs; and royalty payments on sales. We did not have any revenue for the three months ended March 31, 2015.

Revenue arrangements with multiple elements are divided into separate units of accounting if certain criteria are met, including whether the delivered element has stand-alone value to the customer. When deliverables are separable, consideration received is allocated to the separate units of accounting based on the relative selling price of each

deliverable and the appropriate revenue recognition principles are applied to each unit.

We recognize revenue using the proportional performance method when the services are rendered. Under the proportional performance method, revenue is recognized based on cost incurred to date as a percentage of total estimated cost to complete.

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At the inception of a license agreement, we evaluate whether each milestone is substantive on the basis of the contingent nature of the milestone. This evaluation includes an assessment of whether: (a) the consideration is commensurate with either our performance to achieve the milestone or the enhancement of the value of the delivered items as a result of a specific outcome from our performance to achieve the milestone; (b) the consideration relates solely to past performance; and (c) the consideration is reasonable relative to all of the deliverables and payment terms within the arrangement. In making this assessment, we evaluate factors such as the clinical, regulatory, commercial and other risks that must be overcome to achieve the respective milestone, the level of effort and investment required, and whether the milestone consideration is reasonable relative to all deliverables and payment terms in the arrangement. We recognize revenues related to substantive milestones in full in the period in which the substantive milestone is achieved.

We recognize royalty revenue, if any, based upon actual and estimated net sales by the licensee of licensed products in licensed territories, and in the period the sales occur.

Stock-based Compensation

We issue stock-based awards to employees and nonemployees generally in the form of stock options. We account for our stock-based awards in accordance with Financial Accounting Standards Board, or FASB, Accounting Standards Codification, or ASC, Topic 718, *Compensation Stock Compensation*, or ASC 718. ASC 718 requires all stock-based payments to employees, including grants of employee stock options and modifications to existing stock options, to be recognized in the consolidated statements of operations based on their fair values on the date of grant. We account for stock-based awards to nonemployees in accordance with FASB ASC Topic 505-50, *Equity-Based Payments to Non-Employees*, which requires the fair value of the nonemployee award to be remeasured as the award vests. For employee stock-based awards with only service conditions, we recognize compensation on a straight line basis over the requisite service period, which is usually the vesting period of the award, net of estimated forfeitures. We have granted some performance based awards where the vesting of the options is accelerated upon achievement of certain of our operational milestones. In these cases, stock-based compensation expense is accelerated when it is considered probable that our operational milestone will be met.

For modification of stock compensation awards, we record the incremental fair value of the modified awards as compensation on the date of modification for vested awards, or over the remaining vesting period for unvested awards. The incremental compensation is the excess of the fair value of the modified awards on the date of modification over the fair value of the original awards immediately before the modification. Compensation expense related to our stock-based awards is subject to a number of estimates including volatility and the underlying fair value of our common stock, as well as the estimated life of the awards.

For a detailed description of how we estimate fair value for purposes of option grants and the methodology used in measuring stock-based compensation expense, see Stock-based Compensation and Common Stock Valuation below. Following the consummation of this offering, stock option values will be determined based on the traded price of our common stock.

Income Taxes

The consolidated financial statements presented elsewhere in this prospectus reflect provisions for federal, state, local and foreign income taxes. Deferred tax assets and liabilities represent future tax consequences of temporary differences between the financial statement carrying amounts and the tax basis of assets and liabilities and for loss carryforwards using enacted tax rates expected to be in effect in the years in which the differences reverse. A valuation allowance is recorded when it is more likely than not that some or all of the deferred tax assets will not be

realized. We cannot be certain that future U.S. taxable income will be sufficient to realize our deferred tax assets and, accordingly, a full valuation allowance has been provided against our U.S. net deferred tax assets.

We evaluate the tax positions we have taken when preparing our federal, state, local and foreign income tax returns, and determine whether it is more likely than not that a tax position will be sustained upon examination. If

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it is not more likely than not that a position will be sustained, none of the benefit attributable to the position is recognized. The tax benefit to be recognized for any tax position that meets the more-likely-than-not recognition threshold is calculated as the largest amount that is more than 50% likely of being realized upon resolution of the contingency. As of December 31, 2013 and 2014, and March 31, 2015, we have provided a liability of $0.1 million, $0.2 million and $0.3 million, respectively. We account for interest and penalties related to uncertain tax positions as part of our other expenses.

Results of Operations for the Three Months Ended March 31, 2014 and 2015

Revenue

The following is a comparison of revenue for the three-months ended March 31, 2014 and 2015 (in thousands, except percentages):

	Three Months Ended March 31,			
	2014	2015	Decrease	
Revenue from license agreement	$ 4,573	$	$ 4,573	100%

Revenue during the three months ended March 31, 2014 was generated solely from our license agreement with Roche and was recognized on a proportional performance basis. During the three months ended March 31, 2014, we recognized $4.6 million of the total $85.0 million of upfront and milestone payments that were invoiced and collected from Roche. During the year ended December 31, 2014, our license agreement with Roche was terminated. Accordingly, there was no further revenue to be recognized under the license agreement during the three months ended March 31, 2015.

Research and Development

The following is a comparison of research and development expenses for the three-months ended March 31, 2014 and 2015 (in thousands, except percentages):

	Three Months Ended March 31,			
	2014	2015	Increase	
Research and development	$ 1,650	$ 2,219	$ 569	34%

During the three months ended March 31, 2015, our total research and development expenses increased by $0.6 million, or 34%, compared to the three months ended March 31, 2014, primarily due to our preparation of filing an NDA for oral octreotide in acromegaly in the United States as well as activities associated with the initiation of the manufacturing process validation.

The following table is a comparison of the components of our research and development expenses during the three-months ended March 31, 2014 and 2015 (in thousands, except percentages):

	Three Months Ended March 31,			
	2014	2015	Increase (Decrease)	
External research and development expenses:				
Oral octreotide	$ 365	$ 1,464	$ 1,099	301%
Internal research and development expenses	1,285	755	(530)	(41%)
Total research and development expenses	$ 1,650	$ 2,219	$ 569	34%

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Marketing, General and Administrative

The following is a comparison of marketing, general and administrative expenses for the three months ended March 31, 2014 and 2015 (in thousands, except percentages):

	Three Months Ended March 31,			
	2014	2015	Increase	
Marketing.	$	$ 799	$ 799	100%
General and administrative	954	1,132	178	19%
Total marketing, general and administrative expenses.	$ 954	$ 1,931	$ 977	102%

For the three months ended March 31, 2015, our marketing expenses increased by $0.8 million, or 100%, compared to the same period in 2014, related to increased pre-commercial activities related to oral octreotide.

For the three months ended March 31, 2015, our general and administrative expenses increased by $0.2 million, or 19%, compared to the same period in 2014, related to increased intellectual property protection related legal fees and costs associated with hiring our chief executive officer, senior executives and other employees.

Other Expense, net

Other expenses totaled $25,000 for the three months ended March 31, 2014 compared to $89,000 for the three months ended March 31, 2015. The increase was the result of the imputed interest associated with the long-term obligation related to the acquisition of API and trade name from Roche.

Provision for Income Taxes

Our total tax provision was $(129,000) million for the three months ended March 31, 2014, representing an effective tax rate of (6.6%), as compared to a tax provision of $5,000 for the three months ended March 31, 2015, representing an effective tax rate of (0.1%).

Our effective tax rate differs from the statutory rate each year mainly due to a full valuation allowance maintained against U.S. deferred tax assets and due to lower tax rates applied to income of our Israeli subsidiary.

Results of Operations for the Years Ended December 31, 2013 and 2014

Revenue

The following is a comparison of revenue for the years ended December 31, 2013 and 2014 (in thousands, except percentages):

	Year Ended December 31,		Decrease	

	2013	2014		
Revenue from license agreement	$ 73,134	$ 13,166	$ 59,968	82%

Revenues during the years ended December 31, 2013 and 2014 were generated solely from our license agreement with Roche and were recognized on a proportional basis. During the year ended December 31, 2013, we recognized $73.1 million of the total $85.0 million of upfront and milestone payments that were invoiced and collected from Roche. During the year ended December 31, 2014, our license agreement with Roche was terminated and the amounts recognized in 2013 and 2014 represent the entire amount earned under the license agreement.

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Research and Development

The following is a comparison of research and development expenses for the years ended December 31, 2013 and 2014 (in thousands, except percentages):

	Year Ended December 31,			
	2013	2014	Decrease	
Research and development	$ 26,455	$ 11,527	$ 14,928	56%

During the year ended December 31, 2014, our total research and development expenses decreased by $14.9 million, or 56%, compared to the prior year, primarily due to the completion of our Phase 3 clinical trial of oral octreotide in acromegaly, offset by the accrual and expense of $4.4 million for our purchase of API and other supplies related to oral octreotide in connection with the termination of our license agreement with Roche. The decrease in research and development expenses also reflected the reversal of a one-time employee termination liability we previously recorded in 2013. In March 2013, following the signing of the Roche license agreement and in anticipation of transferring our intellectual property related to oral octreotide to Roche, management and the board of directors approved a one-time involuntary employee termination plan. The termination process was expected to be completed within one year.

The estimated fair value of the one-time termination liability of $1.8 million was recorded over the required service period through the involuntary termination date for affected employees. During 2013 and 2014, we paid a total of $0.6 million and $0.5 million, respectively, of termination payments to departing employees. In July 2014, following Roche s decision not to submit a regulatory filing for oral octreotide and its corresponding termination of the license agreement, we canceled the employee termination plan and reversed the majority of the corresponding liability previously recorded in 2013.

The following table is a comparison of the components of our research and development expenses during the years ended December 31, 2013 and 2014 (in thousands, except percentages):

	Year Ended December 31,			
	2013	2014	Decrease	
External research and development expenses:				
Oral octreotide	$ 19,756	$ 8,215	$ 11,541	58%
Internal research and development expenses	6,699	3,312	3,387	51%
Total research and development expenses	$ 26,455	$ 11,527	$ 14,928	56%

General and Administrative

The following is a comparison of general and administrative expenses for the years ended December 31, 2013 and 2014 (in thousands, except percentages):

	Year Ended December 31,			
	2013	2014	Decrease	
General and administrative	$ 8,065	$ 3,469	$ 4,596	57%

For the year ended December 31, 2014, our general and administrative expenses decreased by $4.6 million, or 57%, compared to the prior year, related in part to a reduction of workforce that was previously planned in conjunction with the license agreement with Roche. Our general and administrative employee headcount was

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reduced from eight at December 31, 2013 to three at December 31, 2014. In addition, legal and accounting, recruiting, business development, insurance, travel and facilities costs not allocated to research and development declined by $2.4 million in 2013 compared to 2014.

Other Expense, net

Other expenses totaled $1.2 million for the year ended December 31, 2013 and was $4,000 in the year ended December 31, 2014. The decrease was the result of the repayment of the outstanding principal and accrued interest on a loan agreement. In February 2013, we terminated our existing loan agreement and as of December 31, 2014, we did not have any outstanding credit facilities.

Change in Fair Value of Preferred Stock Warrant Liability

During 2013, we recorded a $60,000 increase in the fair value of warrant liability that reflected changes in the fair value of these preferred stock warrants through the date of a cashless exercise for shares of Series C preferred. These warrants were issued in conjunction with a loan agreement that was repaid in 2013. The amount reflected an adjustment to bring the warrants to their fair value on the day of exercise. There were no outstanding preferred stock warrants as of December 31, 2013 and 2014.

Provision for Income Taxes

Our total tax provision was $1.2 million for the year ended December 31, 2013, representing an effective tax rate of 3.3%, as compared to a tax provision of $0.2 million for the year ended December 31, 2014, representing an effective tax rate of (9.6%). The higher tax provision in 2013 was mainly attributable to a federal alternative minimum tax liability resulting from our U.S. taxable income in 2013.

Our effective tax rate differs from the statutory rate each year primarily due to a full valuation allowance maintained against U.S. deferred tax assets and due to lower tax rates applied to income of our Israeli subsidiary.

Liquidity and Capital Resources

Since our inception and through March 31, 2015, we have raised an aggregate of $259.7 million to fund our operations, of which $86.3 million was through our license agreement with Roche, $161.4 million was from the issuance of private securities, and $12.0 million was from borrowings under a loan agreement. In March 2013, using proceeds from the Roche license agreement, we repaid all outstanding borrowings under our loan agreement and paid an aggregate of $55.0 million in cash as partial consideration for the redemption of certain shares of our preferred stock.

As of March 31, 2015, our cash was $70.9 million, of which $1.3 million was held by our Israeli subsidiary.

Indebtedness

We had a loan agreement with General Electric Capital Corporation which provided funding for an aggregate principal amount of up to $12.0 million. In February 2013, we fully repaid the outstanding borrowings and terminated the loan agreement. As of December 31, 2013 and 2014, and March 31, 2015, we did not have any outstanding borrowing under any loans or credit facilities.

Following the termination of the Roche agreement, we purchased API supplies from Roche to continue the development and manufacturing of oral octreotide, as well as Roche s trade name proposed for oral octreotide. The total consideration of $5.1 million, which is recorded in long-term liabilities on our balance sheet based on discounted value, will be paid in three equal annual installments of $1.7 million beginning in January 2016.

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Plan of Operations and Future Funding Requirements

Our primary uses of capital are, and we expect will continue to be, seeking regulatory approval of oral octreotide and preparation for commercial launch of oral octreotide in the United States, manufacturing of oral octreotide for market consumption and clinical trial uses, clinical trial costs (including an additional Phase 3 clinical trial to support European regulatory approval), compensation and related expenses, third-party clinical and nonclinical research and development services, laboratory and related supplies, legal and other regulatory expenses, and other general operating costs.

We expect that the net proceeds from this offering and our cash as of March 31, 2015 will fund our operating expenses and capital expenditure requirements through at least the end of 2016. During this period, we expect to seek regulatory approval of oral octreotide in the United States and, if granted; launch oral octreotide in the United States; initiate an additional Phase 3 clinical trial of oral octreotide to treat acromegaly to support European regulatory approval; continue clinical development plans for the use of oral octreotide in other indications; and conduct additional nonclinical studies to expand our product pipeline. We have based these estimates on assumptions that may prove to be wrong, and we could use our capital resources sooner than we currently expect. Additionally, the process of testing product candidates in clinical trials is costly, and the timing of progress in these trials is uncertain. Because our oral octreotide and potential product candidates are in various stages of clinical and nonclinical development and the outcome of these efforts is uncertain, we cannot estimate the actual amounts necessary to successfully complete the development and commercialization of oral octreotide and any other product candidates we may develop or whether, or when, we may achieve profitability. Our future capital requirements will depend on many factors, including:

- the costs and timing of future commercialization activities, including product manufacturing, marketing, sales and distribution, for oral octreotide and any other future product candidates for which we receive marketing approval;
- the costs, timing and outcome of regulatory review of oral octreotide and any future product candidates;
- proceeds, if any, received from commercial sales of oral octreotide and any future product candidates for which we receive marketing approval;
- the progress and results of our clinical trials of oral octreotide;
- the scope, progress, results, and costs of nonclinical development, laboratory testing and clinical trials for future product candidates we may develop;
- the number and development requirements of other product candidates that we pursue;
- the costs and timing of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending any intellectual property-related claims; and

the extent to which we acquire or in-license other products and technologies.

Until such time, if ever, as we can generate substantial product sales, we expect to finance our cash needs through a combination of equity offerings, debt financings and license and collaboration arrangements. To the extent that we raise additional capital through future issuance of equity or debt, 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 existing common stockholders. If we raise additional funds through collaboration arrangements, we may have to relinquish valuable rights to our technologies, future revenue streams or drug candidates 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 product candidates that we would otherwise prefer to develop and market ourselves.

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Cash Flows

The following is a summary of cash flows for the years ended December 31, 2013 and 2014 and for the three months ended March 31, 2014 and 2015 (in thousands):

	Year Ended December 31,		Three Months Ended March 31,	
	2013	2014	2014	2015
Net cash provided by (used in) operating activities	$ 46,192	$ (6,400)	$ 2,230	$ (4,923)
Net cash (used in) provided by investing activities	(18)	85	11	6
Net cash (used in) provided by financing activities	(51,815)	33,625		35,628

Net Cash Provided by (Used in) Operating Activities

Net cash provided by operating activities was $46.2 million for the year ended December 31, 2013, compared to net cash used in operating activities of $6.4 million for the year ended December 31, 2014. Net cash provided by operating activities was $2.2 million for the three months ended March 31, 2014, compared to net cash used in operating activities of $4.9 million for the three months ended March 31, 2015. During the year ended December 31, 2013, we collected $75.0 million of the total $85.0 million of upfront and milestone payments that were invoiced to Roche. During the year ended December 31, 2014 and prior to terminating our license agreement with Roche, we collected an additional $11.3 million from Roche. Our spending decreased in 2014 primarily as a result of the completion of our Phase 3 clinical trial of oral octreotide in acromegaly and headcount reduction in both the research and development and general and administrative areas of our operations. During the three months ended March 31, 2014, we collected $10.0 million of the milestone payments invoiced to Roche. During the three months ended March 31, 2015, we used internal cash resources to finance our operating activities. Our spending increased in the three months ended March 31, 2015 primarily as a result of increased activities related to preparing to file our NDA for oral octreotide in acromegaly in the United States, activities associated with the initiation of the manufacturing process validation as well as increased pre-commercial activities related to oral octreotide.

Net Cash (Used in) Provided by Investing Activities

Net cash used in investing activities was $18,000 for the year ended December 31, 2013, compared to cash provided by investing activities of $85,000 for the year ended December 31, 2014. Net cash provided by investing activities was $11,000 for the three months ended March 31, 2014, compared to cash provided by investing activities of $6,000 for the three months ended March 31, 2015. The increase in cash provided by investing activities in the year ended December 31, 2013 as compared to the year ended December 31, 2014 was primarily the result of proceeds from sales of property and equipment during 2014. The decrease in cash provided by investing activities in the three months ended March 31, 2014 as compared to the three months ended March 31, 2015 was primarily the result of acquisition of equipment.

Net Cash (Used in) Provided by Financing Activities

Net cash used in financing activities during the year ended December 31, 2013 of $51.8 million was primarily related to the repayment of borrowings under our loan agreement totaling $11.1 million and a cash redemption payment to the holders of redeemable convertible preferred stock totaling $55.0 million, offset by proceeds from the issuance of the third tranche of Series D redeemable convertible preferred stock and common stock warrants of $14.2 million. Net cash provided by financing activities for the year ended December 31, 2014 of $33.6 million was due to the issuance

of Series E redeemable convertible preferred stock and common stock warrants. We did not generate net cash from financing activities during the three months ended March 31, 2014. Net cash provided by financing activities during the three months ended March 31, 2015 of $35.6 million was mainly due to the sale and issuance of the second tranche of our Series E redeemable convertible preferred stock and common stock warrants.

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Contractual Obligations and Contingent Liabilities

The following summarizes our significant contractual obligations as of December 31, 2014 (in thousands):

Contractual Obligations	Total	Less than 1 Year	1 to 3 Years	3 to 5 Years	More than 5 Years
Operating leases	$ 155	$ 155	$	$	$
Long-term purchase obligation	5,100		3,400	1,700	
Total obligations	$ 5,255	$ 155	$ 3,400	$ 1,700	$

Operating Leases. This amount represents future minimum lease payments under non-cancelable operating leases in effect as of December 31, 2014 for our current facilities in Israel. The minimum lease payments do not include common area maintenance charges or real estate taxes.

Long-term Purchase Obligation. Upon termination of the Roche agreement in 2014, we purchased API supplies from Roche to continue the development and manufacturing of oral octreotide and Roche s proposed trade name for oral octreotide. The undiscounted consideration of $5.1 million will be paid in equal annual installments of $1.7 million beginning in January 2016. We have no further obligations to Roche upon full payment of these amounts.

The table excludes potential payments we may be required to make under manufacturing and CRO agreements as the timing of when these payments will actually be made is uncertain and the payments are contingent upon the initiation and completion of future activities.

There were no material changes outside the ordinary course of business in our contractual obligations during the three months ended March 31, 2015.

Stock-based Compensation and Common Stock Valuation

Stock-based Compensation

We estimate the fair value of our stock-based awards to employees and nonemployees using Black-Scholes, which requires the input of highly subjective assumptions, including (a) the weighted-average expected volatility of our stock, (b) the weighted-average expected term of the award, (c) the weighted-average risk-free interest rate and (d) expected dividends. Due to the lack of a public market for the trading of our common stock and a lack of company-specific historical and implied volatility data, we have based our estimate of expected volatility on the historical volatility of a group of publicly traded companies in the pharmaceutical and biotechnology industries in a similar stage of development as us. For these analyses, we have selected companies with comparable characteristics to ours, including enterprise value and risk profiles, and with historical share price information sufficient to meet the expected life of the stock-based awards. We compute the historical volatility data using the daily closing prices for the selected companies shares during the equivalent period of the calculated expected term of our stock-based awards. We will continue to apply this process until a sufficient amount of historical information regarding the volatility of our own stock price becomes available. We have estimated the expected life of our employee stock options using the simplified method, whereby the expected life equals the average of the vesting term and the original contractual term of the option. The risk-free interest rates for periods within the expected life of the option are based on the U.S. Treasury yield curve in effect during the period the options were granted.

We are also required to estimate forfeitures at the time of grant and revise those estimates in subsequent periods if actual forfeitures differ from estimates. We use historical data to estimate pre-vesting option forfeitures and we record stock-based compensation expense only for those awards that are expected to vest. To the extent that

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actual forfeitures differ from our estimates, the difference is recorded as a cumulative adjustment in the period the estimates were revised. Stock-based compensation expense recognized in the financial statements is based on awards that are ultimately expected to vest.

We have computed the fair value of employee stock options at date of grant using the following weighted-average assumptions:

	Year Ended December 31,		Three Months Ended March 31,	
	2013	2014	2014	2015
Expected volatility	85%	80%		80%
Expected term (in years)	6.25	6.25		6.25
Risk-free interest rate	1.08%	1.79%		1.75%
Expected dividend yield	0%	0%		0%

No stock option grants were made during the three months ended March 31, 2014.

Stock-based compensation for employees and nonemployees were allocated as indicated in the following table (in thousands):

	Year Ended December 31,		Three Months Ended March 31,	
	2013	2014	2014	2015
Research and development	$ 297	$ 424	$ 46	$ 136
General and administrative	448	332	83	85
Total	$ 745	$ 756	$ 129	$ 221

As of March 31, 2015, we had $2.2 million of unrecognized compensation expense, which is expected to be recognized over a weighted-average remaining vesting period of 3.28 years. We expect the impact of our stock-based compensation expense for stock options granted to employees and nonemployees to grow in future periods due to the potential increases in the value of our common stock and future grants to existing and new employees.

During the years ended December 31, 2013 and 2014, we modified stock options granted to certain employees providing for the extension of exercise period post-employment termination, performance based acceleration of vesting terms and changes in exercise prices. For the year ended December 31, 2014, the incremental compensation expense resulting from the modifications was calculated by comparing the fair value of stock options immediately before and immediately after the modification and totaled $0.4 million which included $0.3 million classified as research and development expenses and $0.1 million classified as general and administrative expense.

Common Stock Valuation

We have historically granted stock options at exercise prices determined by our board of directors. We are a private company with no active public market for our common stock. Therefore, our board of directors estimated the per share fair value of our common stock at each grant date using internal and external factors that it believed to be relevant,

including its and management s best estimate of our business condition, prospects, and operating performance at each grant date. In reaching its fair value determinations, our board of directors and management considered a range of objective and subjective factors and assumptions including, among others:

- the prices of our preferred stock issued to or exchanged between investors in arm s length transactions, and the rights, preferences and privileges of our preferred stock as compared to those of our common stock, including the liquidation preferences of our preferred stock;

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our results of operations, financial position, and the status of research and development efforts;

the composition of, and changes to, our management team and board of directors;

the lack of liquidity of our common stock as a private company;

our stage of development and business strategy and the material risks related to our business and industry;

the achievement of enterprise milestones, including entering into collaboration and license agreements;

any external market conditions affecting the life sciences and biotechnology industry sectors; and

the likelihood of achieving a liquidity event for the holders of our common stock and stock options, such as an initial public offering, or IPO, or a sale of our company, given prevailing market conditions.

Common Stock Valuation Methodologies

In preparing for our proposed IPO, we determined that retrospective valuations of the fair value of our common stock for certain prior stock compensation awards were appropriate due to the acceleration of the time frame to a potential liquidity event. In connection with that reexamination, we obtained retrospective valuations of the fair value of our common stock for financial reporting purposes to assist our board of directors in re-evaluating the fair value of our common stock as of these dates.

The valuations discussed below were prepared in accordance with the guidance outlined in the American Institute of Certified Public Accountants Practice Aid, *Valuation of Privately-Held Company Equity Securities Issued as Compensation*, also known as the Practice Aid, which prescribes several valuation approaches for setting the value of an enterprise, such as the cost, market, and income approaches, and various methodologies for allocating the value of an enterprise to its common stock. We generally used the market approach, in particular the guideline company analysis and transaction analysis, based on inputs from comparable public companies equity valuations and comparable acquisition and IPO transactions, to estimate the enterprise value of our company. In addition to the market approach based on our recent transactions, we also utilized the income approach for purposes of the December 16, 2014, March 16, 2015 and June 14, 2015 valuations based upon the potential occurrence of an IPO and/or sale, merger or liquidation (or SML). The resulting values were weighted with the value estimated using the market approach.

Methods Used to Allocate Our Enterprise Value to Classes of Securities

In accordance with the Practice Aid, we considered the various methods for allocating the enterprise value across our classes and series of capital stock to determine the fair value of our common stock at each valuation date. The methods we considered consisted of the following:

Option Pricing Method. Under the option pricing method, or OPM, shares are valued by creating a series of call options with exercise prices based on the liquidation preferences and conversion terms of each equity class. The values of the preferred and common stock are inferred by analyzing these options. The total equity value allocated to the common stock is then divided by the number of shares outstanding at each valuation date to determine the fair value per share. In addition, since our stock is not publicly traded, a discount for lack of marketability is then applied to determine the fair value of our common stock.

Probability-Weighted Expected Return Method, or PWERM. The PWERM is a scenario-based analysis that estimates the value per share based on the probability-weighted present value of expected future investment returns, considering each of the possible outcomes available to us, as well as the economic and control rights of each share class.

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Retrospective Valuations

In preparing for our proposed IPO, we obtained retrospective valuations of the fair value of our common stock for financial reporting purposes to assist our board of directors in re-evaluating the fair value of our common stock as of these dates.

March 28, 2013 and December 16, 2014 Common Stock Valuations

We obtained retrospective valuations of our common stock on March 28, 2013 and December 16, 2014, which represented the dates of recent equity transactions. These retrospective valuations primarily used variations of the OPM approach, then-current rights and attributes of the securities in our capital structure and the terms of the recent capital transactions with third party investors negotiated at arm s length as compared to the results of a guideline company analysis and a guideline transaction analysis, to determine our enterprise value. These rights and attributes of our securities were determined based on their respective liquidation and conversion terms and preferences. In calculating the enterprise value to be allocated to these securities, a series of Black-Scholes call-option models were utilized based on the relative claim amount on an as-converted basis. In addition, for the December 16, 2014 valuation, we used the PWERM approach to include the effect of a potential SML and IPO.

For purposes of the March 28, 2013 and December 16, 2014 valuations, we relied on the following key assumptions in applying the OPM:

- We estimated volatility of 80% for purposes of the March 28, 2013 valuation and 75% for purposes of the December 16, 2014 valuation, based on guideline publicly traded companies and industry benchmarks with an expected term consistent with the timeline to the liquidity event.

- We estimated a weighted-average time to an exit scenario of two years for purposes of the March 28, 2013 valuation and 1.4 years for purposes of the December 16, 2014 valuation, based on the projected time to an SML or IPO.

- We determined the risk-free interest rate based on the yield of a U.S. Treasury bill with a maturity date closest to the estimated time to a sale event for our stockholders. The risk-free interest rate used were 0.25% for purposes of the March 28, 2013 valuation and 0.47% for purposes of the December 16, 2014 valuation.

- We applied a discount for lack of control and marketability, or DLOM, of 15% on both valuation dates, which reflected the prospect of our attaining a liquidity event in the foreseeable future combined with the highly illiquid nature of our common stock as well as the lack of control possessed by common stockholders in light of the rights and privileges of our preferred stock, including anti-dilution protection, redemption rights, protective provisions in our certificate of incorporation and rights to participate in future rounds of financing.

At the December 16, 2014 valuation date, we were considering an IPO. In addition to the OPM approach described above, we also utilized an income approach using the PWERM. The fair value of our common stock was estimated using a probability weighted analysis of the present value of the returns afforded to common stockholders under several future stockholder exit or liquidity event scenarios, either through an IPO or an SML. The present value of the

projected equity value was then calculated by discounting the probability weighted equity value to the December 16, 2014 valuation date. The assumptions underlying the projected IPO pricing include projected market penetration, pricing, FDA approval and other factors related to the potential commercialization of oral octreotide.

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The specific facts and circumstances considered by our board of directors in assessing these key valuation assumptions for the December 16, 2014 retrospective valuations using the PWERM approach included those noted in the following table:

December 16, 2014 Major Assumptions	IPO	Sale/ Merger/ Liquidation
Probability of scenario	33.3%	66.7%
Discount for marketability	15%	15%
Timeline to liquidity	0.8 years	1.8 years
Discount rate common stock	30%	N/A

The values of our common stock estimated in the SML and IPO scenarios were then weighted together and a DLOM was estimated and subtracted to conclude the fair value of our common stock. The resulting estimated fair value of our common stock based on the results of the valuation methodologies described above as of March 28, 2013 was $4.84 per share, as of immediately prior to the redemption of certain of our then outstanding shares of preferred stock, and $5.21 per share immediately following the redemption. The resulting estimated fair value of our common stock based on the results of the valuation methodologies described above was $3.65 per share as of December 16, 2014.

Our board of directors considered these retrospective valuations, together with the other factors described in the preceding paragraphs, in making its retrospective determination of the fair value, which it determined to be $5.21 per share as of March 28, 2013 and $3.65 per share as of December 16, 2014. Our board of directors also considered the fair value of our common stock retrospectively as of August 1, 2014, October 21, 2014, and November 12, 2014 and determined that the termination of the Roche agreement during July 2014 was indicative of a significant change in the fair value of our common stock. As a result, our board of directors determined that the retrospective fair value of our common stock as of August 1, 2014, October 21, 2014, and November 12, 2014 was $3.65 per share. In addition, because the factors we considered in estimating the March 28, 2013 valuation, which included an equity transaction on that date and the signing of the license agreement with Roche, were also either present or contemplated on March 20, 2013, our board of directors determined that the retrospective fair value of our common stock as of March 20, 2013 was $4.84 per share.

March 16, 2015 Valuation

We obtained contemporaneous valuations of our common stock on March 16, 2015 to assist our board of directors in estimating the fair value of our common stock on subsequent grant dates. These contemporaneous valuations used the OPM approach and the PWERM approach to determine the enterprise value of our company.

The OPM, which included a guideline company analysis and a guideline transaction analysis, was developed based on the then-current rights and attributes of the securities in our capital structure and the terms of the recent capital transaction, primarily the issuance of Series E preferred, negotiated in an arm s length with third-party investors. A series of Black-Scholes call-option models was then utilized to allocate the enterprise value to the common stock on an as-converted basis. These rights and attributes of our securities were determined based on their respective liquidation and conversion terms and preferences.

For purposes of the March 16, 2015 valuation, we relied on the following key assumptions in applying the OPM:

We estimated volatility of 75% using guideline publicly traded companies and industry benchmarks with an expected term consistent with the timeline to the liquidity event.

We estimated a weighted-average time to an exit scenario of 1.1 years based on the projected time to an SML or IPO.

We determined the risk-free interest rate based on the yield of a U.S. Treasury bill with a maturity date closest to the estimated time to a sale event for our stockholders. The risk-free interest rate used was 0.47% for purposes of the March 16, 2015 valuation.

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We applied a discount for lack of control and marketability of 15%, which reflected the prospect of our attaining a liquidity event in the foreseeable future combined with the highly illiquid nature of our common stock, as well as the lack of control possessed by common stockholders in light of the rights and privileges of our preferred stock, including anti-dilution protection, redemption rights, protective provisions in our certificate of incorporation and rights to participate in future rounds of financing.

At the March 16, 2015 valuation date, we were in the process of pursuing an IPO. Therefore, we also utilized the PWERM valuation methodology in combination with the OPM described above to allocate the enterprise value to the common stock. Under the PWERM, the value of the common stock was estimated based upon an analysis of future values for our company assuming various investment outcomes, the timing of which was based, in part, on the plans of our board of directors and management. Under the PWERM, share value was derived from the probability-weighted present value of expected future investment returns, considering each of the possible outcomes available to us, as well as the economic and control rights of each share class under possible future stockholder exit or liquidity event scenarios, either through an IPO or an SML, then calculated by discounting the probability weighted equity value to the March 16, 2015 valuation date.

For the March 16, 2015 valuation, significant assumptions for the PWERM included the probability of occurrence of each scenario, timing to the liquidity event, discount rate and discount for lack of marketability. The key valuation assumptions included:

March 16, 2015		
Major Assumptions	**IPO**	**Sale/ Merger/ Liquidation**
Probability of Scenario	50%	50%
Discount for Marketability	15%	15%
Timeline to Liquidity	0.375 years	1.75 years
Discount Rate Common Stock	30%	N/A

The estimated fair value of our common stock as of March 16, 2015 using the combined results of OPM and PWERM was $5.57 per share.

June 14, 2015 Valuation

We obtained a contemporaneous valuation of our common stock on June 14, 2015 to assist our board of directors in estimating the fair value of our common stock on subsequent grant dates. This contemporaneous valuation used the OPM approach, the discounted cash flow, or DCF approach, and the PWERM approach to determine the enterprise value of our Company. The OPM was developed based on the then-current rights and attributes of the securities in our capital structure and the terms of the recent capital transaction, primarily the issuance of Series E preferred, negotiated in an arm s length with third-party investors. These rights and attributes of our securities were determined based on their respective liquidation and conversion terms and preferences.

For the DCF approach, our projected after-tax cash flows were discounted back to present value, using a discount rate. Since it is not possible to project our after-tax cash flows beyond a limited number of years, the DCF method relies on determining a terminal or exit value representing the aggregate value of either the future after-tax cash flows or estimated sale price of the Company after the end of the period for which annual projections are possible. The discount rate, known as the weighted cost of capital, or WACC, accounts for the time value of money and the appropriate degree of risk inherent in the business and the projected cash flows. The DCF approach requires significant assumptions regarding our projected cash flows, terminal or exit value and the discount rate applicable to

our business.

The OPM approach and the DCF approach were equally weighted to arrive at the estimated enterprise value for the SML scenario. We also used the guideline company method and the guideline transaction method in order to evaluate whether the DCF and OPM approaches provided a reliable estimate of our enterprise value. The

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estimated value in the SML scenario was then allocated using an OPM based on the rights and attributes of the securities in our capital structure at the June 14, 2015 valuation date.

For purposes of allocating the estimated SML equity value for the June 14, 2015 valuation, we relied on the following key assumptions in applying the OPM:

- We estimated volatility of 70% using guideline publicly traded companies and industry benchmarks with an expected term consistent with the timeline to the liquidity event.

- We estimated a weighted-average time to an exit scenario of 1.75 years based on the projected time to a SML.

- We determined the risk-free interest rate based on the yield of a U.S. Treasury bill with a maturity date closest to the estimated time to a sale event for our stockholders. The risk-free interest rate used was 0.62% for purposes of the June 14, 2015 valuation.

- We applied a discount for lack of control and marketability of 10%, which reflected the prospect of our attaining a liquidity event in the foreseeable future balanced against the current illiquid nature of our common stock, as well as the lack of control possessed by common stockholders in light of the rights and privileges of our preferred stock, including anti-dilution protection, redemption rights, protective provisions in our certificate of incorporation and rights to participate in future rounds of financing.

At the June 14, 2015 valuation date, we were in the process of pursuing an IPO. Therefore, we also utilized the PWERM valuation methodology in combination with the OPM and DCF approaches described above to allocate the enterprise value to the common stock. Under the PWERM, the value of the common stock was estimated based upon an analysis of future values for our company assuming various investment outcomes, the timing of which was based, in part, on the plans of our board of directors and management. Under the PWERM, share value was derived from the probability-weighted present value of expected future investment returns, considering each of the possible outcomes available to us, as well as the economic and control rights of each share class under possible future stockholder exit or liquidity event scenarios, either through an IPO or an SML, then calculated by discounting the probability weighted equity value to the June 14, 2015 valuation date.

For the June 14, 2015 valuation, significant assumptions for the PWERM included the probability of occurrence of each scenario, timing to the liquidity event, discount rate and discount for lack of marketability. The key valuation assumptions included:

June 14, 2015 **Major Assumptions**	**IPO**	**Sale/ Merger/ Liquidation**
Probability of Scenario	70%	30%
Discount for Marketability	10%	10%
Timeline to Liquidity	0.131 years	1.75 years

Discount Rate	22.5%	22.5%

The estimated fair value of our common stock as of June 14, 2015 was $8.13 per share.

Estimated Offering Price

Our estimate of the fair value of our common stock was $8.13 per share at June 14, 2015, which was determined by our board of directors with the assistance of a contemporaneous valuation of our common stock as of June 14, 2015. This valuation utilized a probability weighted expected return method (PWERM) attributing a 70% probability to an initial public offering and a 30% probability to the scenarios of remaining a private company, sale, merger or liquidation and reflected a 10% discount for lack of marketability. The 70% weighting attributed to an initial public offering reflected our subjective assessment as to the necessity and likelihood of an initial

public offering in light of the working capital provided by our recent financing round, macro-economic and market conditions, including market conditions for initial public offerings of companies similarly situated to ours, our subjective assessment as to the likelihood of FDA approval of our oral octreotide product candidate, our continued progress towards commercialization in the event our oral octreotide product candidate is approved, and our subjective assessment as to the likelihood of successfully executing an initial public offering in the coming months, among other factors. We note that, as is typical in initial public offerings, the offering price was not derived using a formal determination of fair value, but was determined based upon discussions between us and the underwriters. Among the factors considered in setting the estimated range were prevailing market conditions and estimates of our business potential, the general condition of the securities market and the market prices of, and demand for, publicly-traded common stock of generally comparable companies.

In addition, we believe that the difference in value reflected between the offering price and the determination of the fair value of our common stock on June 14, 2015 was primarily the result of the following factors:

- since June 14, 2015, we publicly filed the registration statement of which this prospectus is a part, and our common stock has received approval for listing on The NASDAQ Global Select Market;

- since June 14, 2015, we have continued to advance our preparations for the initiation of a Phase 3 trial in Europe for our oral octreotide product candidate, which is expected to commence later this year;

- the contemporaneous valuation prepared as of June 14, 2015 contains multiple liquidity scenarios, including an initial public offering to which we assigned a probability weighting of 70%. The consideration of different scenarios accounts for some but not all of the difference between the initial public offering price and the valuation as of June 14, 2015;

- the June 14, 2015 valuation took into account the uncertainty surrounding the public offering in terms of the likelihood of success, timing and price. The initial public offering price necessarily assumes that the initial public offering has occurred, that a public market for our common stock has been created, and therefore excludes any discount for lack of marketability of our common stock, which was factored in the June 14, 2015 valuation. Accordingly, the previously used private company valuation methodology is no longer applicable;

- the proceeds of a successful initial public offering would substantially strengthen our consolidated balance sheet by increasing our cash and cash equivalents. Additionally, the completion of this offering provides us with access to the public company debt and equity markets and a lower cost of capital following the public offering. These projected improvements in our consolidated financial position influenced the offering price shown on the cover of this prospectus;

- the price that investors are willing to pay in this offering may take into account other things that have not been expressly considered in our prior valuations but matter to investors in their own subjective and qualitative assessment of our company, are thus not objectively determinable and that valuation models are

not able to quantify; and

in the public markets we believe there are investors who may apply more qualitative valuation criteria to certain of our clinical assets than the valuation methods applied in our valuations.

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Stock Option Grants

The following table summarizes stock options granted from January 1, 2013 through June 14, 2015.

Grant Date	Number of Common Shares Underlying Options Granted	Exercise Price Per Common Share at Grant Date	Reassessed Fair Value Per Common Share[(1)]	Fair Value per Option at Grant Date	Intrinsic Value Per Common Share at Grant Date
June 14, 2015	628,539	$ 8.13	$ 8.13	$ 5.47	$
April 14, 2015	1,507,234	5.57	5.57	3.72	
February 17, 2015	61,322	3.29	3.65	2.62	0.36
February 6, 2015	61,322	3.29	3.65	2.61	0.36
November 17, 2014	91,954	3.29	3.65	2.62	0.36
November 15, 2014	475,083	3.29	3.65	2.61	0.36
October 21, 2014	122,605	2.74	3.65	2.72	0.91
March 20, 2013	27,375	7.03	4.84	3.22	

(1) The fair value of our common stock was reassessed for financial reporting purposes subsequent to the grant date based on retrospective valuations.

Stock Option Modifications

In March 2013, the board of directors effected the following changes to the terms of the then outstanding stock options: (a) an extension of option exercise period to the second anniversary of the termination of employment or consulting services; and (b) acceleration of the option vesting period upon a decision by Roche to file for regulatory approval as defined in the license agreement. In addition, during May 2014 and September 2014, the board of directors modified the exercise price of certain stock options granted to employees and executives. The incremental compensation expense, resulting from comparing the fair value of stock options immediately before and immediately after the modification, for the years ended December 31, 2013 and 2014 totaled $0.2 million and $0.4 million, respectively.

Off-Balance Sheet Arrangements

As of December 31, 2013 and 2014, and March 31, 2015 we did not have any off-balance sheet arrangements.

NOL Carryforwards

At March 31, 2015, we had federal NOL carryforwards of $27.0 million. The federal NOL carryforwards expire at various dates through 2035. At March 31, 2015, we had NOL carryforwards in our Israeli subsidiary of $0.3 million. The foreign NOLs may be carried forward indefinitely, but may not be used to offset future taxable income in the United States.

Under Section 382 of the Internal Revenue Code of 1986, as amended, or Section 382, substantial changes in our ownership may limit the amount of NOL carryforwards that can be utilized annually in the future to offset our U.S. federal taxable income. Specifically, this limitation may arise in the event of a cumulative change in our ownership of more than 50% within any three-year period. Management has determined that we experienced an ownership change for purposes of Section 382 on August 16, 2005 and May 12, 2008. These ownership changes resulted in annual limitations to the amount of NOL carryforwards that can be utilized to offset future taxable income, if any, at the federal level. The annual limit is $0.1 million for 2014 and each year thereafter. These annual limitations resulted in the loss of our ability to utilize $8.9 million in federal NOL carryforwards, which resulted in a write-off of $3.0 million of federal deferred tax assets prior to 2013.

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JOBS Act

In April 2012, the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, was enacted. Section 107 of the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. Thus, an emerging growth company can delay the adoption of certain 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 public companies.

Quantitative and Qualitative Disclosures about Market Risk

The market risk inherent in our financial instruments and in our financial position represents the potential loss arising from adverse changes in interest rates. As of March 31, 2015, we had $70.9 million in cash, consisting of cash in checking accounts at U.S. and Israeli banking institutions. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates. Since we do not hold any cash equivalents, an immediate 100 basis point change in interest rates would not have a material effect on our financial results. As of March 31, 2015, we did not have any outstanding borrowings so that we are not exposed to interest rate risk associated with credit facilities.

In addition, we are subject to currency risk for balances held, or denominated, in currencies other than U.S. dollars. We work to maintain all balances in U.S. dollars until payment in other currencies is required to minimize this currency risk. Fluctuations in the exchange rate between the U.S. dollar and each of the Euro, GBP and NIS over the past 24 months has been approximately 32%, 17% and 30%, respectively. As of March 31, 2015, we held $1.3 million in Israeli banks and petty cash funds to support our Israeli operations, the majority of which is denominated in U.S. dollars. We contract with CROs internationally, primarily for the execution of clinical trials and manufacturing activities. Transactions with these providers are settled in U.S. dollars, Euros or GBP and, therefore, we believe that we have only minimal exposure to foreign currency exchange risks. We do not hedge against foreign currency risks.

We do not believe that inflation and changing prices had a significant impact on our results of operations for any periods presented herein.

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BUSINESS

Overview

We are a late-stage biopharmaceutical company focused on improving the lives of patients suffering from orphan diseases by developing and commercializing novel oral forms of therapies that are available today only by injection. Using our proprietary Transient Permeability Enhancer, or TPE, technology platform, we seek to develop oral therapies that eliminate the significant limitations and burdens generally associated with existing injectable therapies. We have completed a multinational Phase 3 clinical trial of our most advanced TPE platform-based product candidate, oral octreotide, for the treatment of acromegaly, a condition that results in the body s production of excess growth hormone. Octreotide is an analog of somatostatin, a natural inhibitor of growth hormone secretion. We believe that our lead product candidate, if approved by regulatory authorities, will be the first somatostatin analog available for oral administration. Our oral octreotide product candidate has been granted orphan designation in the United States and the European Union for the treatment of acromegaly. We submitted a new drug application, or NDA, to the U.S. Food and Drug Administration, or FDA, on June 15, 2015, seeking approval for the marketing and sale of oral octreotide for the maintenance therapy of adult patients with acromegaly. The FDA has 60 days after receipt of the NDA to preliminarily review and determine if the application is sufficiently complete to permit a substantive review and meets the threshold for filing. In light of our clinical data and feedback from patients and healthcare providers, we believe that oral octreotide, if approved, could become a new standard of care in acromegaly.

Acromegaly is a condition caused by a benign tumor of the pituitary gland that releases excess growth hormone, or GH, which in turn elevates insulin-like growth factor 1, or IGF-1. These elevated hormone levels result in a number of painful and disfiguring symptoms, including some acute, such as headaches, joint pain and fatigue, and some long-term, such as enlarged hands, feet and internal organs, as well as altered facial features. If not treated promptly, acromegaly can lead to serious illness and is associated with premature death, primarily due to cardiovascular disease. According to data published by the Mayo Clinic in 2013, the mortality rate of people afflicted by acromegaly who go untreated is two to three times higher than that of the general population. Recent data from a published study presented at the Endocrine Society s Annual Meeting in 2015 suggest that the global prevalence of acromegaly may be between 85 and 118 cases per million people.

The current standard of care for patients diagnosed with acromegaly consists of lifelong, once-monthly injections of an extended release somatostatin analog, primarily octreotide or lanreotide. These products contain a viscous formulation and are typically administered by a healthcare professional with large-gauge needles into the muscle or deep subcutaneously, that is, deeply under the skin. While injectable somatostatin analogs are generally effective at reducing GH and IGF-1 levels and therefore providing disease control, the injections are associated with significant limitations and patient burdens, including suboptimal symptom control, pain, injection-site reactions and other injection-related side effects, inconvenience, lost work days and emotional issues. The worldwide market for injectable somatostatin analogs is approximately $2.0 billion annually, of which approximately $730 million represents annual sales for the treatment of acromegaly.

Our lead product candidate, oral octreotide, is the first somatostatin analog formulated for oral administration to complete a Phase 3 clinical trial and demonstrate clinical proof of concept in treating patients with acromegaly. In our Phase 3 clinical trial, we observed that oral octreotide maintained reduced levels of GH and IGF-1, or biochemical disease control, and improved symptom control. In this 155-patient Phase 3 clinical trial designed to evaluate oral octreotide in acromegaly patients already controlled on injectable somatostatin analogs, 65% of patients receiving oral octreotide twice a day for up to seven months achieved the primary endpoint, maintenance of biochemical disease control. This biochemical disease control was durable and 86% of patients who completed the seven-month core treatment period of the trial elected to continue on oral therapy during the six-month extension phase for up to a total

of 13 months of treatment after first dosing, rather than switch back to injections. In the majority of patients in our trial, oral octreotide achieved comparable biochemical disease control and reduced incidence and severity of acromegaly symptoms relative to injectable somatostatin analogs currently used to treat this disease. The adverse events observed for oral octreotide were similar to those previously reported for injectable somatostatin analogs, but without injection-site reactions.

Based in part on the data from our Phase 3 clinical trial, we submitted an NDA on June 15, 2015 seeking approval for the marketing and sale of oral octreotide for the maintenance therapy of adult patients with acromegaly. Assuming the FDA accepts for filing, reviews and responds to our NDA in accordance with the goals and policies agreed to by the FDA under the Prescription Drug User Fee Act, or PDUFA, and subject to the FDA s acceptance of the NDA for filing, we anticipate a regulatory decision on marketing approval in April 2016. To support approval by the European Medicines Agency, or the EMA, and subject to final agreement with the EMA on the protocol for this trial, we intend to initiate an additional Phase 3 clinical trial of oral octreotide in acromegaly in the second half of 2015 in the United States and internationally to show parallel comparative safety and effectiveness as required by the EMA. Assuming we receive favorable results from this second Phase 3 clinical trial, we expect to submit a marketing authorization application, or MAA, to the EMA in late 2017 or early 2018. In addition, if we receive regulatory approval of oral octreotide in acromegaly, we expect to initiate a Phase 2 clinical trial in the second half of 2016 for neuroendocrine tumors, or NET, which are currently treated predominantly by injectable somatostatin analogs, and for another new indication.

Approximately 40% of people with acromegaly undergoing treatment in the United States are treated by endocrinologists at a small number of academic institutions with pituitary experts, which we refer to as pituitary centers. The remaining people with acromegaly undergoing treatment are generally treated by community endocrinologists. We believe we will be able to market oral octreotide, if approved, directly to pituitary centers that treat high volumes of patients with acromegaly through our own small, targeted sales force. We also intend to direct our sales and marketing efforts towards the larger number of community endocrinologists. We believe that oral octreotide, if approved, will be embraced by these healthcare providers who are generally hampered by the complexity and resource burden associated with the administration of currently available injectable therapies. Finally, we intend to continue to engage in direct patient outreach efforts. We believe that the clinical benefits and preferences of patients and healthcare professionals for an oral product together with our patient-centric approach could enable oral octreotide, if approved, to become a new standard of care in acromegaly.

We retain worldwide rights to develop and commercialize oral octreotide with no royalty obligations to third parties. We intend to commercialize oral octreotide ourselves in the United States and we plan to explore the strategic merits of collaboration opportunities for commercializing oral octreotide in Europe and the rest of the world. Oral octreotide is currently protected by issued patents lasting until at least 2029 in the United States, United Kingdom and Japan, and pending patent applications in additional jurisdictions that will last until 2029, if granted. We are also pursuing additional patent applications relating to particular uses, dosages and packaging for oral octreotide.

We also intend to use our TPE platform to develop a new line of oral medications, beyond oral octreotide, to help improve the lives of patients suffering from other debilitating diseases that are currently being treated with injectable therapies. In contrast to conventional small molecule drugs, the oral absorption of larger molecules, such as peptides and other protein molecules, is limited due to low intestinal permeability and digestion in the stomach and intestine. Our TPE platform transiently enhances intestine permeability, allowing peptides and other drugs that are otherwise poorly absorbed when administered orally to pass through the intestine and reach therapeutic levels in the blood. We believe our TPE platform is particularly well suited to therapies used in chronic indications for which injections are required and for which the active agent can be administered without adverse safety implications. While our technology will not be appropriate for all drugs that cannot currently be administered orally, based on our nonclinical proof of concept data we believe that we can administer a number of peptide-based drugs orally using our TPE technology and achieve therapeutic levels in the blood.

As we consider new peptide-based drugs to develop using our TPE platform, to reduce the development time and expenses and overall level of investment required we intend to focus our efforts on drugs for which we may utilize the FDA s 505(b)(2) regulatory pathway in the United States and the hybrid application pathway, which is analogous to

the 505(b)(2) regulatory pathway, in Europe. With oral octreotide, we brought a TPE-based product candidate from concept to the first clinical trial within 18 months and then on to clinical proof of concept within an additional 12 months.

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We have assembled an experienced team with extensive drug discovery, development and commercialization capabilities. Our investors include funds affiliated with MPM Capital, Fidelity Securities, Abingworth, 7 Med Health Ventures, F2 Capital, ARCH Venture Partners, Sofinnova Ventures and Rock Springs Capital.

Strategy

Our goal is to become a leading patient-focused biopharmaceutical company by developing and commercializing oral octreotide for acromegaly and other orphan indications, and leveraging our TPE platform to develop and commercialize novel oral products for other debilitating diseases currently treated only by injectable therapies. Our strategy to pursue this goal includes the following elements:

Obtain U.S. regulatory approval of oral octreotide for the treatment of acromegaly. Based in part on the results of our Phase 3 clinical trial, we submitted an NDA to the FDA on June 15, 2015 seeking approval for the marketing and sale of oral octreotide for the maintenance therapy of adult patients with acromegaly. Assuming the FDA reviews and responds to our NDA within 10 months of receipt in accordance with the PDUFA timeline, and subject to the FDA s acceptance of the NDA for filing, we anticipate a regulatory decision from the FDA on marketing approval in April 2016.

Independently commercialize oral octreotide in the United States. In anticipation of receiving marketing approval from the FDA, we plan to build a focused in-house sales and marketing organization to identify pituitary specialists and community endocrinologists who comprise the top prescribers of therapies for acromegaly and prepare to market oral octreotide to these physicians.

Obtain European regulatory approval of oral octreotide for the treatment of acromegaly. To support approval in Europe, subject to final agreement with the EMA on the protocol for the trial, we intend to initiate an additional Phase 3 clinical trial in the second half of 2015, whose key design elements have been agreed with the EMA, to evaluate the comparative safety and efficacy of oral octreotide in acromegaly. Following completion of the trial, assuming favorable results, we expect to submit our MAA to the EMA in late 2017 or early 2018.

Explore collaboration opportunities in Europe and the rest of the world for oral octreotide in acromegaly and other indications. We intend to explore collaborations to commercialize oral octreotide in acromegaly and other orphan indications outside of the United States. However, depending on our evaluation of the strategic merits of these collaboration opportunities, we may decide to retain commercial rights in key markets.

Pursue the development of oral octreotide in additional indications currently treated by injectable therapies, such as NET. We believe that the data generated in our previous clinical trials of oral octreotide provide the necessary safety and pharmacokinetic data to allow us to move directly into Phase 2 clinical trials of oral octreotide in other orphan indications. If we receive regulatory approval of oral octreotide in acromegaly, we plan to initiate a Phase 2 clinical trial of oral octreotide for the symptomatic control of NET in the second half of 2016.

Leverage our proprietary TPE platform to develop a pipeline of new high-value oral therapeutics. We have obtained nonclinical proof of concept data for intestinal absorption of several oral peptides currently available only in injectable forms. Based on these studies, we intend to pursue development of new oral therapies in reliance on the FDA s 505(b)(2) regulatory pathway and the hybrid application pathway in Europe. In addition, we plan to evaluate collaboration opportunities to expand the scope of our pipeline and the utilization of our TPE platform to create novel oral therapies.

Competitive Strengths

We believe we are well positioned to achieve our corporate and strategic goals based on the following key strengths:

Oral octreotide has the potential to become a standard of care in the treatment of acromegaly. In our Phase 3 clinical trial, we observed the ability of oral octreotide to reduce the significant limitations and

burdens associated with existing injectable somatostatin analogs, while also providing comparable biochemical disease control and improved symptom control. Based on this and other clinical data and feedback from patients and healthcare providers, we believe that oral octreotide, if approved, could become a new standard of care in acromegaly.

Oral octreotide is the only somatostatin analog formulated for oral administration to complete a Phase 3 clinical trial. Based in part on the data from our completed Phase 3 clinical trial, we submitted an NDA on June 15, 2015 seeking approval for the marketing and sale of oral octreotide for the maintenance therapy of adult patients with acromegaly. To our knowledge, there are no other oral formulations of somatostatin analogs that have achieved clinical proof of concept or that are in late-stage clinical development.

Treatment of acromegaly is a well-characterized market that we believe we can address with a focused and differentiated commercial infrastructure. Approximately 40% of acromegaly patients are treated by endocrinologists at pituitary centers. The remaining patients are treated by community endocrinologists. We believe we will be able to market oral octreotide, if approved, directly to these pituitary centers through our own small, targeted sales force. We also intend to direct our sales and marketing efforts specifically towards the larger number of community endocrinologists. We believe that the clinical benefits and preferences of patients and healthcare professionals for an oral product, together with our patient-centric approach, could enable oral octreotide, if approved, to become a new standard of care in acromegaly.

Our business model and regulatory strategy target shorter development timelines and lower associated expenses. Our pursuit of the 505(b)(2) regulatory pathway in the United States and the hybrid application pathway in Europe should allow shorter development timelines and reduced development expenses. For oral octreotide, we generated proof of concept clinical data in healthy volunteers three years after we began development, completed our Phase 3 clinical trial in acromegaly within a further four years, and believe that we now have sufficient data to seek U.S. regulatory approval utilizing the FDA s 505(b)(2) regulatory pathway. For comparison, the typical timeline for development of a new chemical entity, or NCE, under a traditional NDA program is over 10 years. We intend to continue to pursue product development opportunities where we believe the FDA s 505(b)(2) regulatory pathway and the hybrid application pathway in Europe are available.

We believe that we have the ability to leverage our proprietary TPE platform to develop additional high-value oral therapeutics. Our TPE technology enhances the absorption through the intestinal wall of drugs that otherwise would not be able to be absorbed efficiently by that route. Using our TPE technology, we have identified multiple potential product candidates that may potentially address areas of unmet medical need. We have obtained nonclinical proof of concept data for intestinal absorption of several peptides that are currently available only in injectable forms. Based on data obtained from these studies, we believe we can develop new oral therapies from already approved injectable therapies using a similar development strategy as we employed with oral octreotide.

Our leadership team has significant drug development and commercial experience and possesses important intellectual capital. Our President and Chief Executive Officer, Mark Leuchtenberger, has extensive experience in commercial operations, business development and preparing biopharmaceutical

companies for product approval and commercialization. Our Chief Development Officer, Roni Mamluk, Ph.D., led the development of oral octreotide and is one of the primary inventors of our TPE technology. Our Chief Financial Officer, Mark J. Fitzpatrick, has more than 20 years of financial management experience in both public and private companies, having most recently served as chief financial officer at Aegerion Pharmaceuticals, Inc., Proteon Therapeutics, Inc. and RenaMed Biologics, Inc. In addition, our Senior Medical Advisor, Gary Patou, M.D., brings over 20 years of extensive experience in clinical and regulatory affairs to the organization, having taken several drugs through development and FDA approval.

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Our Product Candidate Pipeline

Leveraging our TPE platform, we have developed a pipeline of oral product candidates. Our most advanced product candidate is oral octreotide for acromegaly. In addition, if we receive regulatory approval of oral octreotide in acromegaly, we expect to initiate a Phase 2 clinical trial of oral octreotide for the symptomatic control of NETs, in the second half of 2016. We also intend to initiate additional clinical trials of oral octreotide in a new orphan indication, once selected, in late 2016. Using our TPE technology, we have also identified several peptides currently available only in injectable forms that we believe we can develop into oral formulations using a similar development strategy as we employed with oral octreotide. We have obtained nonclinical proof of concept data for various peptides, currently available as injections, and expect that in late 2016 we will select a second product candidate for clinical development and initiate nonclinical development of a third product candidate in 2017.

Our Lead Product Candidate, Oral Octreotide in Acromegaly

Our lead product candidate, oral octreotide, has completed a Phase 3 clinical trial for the treatment of acromegaly. In June 2015, we submitted our NDA for oral octreotide as a maintenance therapy for acromegaly in the United States. The FDA has 60 days after receipt of the NDA to preliminary review and determine if the application is sufficiently complete to permit a substantive review and meets the threshold for filing. Based on the 10-month PDUFA timeline, which begins after the FDA has received our NDA, and subject to the FDA s acceptance of the NDA for filing, we anticipate a regulatory decision on marketing approval in April 2016. In addition to the clinical data we submitted to the FDA, the EMA has advised us that a clinical trial demonstrating non-inferiority of oral octreotide compared to injectable somatostatin analogs as active controls will be required prior to regulatory approval. We have agreed to key elements of the trial design with the EMA and, subject to final agreement on the protocol for the trial, we expect to initiate this trial before the end of 2015, and, if successful, to submit our regulatory filing to the EMA in late 2017 or early 2018.

Overview of Acromegaly

Acromegaly results from the overproduction of GH, most often due to the growth of a benign tumor in the pituitary gland in middle-aged adults. GH, in turn, stimulates the production of IGF-1 in the liver which stimulates the growth of bones and other tissues.

Progression of acromegaly can result in significant health problems such as hypertension, enlargement of the heart, or cardiomyopathy, sleep apnea, type-2 diabetes, and abnormal growths in the colon and uterus. Acromegaly is associated with a number of symptoms, some acute, such as headaches, joint pain and fatigue, and some long-term, such as enlarged hands, feet and internal organs, as well as altered facial features. Because acromegaly is uncommon and physical changes occur gradually, the condition is often not recognized immediately, sometimes not for years. If not treated promptly, acromegaly can lead to serious illness and is associated with premature death, primarily due to cardiovascular disease. However, both surgical and drug treatments are available for acromegaly that can reduce the risk of complications and premature death and significantly improve symptom control.

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Surgery is often the first line of therapy for acromegaly and, in some cases, surgical removal of the pituitary tumor can result in normalization of GH and IGF-1 levels. In many other cases, however, the levels of GH remain elevated even after surgery due to residual tumor and many patients therefore also require a therapeutic intervention. The body s natural inhibitor of excess GH secretion is somatostatin, a peptide hormone. Octreotide and lanreotide, analogs of somatostatin with a significantly longer half-life in the blood than natural somatostatin, have achieved widespread adoption by physicians treating patients afflicted with acromegaly. These somatostatin analogs are routinely administered by injection by a healthcare professional. If not administered with proper technique, the injection may not effectively deliver the medication. There is currently no oral formulation of a somatostatin analog on the market and none, we believe, in clinical development except oral octreotide.

Incidence and Prevalence of Acromegaly and Current Treatment Landscape

There are an estimated 62,300 individuals with acromegaly worldwide, of which an estimated 35,100 receive lifelong injections. The U.S. National Institutes of Health, or NIH, estimates that there are roughly 20,000 individuals with acromegaly in the United States, based on its published prevalence of an estimated 60 cases per million. However, recent data presented at the Endocrine Society s Annual Meeting in 2015 suggest that pituitary tumors may be more prevalent than previously thought, and that the global prevalence of acromegaly may be higher, between 85 and 118 cases per million people. NIH also cites an annual incidence of three to four new cases per million each year.

According to publicly available financial reports, injectable forms of octreotide and lanreotide generate worldwide sales of over $2.0 billion annually for the treatment of acromegaly and NET as well as some smaller indications. Approximately $730 million represents the annual sales for the treatment of acromegaly. The great majority of these sales come from once-monthly long acting formulations that must be administered by intramuscular or deep subcutaneous injections with large-gauge needles. Although we are initially targeting acromegaly with oral octreotide, we believe that this product candidate, if approved, has the potential to become a standard of care for other indications currently treated primarily with injectable somatostatin analogs such as NET.

Current Therapeutic Options and Their Limitations

After surgery, the current standard of care for patients suffering from acromegaly involves injectable somatostatin analogs. These therapies are associated with significant limitations and burdens on patients. Currently, the first therapeutic treatment options are octreotide, marketed by Novartis AG, or Novartis, which is administered monthly and intramuscularly using a large gauge needle, and lanreotide, marketed by Ipsen SA, or Ipsen, another long-acting analog of somatostatin, which is administered monthly using a deep subcutaneous injection. For patients not controlled on these somatostatin analogs, the typical second line of treatment options includes pegvisomant daily injections, marketed by Pfizer, Inc., or Pfizer, and pasireotide LAR, marketed by Novartis, which is another somatostatin analog administered via intramuscular injection.

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Injections of these somatostatin analogs present several issues related to patient comfort and convenience as well as breakthrough, or returning, symptoms of the disease near the end of the dosing cycle prior to the next scheduled injection. These issues include:

Suboptimal control. In a patient-reported outcomes survey that we conducted in 195 acromegaly patients receiving injected somatostatin analogs, or our patient survey, 52% of patients reported that the treatment effects begin to wane near the end of the monthly cycle prior to the next injection, and 32% of controlled patients still experienced some symptoms.

Pain. Injections with somatostatin analogs require a large-gauge needle to slowly inject a viscous solution into the muscle or deep into subcutaneous tissue. Patients report these injections to be very painful. Often, this pain persists for several days after the injection. In our patient survey, 70% of patients said they experienced pain during the injection and approximately half of these patients experienced continuing pain days later.

Injection-site reactions. Patients frequently experience hardness, nodules and swelling at the site of the injection as well as bruising and inflammation.

Lack of convenience. The treatment effectiveness is dependent on proper technique and thus the injections are typically administered by a healthcare professional. The monthly injection schedule for injectable somatostatin analogs and the associated travel to the healthcare provider is inconvenient for many patients.

Emotional impact. In our patient survey, 36% of patients said that they felt a loss of independence due to the requirement for chronic injections that typically require them to visit a healthcare professional.

Lost work days. In our patient survey, 16% of patients said that the treatment burden associated with the injectable therapies caused them to regularly miss work for injections. These patients missed an average of 11 days a year.

Since injectable somatostatin analogs are the standard of care for other pituitary diseases beyond acromegaly, including diseases such as NET, these limitations and burdens are also associated with the treatment of the other indications we intend to pursue with oral octreotide.

Our Solution: Oral Octreotide

Oral octreotide is a novel formulation of octreotide developed utilizing our TPE platform. We designed the product candidate to achieve biochemical disease control and improved symptom control while addressing the pain and treatment burdens commonly experienced with current injectable therapies. We are developing oral octreotide as a pill, liquid-filled solid gelatin capsule formulation, intended to be taken twice a day. We expect

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that patients who are prescribed oral octreotide, if approved, by their physicians will receive a 28-day supply of pills, which may be stored at room temperature. Based on the data from our clinical trials, we believe oral octreotide has the potential to achieve biochemical disease control while providing favorable symptom control and reducing the burden of disease and treatment in patients afflicted with acromegaly.

Clinical Program for Oral Octreotide in Acromegaly

Regulatory Pathway

We are seeking regulatory approval of oral octreotide for the maintenance therapy of acromegaly in the United States utilizing the FDA s 505(b)(2) regulatory pathway. The 505(b)(2) pathway enables us to rely, in part, on the FDA s prior findings of safety and efficacy of an approved product, or published literature, in support of our NDA. In the case of oral octreotide in acromegaly, the approved product to which our NDA submission refers is the short-acting subcutaneous injectable formulation of octreotide that was the original product approved by the FDA before the long-acting formulation was developed. Since this formulation of octreotide has been approved by the FDA in generic form and is therefore no longer proprietary, we are not aware of any third party from which we would be required to obtain any license or acquire any rights to commercialize oral octreotide, if approved. We have conducted a series of Phase 1 clinical trials, including a trial to demonstrate that the bioavailability of octreotide administered in our TPE formulation is comparable to the bioavailability of octreotide administered in the short-acting subcutaneous injectable formulation. We have also conducted a Phase 1 clinical trial to evaluate the bioactivity of oral octreotide in healthy subjects, and a Phase 3 clinical trial to evaluate the safety and efficacy of oral octreotide in patients with acromegaly after seven months of treatment plus after an optional six-month extension phase.

In December 2014, we met with the FDA to discuss our clinical development of oral octreotide, including the full 13-month data from our Phase 3 clinical trial. At this meeting, the FDA advised us that it had not identified an issue that would preclude us from submitting an NDA for review. Accordingly, we submitted our NDA for oral octreotide for maintenance therapy in acromegaly to the FDA on June 15, 2015. The FDA has 60 days after receipt of the NDA to preliminarily review and determine if the application is sufficiently complete to permit a substantive review and meets the threshold for filing.

We also intend to seek regulatory approval of oral octreotide for the treatment of acromegaly in Europe utilizing the hybrid application pathway, which is analogous to the 505(b)(2) regulatory pathway in the United States. In addition to the clinical data we submitted to the FDA, the EMA has advised us that a clinical trial demonstrating non-inferiority of oral octreotide compared to injectable somatostatin analogs as active controls will be required prior to regulatory approval by EMA. We have agreed to key elements of the trial design with the EMA and expect to initiate this trial in the second half of 2015, and, if successful, to submit an MAA to the EMA in late 2017 or early 2018.

Completed Phase 3 Clinical Trial

In March 2012, we initiated a Phase 3 multi-center, open-label, baseline-controlled clinical trial to evaluate the safety and efficacy of oral octreotide in patients with acromegaly who responded to and tolerated treatment with somatostatin analogs. We completed this trial in November 2014 and the results were published in the *Journal of Clinical Endocrinology & Metabolism* in February 2015 and presented at the Endocrine Society s Annual Meeting in March 2015.

Trial Design

A total of 155 patients with acromegaly, each of whom was classified as a responder to a long-acting injectable somatostatin analog, were enrolled in the trial. Two weeks after their last monthly injection of the long-acting injectable somatostatin analog, patients were reassessed to obtain baseline IGF-1 and GH levels. Both the screening and baseline measurements were performed while patients were still on active injection therapy. The 155 patients enrolled in the trial are referred to as the intent to treat, or ITT, group.

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After baseline levels were obtained, no less than one month following their last monthly injection of the long-acting injectable somatostatin analog, a core treatment period with oral octreotide was initiated. This core treatment period consisted of a dose-escalation phase of at least two months in duration, designed to find an appropriate dose of oral octreotide for each individual patient, and a fixed-dose phase of up to five months in duration, during which period the appropriate therapeutic dose identified in the dose-escalation phase was maintained. Since data from our prior clinical trials demonstrated a significant reduction in bioavailability when oral octreotide is administered with a high-fat meal, patients in this Phase 3 clinical trial were required to fast for at least one hour before and at least one to two hours after each dose.

Patients who entered the core treatment phase of the trial initially received a 40 mg daily dose (administered in two pills a day), which was increased to daily doses of 60 mg or 80 mg on an as-required basis to maintain biochemical and/or symptom control, at the discretion of the investigator. For each patient, the core treatment phase lasted for seven months after his or her first dose of oral octreotide. Patients could then opt to continue treatment with oral octreotide during an extension period of up to an additional six months, with a two-week period for final follow-up. Four patients dropped out of the trial after receiving at least one dose of oral octreotide but before a biochemical response could be measured, resulting in a modified intent to treat, or mITT, group of 151 patients.

The primary objective of the trial was to determine the efficacy of oral octreotide in patients with acromegaly, as measured by effect on IGF-1 and GH levels, with responders defined as patients who achieve an IGF-1 level less than 1.3 times the upper limit of normal, or ULN, adjusted for age and an integrated GH level over two hours less than 2.5 ng/mL. Secondary objectives included assessment of safety and tolerability of oral octreotide, and comparison of efficacy of oral octreotide versus long-acting injectable somatostatin analog.

Phase 3 Clinical Trial Design

Trial Results

Of the 155 patients enrolled, four were not evaluable and of the 151 in the mITT group, 49 patients discontinued, the majority during the dose-escalation phase. Of the 151 patients in the mITT group, patients discontinued for a variety of reasons, including treatment failures because the patient could not be controlled on 80 mg, the highest dose available (24); withdrawals due to adverse events (18); or patient choice, sponsor request and lost to follow up (7). Of the 110 patients that completed the dose-escalation phase, 52 patients, or 47%, were receiving the 40 mg daily dose, 25 patients, or 23%, were receiving the 60 mg dose, and 33 patients, or 30%, were receiving the 80 mg dose.

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After completion of the dose-escalation phase, the remaining 110 patients entered the fixed dose phase of the core treatment period and continued on oral octreotide at their respective doses until seven months after first dosing. A total of 102 patients completed the fixed dose phase of the trial, 88 of whom, or 86%, voluntarily chose to remain on oral octreotide during the six-month extension phase, for a total of 13 months of treatment after first dosing. A total of 82 patients completed the six-month extension phase of the trial.

Overall, 65% of patients in the mITT group were classified as responders at the end of the seven-month core treatment phase, which was the primary endpoint for the trial. Applying a worst-case imputation method, whereby all patients who withdrew from the study prematurely (regardless of reason) are treated as non-responders, 53% of patients were classified as responders at the end of the seven-month core treatment phase. By the end of the six-month extension phase, or 13 months after first dosing, the responder rate was 62% in the mITT group. Of the 110 patients that completed the dose-escalation phase, and therefore received an optimized dose of oral octreotride, 75% were classified as responders. For all 151 patients included in the mITT group, the responder rate on long-acting injectable somatostatin analogs was 89% at baseline, prior to initiation of oral octreotide.

Overall Phase 3 Response in mITT Group vs. Baseline

We further assessed the quality of the responses to oral octreotide. The quality of the patient responses on oral octreotide was comparable to the quality of the responses on injectable therapies. In the mITT group, mean GH levels on oral octreotide therapy were below the baseline values on injectable therapies at all timepoints assessed through the end of the extension phase. The median GH level in the mITT group at baseline was 0.77 ng/mL, which dropped to 0.40 ng/mL within two hours of the first dose of oral octreotide and 0.49 ng/mL by the end of the extension phase, 13 months later. IGF-1 levels were stably maintained below 1.3 times the ULN for up to 13 months in the mITT group.

GH and IGF-1 Response in mITT Group Throughout the Duration of the Phase 3 Trial

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We also assessed control of acromegaly symptoms, the incidence of symptoms, and the severity and number of symptoms in patients using oral octreotide in a retrospective analysis performed after completion of the trial. At baseline, 81% of patients in the mITT group, the majority of whom were classified as responders, still had acromegaly symptoms, such as headaches, excessive perspiration, muscle weakness and/or joint pain and swelling. Patients who completed 13 months of treatment reported significantly fewer acromegaly symptoms at the conclusion of the trial than at the time of their baseline screening, and this result was statistically significant, with p-values of less than 0.020. P-value is a conventional statistical method for measuring the statistical significance of clinical results. A p-value of 0.05 or less is generally considered to represent statistical significance, meaning that there is a less than 1-in-20 likelihood that the observed results occurred by chance. There was also a reduction in the severity of symptoms reported. In addition, breakthrough, or returning, symptoms of acromegaly were reported by 36% of patients receiving injections at baseline compared to 22% at 13 months on oral octreotide through a questionnaire conducted in a subset of the patients in the clinical trial.

Reduced Number of Acromegaly Symptoms at Conclusion of Oral Octreotide Trial

(Fixed Dose Population (n = 110))

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The safety profile of oral octreotide was consistent with the known safety profile of octreotide and the disease burden of acromegaly, with the most common adverse events observed in the gastrointestinal system, such as nausea and diarrhea, the nervous system, such as headaches, and the musculoskeletal system, such as joint pain, but without adverse injection-site reactions. No new or unexpected safety signals were observed.

We only performed statistical analysis on the symptom reductions for our Phase 3 trial of oral octreotide in acromegaly and did not perform statistical analysis related to the biochemistry, specifically the reduction in GH and IGF-1 levels.

Planned Phase 3 Clinical Trial

In addition to the clinical data submitted to the FDA with our NDA, the EMA has advised us that a clinical trial demonstrating that oral octreotide is not inferior to injectable somatostatin analogs included in the same study as active controls will be required prior to regulatory approval. Comparative effectiveness is an important regulatory consideration in Europe. We have agreed to key elements of the trial design with the EMA and expect to finalize the protocol and initiate this trial in the second half of 2015.

We believe this trial will be an open-label, randomized, active-controlled study of oral octreotide in patients who have been classified as responders to a once-a-month injectable somatostatin analog based on criteria comparable to the criteria utilized in our completed Phase 3 clinical trial. The new trial is intended to demonstrate non-inferiority, comparing efficacy responses as between two randomized groups of patients who demonstrated response to oral octreotide. We currently expect to enroll approximately 160 patients in the trial in the United States, Europe and other foreign countries with the goal of including at least 40 patients per group in the randomized phase.

Although we have not yet finalized the protocol for this planned trial, we currently expect that patients will enter a run-in phase on oral octreotide no less than one month following their last monthly injection of the long-acting injectable somatostatin analog. We expect that each patient will initially receive a daily dose of 40 mg of oral octreotide, which will be increased up to a maximum of 80 mg daily dose if lower doses are not effective. Similar to the requirements of our first Phase 3 clinical trial, patients will be required to fast for at least one hour before or at least two hours after each dose. As currently planned, patients that are not identified as responders during the run-in phase will not enter the randomized phase but will be switched back to long-acting injectable somatostatin analog and followed for an additional three months. Patients identified as responders will be randomized (1:1) to either a long-acting injectable somatostatin analog or oral octreotide at the appropriate dose identified during the run-in phase. After completion of this randomized controlled phase, we expect that all eligible patients will have the option of entering an extension phase during which period these patients would receive oral octreotide at the dose identified during the run-in phase. The final design of this planned trial remains subject to our ongoing discussions with the EMA and is expected to be finalized in the second half of 2015.

We anticipate that the primary efficacy endpoint for this trial will relate to IGF-1 and GH levels, with responders defined as patients who achieve an IGF-1 level less than 1.3 times the ULN adjusted for age and an integrated GH level over two hours less than 2.5 ng/mL, the same efficacy criteria utilized in our completed Phase 3 clinical trial. In addition, assessment of symptom control and patient reported outcomes are expected to be included.

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Design of Planned Phase 3 to Support EMA Approval

Phase 1 Clinical Trials of Oral Octreotide

Together with a group of academic collaborators, we conducted a series of Phase 1 clinical trials to demonstrate that the bioavailability of octreotide administered in our TPE formulation is comparable to the bioavailability of octreotide administered in the short-acting subcutaneous, or sc, formulation. These trials demonstrated similar pharmacokinetics for oral octreotide and octreotide 0.1 mg sc injection and that a 20 mg oral dose of oral octreotide produced systemic exposure comparable to octreotide 0.1 mg sc injection in healthy volunteers. There was no effect of route of administration on octreotide elimination, and the mean elimination half-life (t1/2) was comparable with the two treatments. However, these studies also demonstrated that the bioavailability of oral octreotide is approximately 90% lower when it is taken with a high-fat meal rather than in the fasted state. Accordingly, our Phase 3 clinical trial required fasting for at least one hour before and at least one to two hours after each dose.

Pharmacokinetics of Oral Octreotide vs. SC Octreotide in Phase 1 Trial

In addition, to demonstrate the bioactivity of oral octreotide, as measured by reduction in GH levels, we conducted a Phase 1 clinical trial in 16 healthy volunteers. In this crossover study, a single 20 mg dose of oral octreotide was shown to suppress mean GH levels below 0.25 ng/mL ($p < 0.05$). This is similar to the effect seen in published results using octreotide injections.

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Suppression of GH Levels in Healthy Volunteers

Also in this trial, we evaluated the ability of oral octreotide to suppress GH levels in healthy subjects whose production of GH had been transiently stimulated by dosing with growth hormone-releasing hormone, or GHRH, and arginine. GHRH and arginine are used in routine clinical testing for deficiencies in GH production. In a healthy person, their administration leads to a large increase in GH levels, which is what was observed in this trial. A single 20 mg dose of oral octreotide lowered the levels of GH by 80% ($p < 0.001$) following dosing with GHRH and arginine.

Data from our Phase 1 bioavailability and bioactivity clinical trials were published in the *Journal of Clinical Endocrinology & Metabolism* in July 2012.

A total of 11 clinical pharmacology studies have evaluated the safety of oral octreotide. In all of these studies, the safety profile of oral octreotide was consistent with the known safety profile of the short-acting octreotide 0.1 mg sc injection. No new or unexpected safety issues were detected during any of the clinical pharmacology studies. In particular, no new safety issues related to the novel formulation or route of administration were observed.

Other Indications for Oral Octreotide

If we receive regulatory approval for oral octreotide in acromegaly, we plan to submit an investigational new drug application, or IND, and initiate a Phase 2 clinical trial of oral octreotide for the symptomatic control of NET in the second half of 2016. We believe that the data generated in the Phase 1 clinical trials of oral octreotide that we have conducted, coupled with the Phase 3 clinical trial data we have generated for oral octreotide in acromegaly, will be sufficient for us to move directly to a Phase 2 clinical trial in NET. In addition, we intend to initiate clinical trials of oral octreotide in a new orphan indication, once selected, in late 2016.

NETs are formed by hormone-producing cells in the body s neuroendocrine system. NETs most frequently form in tissues derived from the embryonic gut such as small intestine, appendix, proximal colon and pancreas. According to an article published in the *Journal of Clinical Oncology* in 2008, the prevalence of NETs in the United States is estimated to be 5.25 cases per 100,000 people. Over 70% of NETs from the gastrointestinal tract and pancreas express somatostatin receptors. Injectable somatostatin analogs have been approved for the treatment of symptom relief of NETs, mainly for a type known as carcinoids. NETs are associated with numerous clinical symptoms, the most debilitating of which is frequent diarrhea. Approximately 80% of patients experience frequent watery stools up to 30 times a day accompanied by abdominal cramping. Approximately 85% of patients also experience episodic flushing resulting in red to violet coloration of the head, neck and upper chest and a mild burning sensation. This flushing can also lead to reduced blood pressure. Two injectable forms of somatostatin analogs marketed by Novartis are currently the only approved therapies for relief of these symptoms.

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Until recently, somatostatin analogs have been indicated only for the treatment of symptoms of carcinoid or gastroentero-NETs. In December 2014, the FDA expanded the label for lanreotide to include the treatment of patients with pancreatic NETs based on its ability to improve progression-free survival in otherwise untreatable cases. This expanded label is expected to result in a substantial increase in the number of NET patients treated with somatostatin analogs.

Octreotide is known to be effective in controlling symptoms of NETs. It is the standard of care for carcinoid, a form of NET, and related symptoms. Approximately 50% of somatostatin analog sales, or approximately $1.0 billion annually, are associated with treatment of NET and we believe that oral octreotide has the potential to capture a significant portion of this market.

Our Proprietary Transient Permeability Enhancer Technology Platform

Our Transient Permeability Enhancer, or TPE, technology is a proprietary platform, developed internally by our scientists, that enhances the absorption through the intestinal wall of drugs that otherwise would not be absorbed efficiently by that route. Using our TPE technology, we can transiently and reversibly open the so-called tight junctions between the cells lining the inner intestinal wall, enabling drug molecules to be absorbed intact. Our TPE formulation is a suspension of water-soluble particles containing a precise combination of medium-chain fatty acid salts and drug substance in a fat-soluble medium. In creating a TPE formulation, we make no chemical modifications to the drug substance.

Oral delivery of peptides and nucleic acids is limited due to their inherent vulnerability to digestive processes and their poor intestinal absorption. The same intestinal absorption limitation applies to certain small molecules that have poor bioavailability. The cells at the surface of the intestine, columnar epithelial cells, are connected by tight junctions that form a barrier preventing permeation by water-soluble molecules as well as by viruses and bacteria. Our TPE technology induces the transient opening of these tight junctions, allowing peptides and other macromolecules up to a certain size, but not toxins, viruses and bacteria, to cross the intestinal barrier and enabling access to the blood.

The permeability of intestinal tight junctions is known to be altered by a number of dietary factors such as fatty acids, polysaccharides and flavonoids. Transient, reversible opening of the tight junctions and an increase in epithelial permeability are a normal part of intestinal physiology. These permeability adjustments allow the gut to balance two opposing functions: creating a barrier to the passage of microorganisms while facilitating the absorption of nutrients following a meal. In developing the TPE platform, our goal was to establish the ability to reproducibly induce transient increases in the permeability of tight junctions, allowing absorption of specifically formulated drug molecules.

We have conducted extensive nonclinical studies to demonstrate the ability of our TPE technology to increase the permeability of the intestinal epithelial layer and therefore absorb molecules of different shapes, sizes and doses. As a result of these studies, we believe that our TPE technology can be applied to multiple additional peptide drug products as well as small molecules with poor bioavailability.

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Our TPE Platform

Other Product Candidates

We believe that our TPE platform can serve as the foundation for a pipeline of proprietary oral versions of injectable drugs. The technology is particularly well suited for drugs that are used for certain chronic indications, where frequent injections are currently required. To reduce the development time and overall level of investment required, we intend to focus on orphan indications and, where possible, follow the FDA s 505(b)(2) regulatory pathway in the United States or the hybrid application pathway in Europe. With oral octrotide, our team completed the nonclinical work necessary to submit an IND for a TPE-based product within 18 months of initiating work on the product, and then generated clinical proof of concept data within an additional 12 months.

Using our TPE platform, we have also identified several peptides currently available only in injectable forms that we believe we can develop as oral products using a similar strategy as we employed with oral octreotide. We have obtained nonclinical proof of concept data for some of these product candidates. Our intention is to select our second product candidate for clinical development in late 2016 and to initiate nonclinical development of a third product candidate in 2017.

Prior License Agreement with Roche

In January 2013, we entered into a license agreement with F. Hoffmann-La Roche Ltd. and Hoffmann-La Roche Inc., collectively Roche, for the development and commercialization of oral octreotide. Under the terms of the license agreement, we had responsibility for continued clinical development through completion of our Phase 3 clinical trial, establishment of commercial-scale manufacturing and completion of ongoing nonclinical activities. Roche assumed responsibility for development and commercialization thereafter. The agreement provided for an upfront payment of $65.0 million, future consideration of up to $530 million in development and commercial milestones, and the right to receive tiered, double-digit royalties on net sales of oral octreotide.

In January 2014, we received the clinical results from the seven-month core treatment period of the oral octreotide Phase 3 clinical trial. These results did not include the six-month extension period of the trial, which allowed patients the opportunity to choose to continue on oral therapy. In May 2014, Roche conducted a pre-NDA meeting with the FDA. In July 2014, Roche elected to terminate the license agreement and transitioned oral octreotide and all materials related to the clinical development programs back to us. We subsequently entered into a termination agreement with Roche, which included our purchase of active pharmaceutical ingredient for future manufacturing of oral octreotide and a trademark associated with oral octreotide for an aggregate of $5.1 million payable over three years. We have no further obligations to Roche.

In October 2014, we completed analyses of the full 13-month clinical results from our Phase 3 clinical trial of oral octreotide. Subsequently, in December 2014, we met with the FDA to discuss our clinical development of oral octreotide, including the full 13-month data from our Phase 3 clinical trial. Based on the results of this meeting, we submitted an NDA to the FDA on June 15, 2015.

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Commercialization Strategy

We retain worldwide rights to develop and commercialize oral octreotide with no royalty obligations to third parties. We intend to commercialize oral octreotide ourselves in the United States employing a strategy that differentiates our product candidate, if approved, and is tailored to the needs of patients and their physicians. We have been conducting market research and other pre-commercial activities in the United States since 2010 to better understand satisfaction levels and key unmet needs with respect to current treatments for acromegaly and to build awareness of our product candidate. This market research has been conducted with endocrinologists, nurses and people with acromegaly. In surveys commissioned by us, more than 80% of people with acromegaly expressed a preference for an oral treatment, and endocrinologists surveyed predicted that an oral treatment would ultimately be prescribed for a majority of their patients. Endocrinologists indicated that effectiveness in at least 50% of patients treated would be sufficient for an oral treatment to be successful. To assess the attitudes of commercial third-party payors toward reimbursement for oral octreotide, we conducted research with 12 such payors collectively representing 111 million covered lives. Payors representing nearly 90% of these covered lives said they would reimburse an oral treatment assuming pricing was in a range comparable to existing injectable therapies, octreotide and lanreotide.

We believe the current U.S. market for acromegaly treatments is concentrated. Approximately 40% of people with acromegaly in the United States undergoing treatment are treated by endocrinologists at a small number of pituitary centers. The remaining people with acromegaly undergoing treatment are treated by community endocrinologists. We believe we will be able to market oral octreotide, if approved, directly to pituitary centers that treat high volumes of patients with acromegaly through our own small, targeted sales force. We also intend to direct our sales and marketing efforts towards the larger number of community endocrinologists. We believe that oral octreotide, if approved, will be embraced by these healthcare providers who are generally hampered by the complexity and resource burden associated with the administration of currently available injectable therapies. Finally, we intend to engage in direct patient outreach efforts. We believe that the combination of clinical benefits and preferences of patients and healthcare professionals for an oral product together with our patient-centric commercial approach could enable oral octreotide, if approved, to become a new standard of care in acromegaly.

We intend to seek approval to commercialize oral octreotide in Europe through the completion of the Phase 3 trial required by the EMA and subsequent submission of an MAA. We plan to explore the strategic merits of collaboration opportunities for commercializing oral octreotide in Europe and the rest of the world in order to maximize the availability of the product candidate, if approved, to patients. However, depending on our evaluation of the strategic merits of these collaboration opportunities, we may decide to retain commercial rights in key markets.

Manufacturing

We depend on third-party suppliers and contract manufacturing organizations, or CMOs, for all of our required raw materials and drug substance and to manufacture and package drug product for clinical and commercial use. We plan to establish a distribution channel in the United States utilizing third-party logistics and a specialty pharmacy to distribute product directly to patients.

We have qualified Novetide Ltd., a subsidiary of Teva Pharmaceuticals Industries Ltd., in Israel, and Bachem Americas Inc., in the United States, as suppliers of the generic active pharmaceutical ingredient, or API, octreotide acetate. We believe that the manufacturing scale and capacity at both suppliers is sufficient to supply our expected market demands for the foreseeable future.

All excipients, or substances formulated together with the API, used in manufacture of oral octreotide are readily available. The octreotide API is formulated with our TPE technology and filled into capsules and enteric-coated by

Lyophilization Services of New England Inc. and Encap Drug Delivery, a division of Capsugel, in Scotland. All manufacturers periodically undergo inspections by regulatory authorities.

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Oral octreotide is refrigerated and our NDA includes stability data covering 24 months under these storage conditions. We have obtained data regarding additional one-month storage at room temperature, which supports storage of oral octreotide at room temperature. The FDA has indicated that the testing parameters for our control strategy and product release and stability specifications are acceptable. The manufacturing process for the API has been validated at both of our manufacturers. Process validation of certain batches of oral octreotide manufactured at the CMOs is ongoing and we believe it will be completed ahead of our planned commercial launch.

Competition

Our industry is highly competitive and subject to rapid and significant technological change as researchers learn more about diseases and develop new technologies and treatments. Our potential competitors include primarily large pharmaceutical, biotechnology companies and specialty pharmaceutical companies. Key competitive factors affecting the commercial success of oral octreotide and any other product candidates we may develop are likely to be efficacy, safety and tolerability profile, reliability, convenience of administration, price and reimbursement.

The current treatment options for patients suffering from acromegaly all involve injectable therapies. Novartis markets octreotide LAR, which is administered monthly and intramuscularly using a large gauge needle. Ipsen markets lanreotide, another long-acting analog of somatostatin, like octreotide, which is administered monthly using a deep subcutaneous injection. Both therapies, which are currently the first drug treatment options for patients, involve side effects related to the injections and inconvenience due to the timing and requirements of the injections. For patients not controlled on these somatostatin analogs, Pfizer markets pegvisomant daily injections and Novartis also markets pasireotide LAR, which is another somatostatin analog administered via intramuscular injection. Pegvisomant daily injections and pasireotide LAR are significantly more costly than injectable octreotide and lanreotide. The label for pasireotide LAR includes a warning about hyperglycemia and diabetes, which can sometimes be severe. The label advises healthcare professionals administering pasireotide LAR to monitor glucose levels periodically during therapy and to monitor glucose levels more frequently in the months that follow initiation or discontinuation of therapy and following dose adjustment. We are aware of other companies involved in early-stage nonclinical and clinical studies of similar somatostatin analogs, but all involve administration via injection.

Many of our existing or potential competitors have substantially greater financial, technical and human resources than we do and significantly greater experience in the discovery and development of product candidates, obtaining FDA and other regulatory approvals of products and the commercialization of those products. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a small number of our competitors. Accordingly, our competitors may be more successful than we may be in obtaining FDA approval of drugs and achieving widespread market acceptance. Our competitors drugs, or drugs they may develop in the future, may be more effective, or more effectively marketed and sold, than any drug we may commercialize and may render oral octreotide or any future product candidates we may develop obsolete or non-competitive before we can recover the expenses of developing and commercializing oral octreotide or any future product candidates we may develop. Our competitors may also obtain FDA or other regulatory approval of their products more rapidly than we may obtain approval of ours. We anticipate that we will face intense and increasing competition as new drugs enter the market and more advanced technologies become available. If we are unable to compete effectively, our opportunity to generate revenue from the sale of oral octreotide or any future product candidates we may develop, if approved, will be adversely affected.

Intellectual Property

We strive to protect the proprietary technology that we believe is important to our business, including seeking and maintaining patents intended to cover our product candidates and compositions, their methods of use and processes for

their manufacture, and any other aspects of inventions that are commercially important to the development of our business. We also rely on trade secrets to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection.

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We plan to continue to expand our intellectual property estate by filing patent applications directed to compositions, methods of treatment, and dosage regimens identified in the course of our business. Our success will depend on our ability to obtain and maintain patent and other proprietary protection for commercially important technology, inventions and know-how related to our business, defend and enforce our patents, preserve the confidentiality of our trade secrets and operate without infringing the valid and enforceable patents and proprietary rights of third parties. We also rely on know-how, continuing technological innovation and in-licensing opportunities to develop and maintain our proprietary position. We seek to obtain domestic and international patent protection, and endeavor to promptly file patent applications for new commercially valuable inventions.

The patent positions of biopharmaceutical companies like us are generally uncertain and involve complex legal, scientific and factual questions. In addition, the coverage claimed in a patent application can be significantly reduced before the patent is issued, and patent scope can be reinterpreted by the courts after issuance. Moreover, many jurisdictions permit third parties to challenge issued patents in administrative proceedings, which may result in further narrowing or even cancellation of patent claims. We cannot predict whether the patent applications we are currently pursuing will issue as patents in any particular jurisdiction or whether the claims of any issued patents will provide sufficient protection from competitors.

Because patent applications in the United States and certain other jurisdictions are maintained in secrecy for 18 months or potentially even longer, and since publication of discoveries in the scientific or patent literature often lags behind actual discoveries, we cannot be certain of the priority of inventions covered by pending patent applications. Moreover, we may have to participate in interference proceedings or derivation proceedings declared by the U.S. Patent and Trademark Office, or the USPTO, to determine priority of invention.

Patents

As of March 31, 2015, our patent portfolio included two patents issued in the United States; patents issued in foreign jurisdictions; patent applications pending in the United States; and patent applications pending in various foreign jurisdictions. These patents and patent applications include narrow and broad claims directed to octreotide compositions formulated with our TPE technology; capsules containing such compositions; methods of treatment using such compositions; and methods of making various compositions with our TPE technology.

One patent family that we own includes two issued U.S. patents and one pending patent application with claims directed to capsules containing octreotide compositions, and methods of treating various conditions with related octreotide compositions. Other patents in this family have issued in Hong Kong, Japan, New Zealand, South Africa, and the United Kingdom, and patent applications are pending in other jurisdictions, including Brazil, Canada, China, Europe, Israel, Korea, Mexico, Russia, Australia, and Japan. Patents in this family are expected to expire in 2029, absent any adjustments or extensions.

We also own one pending U.S. provisional patent application with claims directed to further uses of octreotide. No U.S. nonprovisional or Patent Cooperation Treaty, or PCT, or foreign filings have yet been made, which claim priority to this U.S. provisional patent application. Patents issuing from any U.S. nonprovisional and foreign-filed patent applications claiming priority to this application are expected to expire in 2035, absent any adjustments or extensions.

We also own two pending U.S. provisional patent applications directed to a dosage regimen for octreotide and also directed to methods of treating acromegaly with certain octreotide-containing compositions and dosage regimens. No U.S. nonprovisional or PCT or foreign filings have yet been made, which claim priority to these U.S. provisional patent applications. Patents issuing from any U.S. nonprovisional and foreign-filed applications claiming priority to this application are expected to expire in 2036, absent any adjustments or extensions.

Finally, we own two patent applications directed to proprietary packaging for distribution of octreotide. One of these is a U.S. nonprovisional patent application, which, if issued, is expected to expire in 2035, absent any

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adjustments or extensions. No PCT or foreign filings have yet been made, which claim priority to this U.S. nonprovisional patent application. The other patent application is a U.S. design patent application, which, if issued, is expected to expire 15 years after issuance.

Patent Term

The base term of a U.S. utility patent is 20 years from the filing date of the earliest-filed non-provisional patent application from which the patent claims priority. The base term of a U.S. design patent is 15 years from issuance once the Patent Law Treaties Implementation Act of 2012 takes effect on May 13, 2015. The term of a U.S. patent can be lengthened by patent term adjustment, which compensates the owner of the patent for administrative delays at the USPTO. In some cases, the term of a U.S. patent is shortened by terminal disclaimer that reduces its term to that of an earlier-expiring patent.

Government Regulation

Government authorities in the United States at the federal, state and local level and in other countries extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, post-approval monitoring and reporting, marketing and export and import of drug products such as our lead product candidate, oral octreotide. Generally, before a new drug can be marketed, considerable data demonstrating its quality, safety and efficacy must be obtained, organized into a format specific to each regulatory authority, submitted for review and approved by the regulatory authority.

United States Drug Development

In the United States, the FDA regulates drugs under the Food, Drug, and Cosmetic Act, or FDCA, and its implementing regulations. Drugs are also subject to other federal, state and local statutes and regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or after approval, may subject an applicant to administrative or judicial sanctions. These sanctions could include, among other actions, the FDA s refusal to approve pending applications, withdrawal of an approval, a clinical hold, untitled or warning letters, voluntary product recalls or withdrawals from the market, product seizures, total or partial suspension of production or distribution injunctions, fines, refusals of government contracts, restitution, disgorgement, or civil or criminal penalties. Any agency or judicial enforcement action could have a material adverse effect on us.

Oral octreotide must be approved by the FDA through the NDA process before it may be legally marketed in the United States. The process required by the FDA before a drug may be marketed in the United States generally involves the following:

- completion of extensive nonclinical or nonclinical laboratory tests, animal studies and formulation studies in accordance with applicable regulations, including the FDA s Good Laboratory Practice, or GLP, regulations;

- submission to the FDA of an IND, which must become effective before human clinical trials may begin;

performance of adequate and well-controlled human clinical trials in accordance with applicable IND and other clinical study related regulations, sometimes referred to as good clinical practices, or GCPs, to establish the safety and efficacy of the proposed drug for its proposed indication;

submission to the FDA of an NDA;

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a determination by the FDA within 60 days of its receipt of an NDA to file the NDA for review;

satisfactory completion of an FDA pre-approval inspection of the manufacturing facility or facilities where the drug is produced to assess compliance with the FDA s current good manufacturing practice requirements, or cGMP, to assure that the facilities, methods and controls are adequate to preserve the drug s identity, strength, quality and purity;

potential FDA audit of the clinical trial sites that generated the data in support of the NDA; and

FDA review and approval of the NDA prior to any commercial marketing or sale of the drug in the United States.

The data required to support an NDA are generated in two distinct development stages: nonclinical and clinical. For new chemical entities, the nonclinical development stage generally involves synthesizing the active component, developing the formulation and determining the manufacturing process, as well as carrying out non-human toxicology, pharmacology and drug metabolism studies in the laboratory, which support subsequent clinical testing. The conduct of the nonclinical tests must comply with federal regulations and requirements including GLPs. The sponsor must submit the results of the nonclinical tests, together with manufacturing information, analytical data, any available clinical data or published literature and a proposed clinical protocol, to the FDA as part of the IND. An IND is a request for authorization from the FDA to administer an investigational drug product to humans. The central focus of an IND submission is on the general investigational plan and the protocol(s) for human studies. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA raises concerns or questions regarding the proposed clinical trials and places the IND on clinical hold within that 30-day time period. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. The FDA may also impose clinical holds on a drug candidate at any time before or during clinical trials due to safety concerns or non-compliance. Accordingly, we cannot be sure that submission of an IND will result in the FDA allowing clinical trials to begin, or that, once begun, issues will not arise that could cause the trial to be suspended or terminated.

The clinical stage of development involves the administration of the drug candidate to healthy volunteers and/or patients under the supervision of qualified investigators, generally physicians not employed by or under the trial sponsor s control, in accordance with GCPs, which include the requirement that all research subjects provide their informed consent for their participation in any clinical trial. Clinical trials are conducted under protocols detailing, among other things, the objectives of the clinical trial, dosing procedures, subject selection and exclusion criteria, and the parameters to be used to monitor subject safety and assess efficacy. Each protocol, and any subsequent amendments to the protocol, must be submitted to the FDA as part of the IND. Further, each clinical trial must be reviewed and approved by an independent institutional review board, or IRB, at or servicing each institution at which the clinical trial will be conducted. An IRB is charged with protecting the welfare and rights of trial participants and considers such items as whether the risks to individuals participating in the clinical trials are minimized and are reasonable in relation to anticipated benefits. The IRB also approves the informed consent form that must be provided to each clinical trial subject or his or her legal representative and must monitor the clinical trial until completion. There are also requirements governing the reporting of ongoing clinical trials and completed clinical trial results to public registries.

Clinical trials are generally conducted in three sequential phases, known as Phase 1, Phase 2 and Phase 3 clinical trials, and may overlap. Phase 1 generally involves a small number of healthy volunteers who are initially exposed to a

single dose and then multiple doses of the product candidate. The primary purpose of these studies is to assess the metabolism, pharmacological action, side effect tolerability and safety of the drug. Phase 2 trials typically involve studies in disease-affected patients to determine the dose required to produce the desired benefits. At the same time, safety and further pharmacokinetic and pharmacodynamic information is collected, as well as identification of possible adverse effects and safety risks and preliminary evaluation of efficacy. Phase 3 trials generally involve large numbers of patients at multiple sites, and are designed to provide the data necessary to demonstrate the effectiveness of the product for its intended use, its safety in use, and to establish the overall benefit/risk relationship of the product and provide an adequate basis for product approval. Phase 3 trials may

include comparisons with placebo and/or other comparator treatments. The duration of treatment is often extended to mimic the actual use of a product during marketing. Generally, two adequate and well-controlled Phase 3 clinical trials are required by the FDA for approval of an NDA.

Post-approval trials, sometimes referred to as Phase 4 clinical trials, may be conducted after initial marketing approval. These studies are used to gain additional experience from the treatment of patients in the intended therapeutic indication. In certain instances, FDA may mandate the performance of Phase 4 trials.

Progress reports detailing the results of the clinical trials, among other information, must be submitted at least annually to the FDA, and written IND safety reports must be submitted to the FDA and the investigators for serious and unexpected adverse events, findings from other studies that suggest a significant risk to humans exposed to the drug, findings from animal or *in vitro* testing that suggest a significant risk to human subjects, and any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, if at all. The FDA or the clinical trial sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB s requirements or if the drug has been associated with unexpected serious harm to patients. Additionally, some clinical trials are overseen by an independent group of qualified experts organized by the clinical trial sponsor, known as a data safety monitoring board or committee. This group provides authorization for whether or not a trial may move forward at designated check points based on access to certain data from the study. The clinical trial sponsor may also suspend or terminate a clinical trial based on evolving business objectives and/or competitive climate.

Concurrent with clinical trials, companies usually complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the drug as well as finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the drug candidate and, among other things, must develop methods for testing the identity, strength, quality and purity of the final drug product. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the drug candidate does not undergo unacceptable deterioration over its shelf life.

NDA and FDA Review Process

Following trial completion, trial data are analyzed to assess safety and efficacy. The results of nonclinical studies and clinical trials are then submitted to the FDA in an NDA along with proposed labeling for the product and information about the manufacturing process and facilities that will be used to ensure product quality, results of analytical testing conducted on the chemistry of the drug, and other relevant information. The NDA is a request for approval to market the drug and must contain proof of safety, purity, potency and efficacy, which is demonstrated by extensive nonclinical and clinical testing. The application includes both negative or ambiguous results of nonclinical studies and clinical trials as well as positive findings. Data may come from company-sponsored clinical trials intended to test the safety and effectiveness of a use of a product, or from a number of alternative sources, including studies initiated by investigators. To support marketing approval, the data submitted must be sufficient in quality and quantity to establish the safety and effectiveness of the investigational drug product to the satisfaction of the FDA. The submission of an NDA is subject to the payment of substantial user fees; a waiver of such fees may be obtained under certain limited circumstances. FDA approval of an NDA must be obtained before marketing a drug in the United States.

In addition, under the Pediatric Research Equity Act, or PREA, an NDA or supplement to an NDA must contain data to assess the safety and effectiveness of the drug for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA may grant deferrals for submission of data or full or partial waivers. An NDA

applicant must submit to the FDA a pediatric study plan typically 60 days after an end-of-Phase 2 meeting with the agency. Because oral octreotide received orphan drug designation for the treatment of acromegaly, we do not need to comply with the requirements of PREA at this time. If, however, we seek other indications for oral octreotide or pursue approval of any other product candidate that does not have orphan drug designation, we may need to comply with PREA or otherwise seek a waiver**.**

The FDA reviews all NDAs submitted before it accepts them for filing and may request additional information rather than accepting an NDA for filing. The FDA must make a decision on accepting an NDA for filing within 60 days of receipt. Once the submission is accepted for filing, the FDA begins an in-depth review of the NDA. The decision to accept the NDA for filing means that the FDA has made a threshold determination that the application is sufficiently complete to permit a substantive review. Under the goals and policies agreed to by the FDA under the Prescription Drug User Fee Act, or PDUFA, the FDA has ten months from the receipt of an NDA in which to complete its initial review of a standard NDA and respond to the applicant. The FDA does not always meet its PDUFA goal dates for standard NDAs, and the review process is often significantly extended by FDA requests for additional information or clarification.

After the NDA submission is accepted for filing, the FDA reviews the NDA to determine, among other things, whether the proposed product is safe and effective for its intended use, and whether the product is being manufactured in accordance with cGMPs to assure and preserve the product s identity, strength, quality and purity. The FDA may refer applications for novel drug products or drug products which present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions. The FDA will likely re-analyze the clinical trial data, which could result in extensive discussions between the FDA and us during the review process. The review and evaluation of an NDA by the FDA is extensive and time consuming and may take longer than originally planned to complete, and we may not receive a timely approval, if at all.

Before approving an NDA, the FDA will conduct a pre-approval inspection of the manufacturing facilities for the new product to determine whether they comply with cGMPs. The FDA will not approve the product unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. In addition, before approving an NDA, the FDA may also audit data from clinical trials to ensure compliance with GCP requirements. After the FDA evaluates the application, manufacturing process and manufacturing facilities, it may issue an approval letter or a Complete Response Letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications. A Complete Response Letter indicates that the review cycle of the application is complete and the application will not be approved in its present form. A Complete Response Letter usually describes all of the specific deficiencies in the NDA identified by the FDA. The Complete Response Letter may require additional clinical data and/or an additional pivotal Phase 3 clinical trial(s), and/or other significant and time-consuming requirements related to clinical trials, nonclinical studies or manufacturing. If a Complete Response Letter is issued, the applicant may either resubmit the NDA, addressing all of the deficiencies identified in the letter, or withdraw the application. Even if such data and information are submitted, the FDA may ultimately decide that the NDA does not satisfy the criteria for approval. Data obtained from clinical trials are not always conclusive, and the FDA may interpret data differently than we interpret the same data.

There is no assurance that the FDA will ultimately approve a drug product for marketing in the United States, and we may encounter significant difficulties or costs during the review process. If a product receives marketing approval, the approval may be significantly limited to specific diseases and dosages or the indications for use may otherwise be

limited, which could restrict the commercial value of the product. Further, the FDA may require that certain contraindications, warnings or precautions be included in the product labeling or may condition the approval of the NDA on other changes to the proposed labeling, development of adequate controls and specifications, or a

commitment to conduct post-market testing or clinical trials and surveillance to monitor the effects of approved products. For example, the FDA may require Phase 4 testing which involves clinical trials designed to further assess drug safety and effectiveness and may require testing and surveillance programs to monitor the safety of approved products that have been commercialized. The FDA may also place other conditions on approvals including the requirement for a risk evaluation and mitigation strategy, or REMS, to assure the safe use of the drug. If the FDA concludes a REMS is needed, the sponsor of the NDA must submit a proposed REMS; the FDA will not approve the NDA without an approved REMS, if required. A REMS could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. Any of these limitations on approval or marketing could restrict the commercial promotion, distribution, prescription or dispensing of products. Product approvals may be withdrawn for non-compliance with regulatory requirements or if problems occur following initial marketing.

505(b)(2) Approval Process

Section 505(b)(2) of the FDCA provides an alternate regulatory pathway for the FDA to approve a new drug and permits reliance for such approval on published literature or an FDA finding of safety and effectiveness for a previously approved drug product. Specifically, section 505(b)(2) permits the filing of an NDA where one or more of the investigations relied upon by the applicant for approval were not conducted by or for the applicant and for which the applicant has not obtained a right of reference. The applicant may rely upon published literature and/or the FDA s findings of safety and effectiveness for a previously approved drug. Typically, 505(b)(2) applicants must perform additional trials to support the change from the previously approved drug and to further demonstrate the new drug s safety and effectiveness. The FDA may then approve the new product candidate for all or some of the labeled indications for which the referenced product has been approved, as well as for any new indication sought by the section 505(b)(2) applicant.

Our lead product candidate, oral octreotide, is based upon an already approved version of the same drug in an immediate-release formulation for subcutaneous injection, rather than a new chemical entity product candidate. Accordingly, we expect to be able to rely on information from previously conducted studies involving the immediate-release subcutaneous octreotide product in our clinical development plans and our NDA submission.

Post-Marketing Requirements

Following approval of a new product, a pharmaceutical company and the approved product are subject to continuing regulation by the FDA, including, among other things, monitoring and recordkeeping activities, reporting to the applicable regulatory authorities of adverse events with the product, providing the regulatory authorities with updated safety and efficacy information, and product sampling and distribution requirements in accordance with the Prescription Drug Marketing Act, a part of the FDCA. Modifications or enhancements to the product or its labeling or changes of the site of manufacture are often subject to the approval of the FDA and other regulators, which may or may not be received or may result in a lengthy review process.

Prescription drug advertising is subject to federal, state and foreign regulations. In the United States, the FDA regulates prescription drug promotion and advertising, including direct-to-consumer advertising. Prescription drug promotional materials must be submitted to the FDA in conjunction with their first use. In addition, a pharmaceutical company must comply with restrictions on promoting drugs for uses or in patient populations that are not described in the drug s approved labeling (known as off-label use), limitations on industry-sponsored scientific and educational activities, and requirements for promotional activities involving the internet. Although physicians may prescribe legally available drugs for off-label uses, manufacturers may not market or promote such off-label uses.

In the United States, once a product is approved, its manufacture is subject to comprehensive and continuing regulation by the FDA. The FDA regulations require that products be manufactured in specific approved facilities and in accordance with cGMPs. We rely, and expect to continue to rely, on third parties for the production of clinical and commercial quantities of our products in accordance with cGMP regulations. cGMP

regulations require among other things, quality control and quality assurance as well as the corresponding maintenance of records and documentation and the obligation to investigate and correct any deviations from cGMP. Drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMPs and other laws. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance. These regulations also impose certain organizational, procedural and documentation requirements with respect to manufacturing and quality assurance activities. NDA holders using contract manufacturers, laboratories or packagers are responsible for the selection and monitoring of qualified firms, and, in certain circumstances, qualified suppliers to these firms. These firms and, where applicable, their suppliers are subject to inspections by the FDA at any time, and the discovery of violative conditions, including failure to conform to cGMPs, could result in enforcement actions that interrupt the operation of any such facilities or the ability to distribute products manufactured, processed or tested by them. Discovery of problems with a product after approval may result in restrictions on a product, manufacturer, or holder of an approved NDA, including, among other things, recall or withdrawal of the product from the market.

The FDA also may require post-marketing testing, known as Phase 4 testing, REMS and surveillance to monitor the effects of an approved product or place conditions on an approval that could restrict the distribution or use of the product. Discovery of previously unknown problems with a product or the failure to comply with applicable FDA requirements can have negative consequences, including adverse publicity, judicial or administrative enforcement, untitled or warning letters from the FDA, mandated corrective advertising or communications with doctors, and civil or criminal penalties, among others. Newly discovered or developed safety or effectiveness data may require changes to a product s approved labeling, including the addition of new warnings and contraindications, and also may require the implementation of other risk management measures. Also, new government requirements, including those resulting from new legislation, may be established, or the FDA s policies may change, which could delay or prevent regulatory approval of our products under development and impact approved products already on the market.

Other Regulatory Matters

The distribution of pharmaceutical products is subject to additional requirements and regulations, including extensive record-keeping, licensing, storage and security requirements intended to prevent the unauthorized sale of pharmaceutical products.

The failure to comply with regulatory requirements subjects firms to possible legal or regulatory action. Depending on the circumstances, failure to meet applicable regulatory requirements can result in criminal prosecution, fines or other penalties, injunctions, voluntary recall, seizure of products, total or partial suspension of production, denial or withdrawal of product approvals, exclusion from federal healthcare programs, or refusal to allow a firm to enter into supply contracts, including government contracts. In addition, even if a firm complies with FDA and other requirements, new information regarding the safety or effectiveness of a product could lead the FDA to modify or withdraw product approval. Prohibitions or restrictions on sales or withdrawal of future products marketed by us could materially affect our business in an adverse way.

Changes in regulations, statutes or the interpretation of existing regulations could impact our business in the future by requiring, for example: (i) changes to our manufacturing arrangements; (ii) additions or modifications to product labeling; (iii) the voluntary recall or discontinuation of our products; or (iv) additional record-keeping requirements. If any such changes were to be imposed, they could adversely affect the operation of our business.

Orphan Designation and Exclusivity

The FDA may grant orphan drug designation to drugs intended to treat a rare disease or condition that affects fewer than 200,000 individuals in the United States. Alternatively, orphan drug designation may be available if

the disease of the condition affects more than 200,000 individuals in the United States and there is no reasonable expectation that the cost of developing and making the drug for this type of disease or condition will be recovered from sales in the United States.

Orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages, and user-fee waivers. In addition, if a product is the first to receive FDA approval of the indication for which it has orphan designation, the product is entitled to orphan drug exclusivity, which means the FDA may not approve any other application to market the same drug for the same indication for a period of seven years, except in limited circumstances, such as a showing of clinical superiority over the product with orphan exclusivity.

U.S. Marketing Exclusivity

Market exclusivity provisions under the FDCA can also delay the submission or the approval of certain marketing applications. The FDA provides three years of marketing exclusivity for an NDA, or supplement to an existing NDA, if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, for example new indications, dosages or strengths of an existing drug. This three-year exclusivity covers only the modification for which the drug received approval on the basis of the new clinical investigations and does not prohibit the FDA from approving ANDAs for drugs containing the active agent for the original indication or condition of use. Three-year exclusivity will not delay the submission or approval of a full NDA. However, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the nonclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness. Orphan drug exclusivity, as described below, may offer a seven-year period of marketing exclusivity, except in certain circumstances. Pediatric exclusivity is another type of regulatory market exclusivity in the United States. Pediatric exclusivity, if granted, adds six months to existing exclusivity periods and patent terms. This six-month exclusivity, which runs from the end of other exclusivity protection and patent term, may be granted based on the voluntary completion of a pediatric trial in accordance with an FDA-issued Written Request for such a trial.

Other Regulations

We are also subject to numerous federal, state and local laws relating to such matters as safe working conditions, manufacturing practices, environmental protection, fire hazard control and disposal of hazardous or potentially hazardous substances. We may incur significant costs to comply with such laws and regulations now or in the future.

European Orphan Designation and Exclusivity

In the European Union, the EMA s Committee for Orphan Medicinal Products, or COMP, grants orphan drug designation to promote the development of products that are intended for the diagnosis, prevention or treatment of life-threatening or chronically debilitating conditions that affect not more than five in 10,000 persons in the European Union Community, or when, without incentives, it is unlikely that sales of such products in the European Union would be sufficient to justify the necessary investment in developing the products. Additionally, orphan drug designation is only available where no satisfactory method of diagnosis, prevention, or treatment of the condition has been authorized (or the product would be a significant benefit to those affected).

In the European Union, orphan drug designation entitles a party to financial incentives such as reduction of fees or fee waivers and 10 years of market exclusivity is granted following medicinal product approval. This period may be reduced to six years if the orphan drug designation criteria are no longer met, including where it is shown that the

product is sufficiently profitable not to justify maintenance of market exclusivity. Market exclusivity would not prevent the approval of a similar drug that is shown to be safer, more effective or otherwise clinically superior.

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Orphan drug designation must be requested before submitting an application for marketing approval. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

Coverage and Reimbursement

Sales of any products for which we receive regulatory approval for commercial sale will depend in part on the availability of coverage and adequate reimbursement from third-party payors, including government healthcare program administrative authorities, managed care organizations, private health insurers, and other entities. Patients who are prescribed medications for the treatment of their conditions, and their prescribing physicians, generally rely on third-party payors to reimburse all or part of the costs associated with their prescription drugs. Patients are unlikely to use our products unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of our products. Therefore, our products, once approved, may not obtain market acceptance unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of our products.

The process for determining whether a third-party payor will provide coverage for a drug product typically is separate from the process for setting the price of a drug product or for establishing the reimbursement rate that the payor will pay for the drug product once coverage is approved. Third-party payors may limit coverage to specific drug products on an approved list, also known as a formulary, which might not include all of the FDA-approved drugs for a particular indication. A decision by a third-party payor not to cover our product candidates could reduce physician utilization of our products once approved. Moreover, a third-party payor s decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved or that any required patient cost-sharing amount will be acceptable to the patient. Adequate third-party reimbursement may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development. Additionally, coverage and reimbursement for drug products can differ significantly from payor to payor and among the insured lives of an individual payor depending upon the benefits applicable to the insured person. One third-party payor s decision to cover a particular drug product or service does not ensure that other payors will also provide coverage for the medical product or service, or will provide coverage at an adequate reimbursement rate. As a result, the coverage determination process will require us to provide scientific and clinical support for the use of our products to each payor separately and will be a time-consuming process.

The containment of healthcare costs has become a priority of federal, state and foreign governments, and the prices of drugs have been a focus in this effort. Third-party payors are increasingly challenging the prices charged for drug products and medical services, examining the medical necessity and reviewing the cost effectiveness of drug products and medical services, in addition to questioning safety and efficacy. If these third-party payors do not consider our products to be cost-effective compared to other available therapies, they may not cover our products after FDA approval or, if they do, the level of payment may not be sufficient to allow us to sell our products at a profit.

The American Recovery and Reinvestment Act of 2009 provides funding for the federal government to compare the effectiveness of different treatments for the same illness. The Department of Health and Human Services, the Agency for Healthcare Research and Quality and the National Institutes for Health develop research plans and periodically report on the status of the research and related expenditures to Congress. Although the results of the comparative effectiveness studies are not intended to mandate coverage policies for governmental or private payors, it is not clear what effect, if any, the research will have on the sales of our product candidates, if any such product or the condition that it is intended to treat is the subject of a study. It is also possible that comparative effectiveness research demonstrating benefits in a competitor s product could adversely affect the sales of our product candidates, once approved.

In addition, in some foreign countries, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing vary widely from country to country. For example,

the European Union provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. A member state may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our products. Historically, products launched in the European Union do not follow price structures of the United States and generally tend to be significantly lower.

Anti-Kickback and False Claims Laws and Other Regulatory Matters

In the United States, among other things, the research, manufacturing, distribution, sale and promotion of drug products and medical devices are potentially subject to regulation and enforcement by various federal, state and local authorities in addition to the FDA, including the Centers for Medicare & Medicaid Services, other divisions of the United States Department of Health and Human Services (e.g., the Office of Inspector General), the Drug Enforcement Administration, the Consumer Product Safety Commission, the Federal Trade Commission, the Occupational Safety & Health Administration, the Environmental Protection Agency, state attorneys general and other state and local government agencies. Our current and future business activities, including for example, sales, marketing and scientific/educational grant programs must comply with healthcare regulatory laws, including the Federal Anti-Kickback Statute, the Federal False Claims Act, as amended, the privacy regulations promulgated under the Health Insurance Portability and Accountability Act, or HIPAA, as amended, physician payment transparency laws, and similar state laws. Pricing and rebate programs must comply with the Medicaid Drug Rebate Program requirements of the Omnibus Budget Reconciliation Act of 1990, as amended, and the Veterans Health Care Act of 1992, as amended. If products are made available to authorized users of the Federal Supply Schedule of the General Services Administration, additional laws and requirements apply. The handling of any controlled substances must comply with the U.S. Controlled Substances Act and Controlled Substances Import and Export Act. Products must meet applicable child-resistant packaging requirements under the U.S. Poison Prevention Packaging Act. All of these activities are also potentially subject to federal and state consumer protection and unfair competition laws.

The Federal Anti-Kickback Statute makes it illegal for any person, including a prescription drug manufacturer (or a party acting on its behalf) to knowingly and willfully solicit, receive, offer, or pay any remuneration that is intended to induce the referral of business, including the purchasing, leasing, ordering or arranging for or recommending the purchase, lease or order of, any good, facility, item or service for which payment may be made, in whole or in part, under a federal healthcare program, such as Medicare or Medicaid. The term remuneration has been broadly interpreted to include anything of value. The Federal Anti-Kickback Statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on one hand and prescribers, purchasers and formulary managers on the other. Although there are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution, the exceptions and safe harbors are drawn narrowly. Practices that involve remuneration that may be alleged to be intended to induce prescribing, purchases or recommendations may be subject to scrutiny if they do not qualify for an exception or safe harbor. Failure to meet all of the requirements of a particular applicable statutory exception or regulatory safe harbor does not make the conduct per se illegal under the Federal Anti-Kickback Statute. Instead, the legality of the arrangement will be evaluated on a case-by-case basis based on a cumulative review of all of its facts and circumstances. Additionally, the intent standard under the Federal Anti-Kickback Statute was amended by the Patient Protection and Affordable Care Act, as amended by the Health Care Education and Reconciliation Act of 2010, or collectively the ACA, to a stricter standard such that a person or entity no longer needs to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. In addition, the ACA codified case law 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 False Claims Act. Violations of this law are punishable by up to five years in prison, criminal fines, administrative civil

money penalties, and exclusion from participation in federal healthcare programs. In addition, many states have adopted laws similar

to the Federal Anti-Kickback Statute. Some of these state prohibitions apply to the referral of patients for healthcare services reimbursed by any insurer, not just federal healthcare programs such as Medicare and Medicaid. Due to the breadth of these federal and state anti-kickback laws, and the potential for additional legal or regulatory change in this area, it is possible that our future business activities, including our sales and marketing practices and/or our future relationships with endocrinologists and other healthcare providers might be challenged under anti-kickback laws, which could harm us.

The Federal False Claims Act prohibits anyone from, among other things, knowingly presenting, or causing to be presented, for payment to federal programs (including Medicare and Medicaid) claims for items or services, including drugs, that are false or fraudulent. This statute has been interpreted to prohibit presenting claims for items or services not provided as claimed, or claims for medically unnecessary items or services. Although we would not submit claims directly to payors, manufacturers can be held liable under these laws if they are deemed to cause the submission of false or fraudulent claims by, for example, providing inaccurate billing or coding information to customers or promoting a product off-label. In addition, our future activities relating to the reporting of wholesaler or estimated retail prices for our products, the reporting of prices used to calculate Medicaid rebate information and other information affecting federal, state and third-party reimbursement for our products, and the sale and marketing of our products, are subject to scrutiny under this law. For example, pharmaceutical companies have been found liable under the Federal False Claims Act in connection with their off-label promotion of drugs. Penalties for a False Claims Act violation include three times the actual damages sustained by the government, plus mandatory civil penalties of between $5,500 and $11,000 for each separate false claim, the potential for exclusion from participation in federal healthcare programs, and, although the Federal False Claims Act is a civil statute, conduct that results in a False Claims Act violation may also implicate various federal criminal statutes. If the government were to allege that we were, or convict us of, violating these false claims laws, we could be subject to a substantial fine and may suffer a decline in our stock price. In addition, private individuals have the ability to bring actions under the Federal False Claims Act and certain states have enacted laws modeled after the Federal False Claims Act.

Similarly, the civil monetary penalties statute imposes penalties against any person or entity who, among other things, is determined to have presented or caused to be presented a claim to a federal health program that the person knows or should know is for an item or service that was not provided as claimed or is false or fraudulent.

Additionally, HIPAA created federal criminal statutes that prohibit, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, including private third-party payors and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services.

The ACA included a provision commonly referred to as the Sunshine Act, which requires certain pharmaceutical manufacturers to track and report annually certain financial arrangements with physicians and teaching hospitals, including any transfer of value provided, as well as any ownership or investment interests held by physicians and their immediate family members. Covered manufacturers are required to submit reports to CMS by the 90th day of each subsequent calendar year. The information reported for the first reporting period was publicly available on a searchable website in September 2014. Information reported for subsequent reporting periods will also be publicly available and searchable on the CMS website. There are also an increasing number of state laws that require manufacturers to make reports to states on pricing and marketing information. Many of these laws contain ambiguities as to what is required to comply with the laws. In addition, given the lack of clarity with respect to these laws and their implementation, our reporting actions could be subject to the penalty provisions of the pertinent state and federal authorities. These laws may affect our sales, marketing and other promotional activities by imposing administrative and compliance burdens on us.

In addition, we may be subject to data privacy and security regulation by both the federal government and the states in which we conduct our business. HIPAA, as amended by the Health Information Technology for

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Economic and Clinical Health Act, or HITECH, and their respective implementing regulations, including the final omnibus rule published on January 25, 2013, imposes specified requirements relating to the privacy, security and transmission of individually identifiable health information. Among other things, HITECH makes certain of HIPAA s privacy and security standards directly applicable to business associates, defined as independent contractors or agents of covered entities that create, receive, maintain or transmit protected health information in connection with providing a service for or on behalf of a covered entity. HITECH also created four new tiers of civil monetary penalties and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorneys fees and costs associated with pursuing federal civil actions. In addition, state laws govern the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

The failure to comply with applicable regulatory requirements subjects us to possible legal or regulatory action. Depending on the circumstances, failure to meet applicable regulatory requirements can result in significant criminal, civil and/or administrative penalties, damages, fines, disgorgement, exclusion from participation in federal healthcare programs, such as Medicare and Medicaid, injunctions, recall or seizure of products, total or partial suspension of production, denial or withdrawal of product approvals, refusal to allow us to enter into supply contracts, including government contracts, contractual damages, reputational harm, administrative burdens, diminished profits and future earnings, and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

We intend to develop a comprehensive compliance program that establishes internal controls to facilitate adherence to the law and program requirements to which we will or may become subject because we intend to commercialize products that could be reimbursed under a federal healthcare program and other governmental healthcare programs.

Affordable Health Care Act and Other Reform Initiatives

In the United States and some foreign jurisdictions, there have been, and likely will continue to be, a number of legislative and regulatory changes and proposed changes regarding the healthcare system directed at broadening the availability of healthcare and containing or lowering the cost of healthcare.

In March 2010, the ACA, was enacted. The ACA includes measures that have significantly changed, and are expected to continue to significantly change, the way healthcare is financed by both governmental and private insurers. Among the provisions of the ACA of greatest importance to the pharmaceutical industry are the following:

The Medicaid Drug Rebate Program requires pharmaceutical manufacturers to enter into and have in effect a national rebate agreement with the Secretary of the Department of Health and Human Services in exchange for state Medicaid coverage of most of the manufacturer s drugs. ACA made several changes to the Medicaid Drug Rebate Program, including increasing pharmaceutical manufacturers rebate liability by raising the minimum basic Medicaid rebate on most branded prescription drugs and biologic agents to 23.1% of average manufacturer price, or AMP, and adding a new rebate calculation for line extensions (i.e., new formulations, such as extended release formulations) of solid oral dosage forms of branded products, as well as potentially impacting their rebate liability by modifying the statutory definition of AMP.

The ACA expanded the types of entities eligible to receive discounted 340B pricing, although, with the exception of children s hospitals, these newly eligible entities will not be eligible to receive discounted 340B

pricing on orphan drugs used in orphan indications. In addition, because 340B pricing is determined based on AMP and Medicaid drug rebate data, the revisions to the Medicaid rebate formula and AMP definition described above could cause the required 340B discounts to increase. The ACA imposed a requirement on manufacturers of branded drugs and biologic agents to provide a 50% discount off the negotiated price of branded drugs dispensed to Medicare Part D beneficiaries in the coverage gap (i.e., donut hole).

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

The ACA included the Sunshine Act, which required certain pharmaceutical manufacturers to track and annually report to CMS certain financial arrangements with physicians and teaching hospitals, including any transfer of value provided, as well as any ownership or investment interests held by physicians and their immediate family members.

The ACA established 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 research conducted by the Patient-Centered Outcomes Research Institute may affect the market for certain pharmaceutical products.

The ACA created the Independent Payment Advisory Board which has the authority to recommend certain changes to the Medicare program to reduce expenditures by the program that could result in reduced payments for prescription drugs. Under certain circumstances, these recommendations will become law unless Congress enacts legislation that will achieve the same or greater Medicare cost savings.

The ACA established the Center for Medicare and Medicaid Innovation within CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending. Funding has been allocated to support the mission of the Center for Medicare and Medicaid Innovation through 2019.

Many of the details regarding the implementation of the ACA are yet to be determined, and at this time, it remains unclear the full effect that the ACA would have on our business.

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

European Union Drug Development

In the European Union, oral octreotide and any future product candidates we may develop will also be subject to extensive regulatory requirements. As in the United States, medicinal products can only be marketed if marketing

authorizations from the competent regulatory agencies have been obtained.

Similar to the United States, the various phases of nonclinical and clinical research in the European Union are subject to significant regulatory controls. Although the EU Clinical Trials Directive 2001/20/EC has sought to harmonize the EU clinical trials regulatory framework, setting out common rules for the control and authorization of clinical trials in the EU, the EU Member States have transposed and applied the provisions of the Directive differently. This has led to significant variations in the member state regimes. Under the current regime, before a clinical trial can be initiated it must be approved in each of the EU countries where the trial is to

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be conducted by two distinct bodies: the National Competent Authority, or NCA, and one or more Ethics Committees, or ECs. Under the current regime all suspected unexpected serious adverse reactions to the investigated drug that occur during the clinical trial have to be reported to the NCA and ECs of the Member State where they occurred.

On April 16, 2014, the European Commission adopted new clinical trials legislation in an effort to ensure that the rules for conducting clinical trials in the EU will be identical. The new legislation, among other things, will implement a streamlined application procedure with a single entry point for review, harmonize the process for assessing applications for clinical trials, simplify reporting procedures, and increase transparency regarding clinical trials and their outcomes. The legislation, however, is not effective until May 28, 2016, at the earliest. Until then, the current law, Clinical Trials Directive 2001/20/EC, continues to govern all clinical trials performed in the EU.

European Union Drug Review and Approval

In the European Economic Area, or EEA, which is comprised of the 27 Member States of the European Union plus Norway, Iceland and Liechtenstein, medicinal products can only be commercialized after obtaining a Marketing Authorization, or MA. There are two types of marketing authorizations:

The *Community MA*, which is issued by the European Commission through the Centralized Procedure, based on the opinion of the Committee for Medicinal Products for Human Use, or CHMP, of the European Medicines Agency, or EMA, and which is valid throughout the entire territory of the EEA. The Centralized Procedure is mandatory for certain types of products, such as biotechnology medicinal products, orphan medicinal products, such as oral octreotide, and medicinal products containing a new active substance indicated for the treatment of AIDS, cancer, neurodegenerative disorders, diabetes, auto-immune and viral diseases. The Centralized Procedure is optional for products containing a new active substance not yet authorized in the EEA, or for products that constitute a significant therapeutic, scientific or technical innovation or which are in the interest of public health in the EU.

National MAs, which are issued by the competent authorities of the Member States of the EEA and only cover their respective territory, are available for products not falling within the mandatory scope of the Centralized Procedure. Where a product has already been authorized for marketing in a Member State of the EEA, this National MA can be recognized in another Member States through the Mutual Recognition Procedure. If the product has not received a National MA in any Member State at the time of application, it can be approved simultaneously in various Member States through the Decentralized Procedure. Under the Decentralized Procedure an identical dossier is submitted to the competent authorities of each of the Member States in which the MA is sought, one of which is selected by the applicant as the Reference Member State, or RMS. The competent authority of the RMS prepares a draft assessment report, a draft summary of the product characteristics, or SPC, and a draft of the labeling and package leaflet, which are sent to the other Member States (referred to as the Member States Concerned) for their approval. If the Member States Concerned raise no objections, based on a potential serious risk to public health, to the assessment, SPC, labeling, or packaging proposed by the RMS, the product is subsequently granted a national MA in all the Member States (i.e. in the RMS and the Member States Concerned).

Under the above described procedures, before granting the MA, the EMA or the competent authorities of the Member States of the EEA make an assessment of the risk-benefit balance of the product on the basis of scientific criteria concerning its quality, safety and efficacy.

Employees

As of June 30, 2015, we had 22 full-time employees, the majority of whom are located in Israel. While none of our employees are represented by a labor union or party to any collective bargaining agreement certain

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provisions of the collective bargaining agreements between the Histadrut (General Federation of Labor in Israel) and the Coordination Bureau of Economic Organizations (including the Industrialists Associations) are applicable to our employees by extension orders issued by the Israel Ministry of Economy (previously the Israeli Ministry of Trade, Industry and Labor).

Israeli labor laws principally govern the length of the workday, minimum wages for employees, procedures for hiring and dismissing employees, determination of severance pay, annual leave, sick days, advance notice of termination of employment, equal opportunity and anti-discrimination laws and other conditions of employment. Subject to certain exceptions, Israeli law generally requires severance pay upon the retirement, death or dismissal of an employee, and requires us and our employees to make payments to the National Insurance Institute, which is similar to the U.S. Social Security Administration. Our Israeli employees have defined-benefit pension plans that comply with applicable Israeli legal requirements, which also include the mandatory pension payments required by applicable law and allocations for severance pay.

We have never experienced any employment-related work stoppages and believe our relationship with our employees is good.

Property and Facilities

Our wholly owned Israeli subsidiary leases premises located in Jerusalem, Israel. The premises are in a commercial office building and house our office space of 3,940 square feet and our laboratory facilities of 3,563 square feet, where we currently conduct our research and development activities.

We lease these premises from an unaffiliated third party, pursuant to a lease that expires on September 4, 2015. In addition, we have three additional one-year lease renewal periods that can be exercised at our option. The last renewal period expires on September 4, 2018. Our annual rental costs with respect to this lease for 2014 were $305,000, and our expected rental costs for 2015 will be approximately the same.

Effective on May 12, 2015, we entered into a sublease for 6,546 square feet of commercial office space in Newton, Massachusetts, which will house our U.S. headquarters. These premises are leased from the current tenant of the space, pursuant to a sublease that expires on March 31, 2016. Our expected annualized rent for the period beginning May 12, 2015 and ending March 31, 2016 will be $229,110, payable in monthly installments of $19,092.50.

Legal Proceedings

From time to time, we may become involved in litigation relating to claims arising from the ordinary course of business. Our management believes that there are currently no claims or actions pending against us, the ultimate disposition of which could have a material adverse effect on our results of operations, financial condition or cash flows.

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MANAGEMENT

Executive Officers and Directors

Below is a list of the names, ages and positions of the individuals who serve as our executive officers, key persons and directors as of June 30, 2015.

Name	Age	Position
Executive Officers		
Mark Leuchtenberger	58	President, Chief Executive Officer and Director
Roni Mamluk, Ph.D.	48	Chief Development Officer
Mark J. Fitzpatrick	52	Chief Financial Officer, Treasurer and Secretary
Chaime Orlev	44	Vice President, Finance and Administration
Key Persons		
Dana Gelbaum	41	Vice President, Commercial Planning
Gary Patou, M.D.	56	Senior Medical Advisor
Non-Employee Directors		
David Stack(1)(3)	64	Chairman of the Board of Directors
Dror Brandwein(4)	56	Director
Todd Foley(1)(3)	43	Director
Ansbert Gadicke, M.D.	57	Director
Bard Geesaman, M.D., Ph.D.(2)	48	Director
Vincent Miles, Ph.D.(4)	64	Director
Scott Minick(2)(3)	63	Director
John Scarlett, M.D.(1)(2)	64	Director

(1) Member of the Compensation Committee.
(2) Member of the Audit Committee.
(3) Member of the Nominating and Corporate Governance Committee.
(4) Has indicated to us his intention to resign from our board of directors upon the closing of this offering.

Executive Officers

Mark Leuchtenberger has served as our President and Chief Executive Officer and as a member of our board of directors since March 2015. Prior to joining us, Mr. Leuchtenberger was President and Chief Executive Officer and director of Acusphere, Inc. (OTCMKTS: ACUS), a biopharmaceutical company, or Acusphere, from September 2013 to January 2015. Prior to Acusphere, from March 2010 to February 2013, Mr. Leuchtenberger served as President, Chief Executive Officer and a director at Rib-X Pharmaceuticals, Inc. (now Melinta Therapeutics, Inc.), a biopharmaceutical company. Prior to that, from 2006 to 2009, Mr. Leuchtenberger served as President and Chief Executive Officer of Targanta Therapeutics Corporation, where he led the company s initial public offering in 2007 and its acquisition in 2009. From 2002 to 2006, Mr. Leuchtenberger served as the President and Chief Executive Officer of Therion Biologics Corporation, or Therion. Prior to Therion, Mr. Leuchtenberger was a senior officer at Biogen Inc., where he led the late-stage development of Avonex and its launch in the United States and subsequently managed North American and international commercial operations. He is a director and past chairman of the Massachusetts Biotechnology Council Board of Directors, and currently serves as a trustee for Beth Israel Deaconess Medical Center and Chairman of the Advisory Committee for the MassDevelopment Emerging Technology Fund. He

is a co-founder of Albor Biologics, Inc. and Alvos Therapeutics, Inc. Mr. Leuchtenberger received his M.B.A. from the Yale School of Management and his B.A. from Wake Forest University. He served as non-executive Chairman of the Board of Directors of Xenetic Biosciences, Inc. (OTCMKTS: XBIO), a biopharmaceutical company developing next-generation biologic drugs and novel oncology therapeutics, from May 2014 to April 2015. We believe Mr. Leuchtenberger s position as our President and Chief Executive Officer as well as his extensive experience in commercial operations, business development and preparing biopharmaceuticals companies for product approval and commercialization make him a critical member of our board of directors.

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Roni Mamluk, Ph.D. has served as our Chief Development Officer since March 2015. She served as our Chief Executive Officer from April 2013 to March 2015 and held various roles of increasing responsibility, including Chief Operating Officer and Vice President, Research and Development, from 2006 to April 2013. She also served as a member of our board of directors from April 2013 to March 2015. Since joining us, Dr. Mamluk has played a leading role in developing, and is one of the primary inventors of, our proprietary Transient Permeability Enhancer, or TPE, technology platform. She has also led the development of oral octreotide and ongoing improvements to our TPE platform. Dr. Mamluk joined us from Adnexus Therapeutics, Inc., where she established and led nonclinical research and development. Dr. Mamluk received her B.A. and Ph.D. from the Hebrew University. She also participated in a post-doctoral fellowship at Children s Hospital/Harvard Medical School in the field of angiogenesis.

Mark J. Fitzpatrick has been our Chief Financial Officer since June 2015. Prior to joining us, he was Chief Financial Officer at Aegerion Pharmaceuticals, Inc. (NASDAQ: AEGR), a biopharmaceutical company specializing in the treatment of rare diseases, from May 2011 to June 2015. From July 2007 to April 2011, Mr. Fitzpatrick served as Chief Financial Officer of Proteon Therapeutics, Inc. (NASDAQ: PRTO), a biopharmaceutical company. He also held Chief Financial Officer positions at RenaMed Biologics, Inc., Dynogen Pharmaceuticals, Inc., WorldStreet Corporation, and Diacrin, Inc., and has more than 20 years of financial management experience in both public and private companies. Mr. Fitzpatrick received his B.S. in Accounting from Boston College in 1984 and earned a Certified Public Accountant certificate in the Commonwealth of Massachusetts in 1987.

Chaime Orlev has been our Vice President, Finance and Administration since December 2011. Mr. Orlev joined us in June 2010 as the Director of Finance. Prior to joining us, he was a financial consultant to several Israeli biotechnology and medical device companies from 2008 to 2010. From 2008 to 2009, Mr. Orlev served as Chief Financial Officer of Oramed Pharmaceuticals Inc. Mr. Orlev served as Chief Financial Officer of Gammacan International Inc. from 2005 to 2008 and as Vice President, Finance and Chief Financial Officer of Huntleigh from 2001 to 2004. Mr. Orlev received his M.B.A. from the Leon Recanati Graduate School of Business Administration at the Tel Aviv University and a B.A. in Business Administration from the College of Business in Israel. Mr. Orlev is a Certified Public Accountant under the laws of Israel.

Key Persons

Dana Gelbaum has been our Vice President, Commercial Planning since December 2011. Ms. Gelbaum joined us in February 2009 as Director of Business Development. Prior to joining us, she was Director of Business Development at Recoly N.V., a biotechnology company that is developing product candidates to treat hemophilia A patients. Previously, Ms. Gelbaum was an Associate at Johnson & Johnson Development Corporation, Johnson & Johnson s investment arm, focusing on investments in biopharmaceutical companies in Europe and medical device companies in Israel. Ms. Gelbaum received her M.Sc. and M.B.A. from Tel Aviv University.

Gary Patou, M.D. has served as our Senior Medical Advisor since August 2014. Since August 2009, Dr. Patou has served as Chief Medical Officer for Pacira Pharmaceuticals, Inc. (NASDAQ: PCRX), or Pacira, a specialty pharmaceutical company. In addition, he has been a Managing Director at MPM Capital, Inc., or MPM, a venture capital fund focused on life sciences companies, since 2005. Prior to joining Pacira, Dr. Patou was Chief Medical Officer at Peplin Inc. from July 2006 to April 2007, Chief Medical Officer of Cerimon Pharmaceuticals, Inc. from June 2005 to June 2006, and Executive Vice President and Chief Medical Officer of Oscient Pharmaceuticals Corp. from February 2004 to April 2005 just after its merger with GeneSoft Pharmaceuticals, Inc., or GeneSoft. Before GeneSoft, Dr. Patou worked at SmithKline Beecham Pharmaceuticals, now a unit of GlaxoSmithKline, as Senior Vice President and Director, Project and Portfolio Management, managing all of the company s pharmaceutical development projects. He also serves on the board of directors at Xenon Pharmaceuticals Inc. (NASDAQ: XENE). Dr. Patou has held a number of academic appointments at University College & Middlesex School of Medicine and

received his B.Sc. from University of London and his M.D. from University College London.

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Non-Employee Directors

David Stack joined our board of directors in November 2014 as Chairman. Since 2007, Mr. Stack has served as President, Chief Executive Officer and Chairman of Pacira Pharmaceuticals, Inc. (NASDAQ: PCRX). Mr. Stack has also been a Managing Director of MPM since 2005. From 2001 to 2004, he was President and Chief Executive Officer of The Medicines Company (NASDAQ: MDCO). Previously, Mr. Stack was President and General Manager at Innovex, Inc. He was Vice President, Business Development/Marketing at Immunomedics, Inc. (NASDAQ: IMMU) from 1993 until 1995. Prior to that, Mr. Stack was with Roche Laboratories from 1981 until 1993, where he eventually served as Director of Business Development and Planning for Infectious Disease, Oncology, and Virology and was the Therapeutic World Leader for Infectious Disease. Mr. Stack received his B.S. from Albany College of Pharmacy and a B.S. from Siena College. We believe Mr. Stack s qualifications to sit on our board of directors include his extensive experience in the life sciences sector, his financial expertise and his years of experience providing strategic and financial advisory services to biopharmaceutical organizations.

Dror Brandwein joined our board of directors in December 2012. Mr. Brandwein serves as the Chief Executive Officer of the 7 Main Group, a family office that specializes in long-term minority partnerships in industrial companies, a position he has held since 2008. Since 1999, Mr. Brandwein has served as a director of Bolder Ltd., a provider of consulting and managerial services. From 1992 to 2006, Mr. Brandwein was a founder and co-managing partner of Leshem Brandwein & Co., which later merged with Meitar, Liquornik, Geva & Co. to form Meitar Liquornik Geva Leshem Brandwein, a leading Israeli law firm. Mr. Brandwein received his LL.B. from the Hebrew University and graduated from the Owner/President Management program of Harvard Business School. We believe Mr. Brandwein s extensive managerial experience qualifies him to serve on our board of directors. Mr. Brandwein has indicated to us his intention to resign from our board of directors upon the closing of this offering.

Todd Foley joined our board of directors in May 2008. Mr. Foley is a Managing Partner at MPM Capital, where he has focused primarily on biotechnology investments. Mr. Foley joined MPM in 1999 and has been a partner since 2007. Prior to MPM, Mr. Foley s career in the life science industry included positions in Business Development at Genentech, Inc., a biotechnology company and subsidiary of F. Hoffman-La Roche, and in management consulting with Arthur D. Little. Mr. Foley currently serves on the boards of various biotechnology and healthcare companies, including Valeritas, Inc., OSS Healthcare Inc., Iconic Therapeutics, Inc., Rhythm Holding Company, LLC, Clinical Ink, Inc., Semma Therapeutics, Inc. and Selexys Pharmaceuticals Corporation. He received his B.S. from the Massachusetts Institute of Technology, or MIT, and an M.B.A. from Harvard Business School. We believe Mr. Foley s extensive business strategy and financial background and experience serving on the boards of several life science companies qualify him to serve on our board of directors.

Ansbert Gadicke, M.D. joined our board of directors in December 2014. Dr. Gadicke co-founded MPM s venture investing activities in 1997. Prior to that, Dr. Gadicke led MPM s Advisory and Investment Banking business from 1992 to 1996, and was in Boston Consulting Group s Health Care Group from 1989 to 1992. He is a member of the board of directors of biotechnology companies, Mitobridge, Inc., OSS Healthcare, Inc., Radius Health, Inc. (NASDAQ:RDUS), Raze Therapeutics, Inc., Sideris Pharmaceuticals, Inc. and TriNetX, Inc. Dr. Gadicke has held research positions in biochemistry and molecular biology at the Whitehead Institute at MIT and the Biochemistry Department at Harvard University. Dr. Gadicke has been published in leading scientific journals such as *Nature* and *Cell*. Dr. Gadicke is also a member of the Board of Fellows of Harvard Medical School and the Research Advisory Council of Massachusetts General Hospital. Dr. Gadicke received his M.D. from J.W. Goethe University. We believe Dr. Gadicke s extensive experience in the healthcare industry and in investment management qualify him to serve on our board.

Bard Geesaman, M.D., Ph.D. joined our board of directors in 2004. Since January 2012, Dr. Geesaman has served as a Managing Director at MPM. From 2012 to 2015, he was Executive Director, Life Sciences of the X PRIZE Foundation. He is the founder of Solasia Pharma K.K., a specialty pharmaceutical company that

develops and commercializes oncology drugs. From 2003 to 2007 he served as the Vice President, Medical Development for Elixir Pharmaceuticals Inc., where he oversaw clinical strategy for drug development and the human genetics program, and was a member of the company s business development team. Dr. Geesaman is a General Partner at F2 and F3 Ventures, two UK-based venture capital funds, and has served on their board of directors since 2004. Dr. Geesaman became board certified in Internal Medicine in 2000, after completing a Clinical Fellowship at the Massachusetts General Hospital. He received his Ph.D. from MIT, an M.D. from Harvard Medical School and a B.S. from University of California, Berkeley. We believe Dr. Geesaman s managerial experience and extensive experience in the healthcare industry qualify him to serve on our board.

Vincent Miles, Ph.D. joined our board of directors in July 2012. Dr. Miles has been a partner at Abingworth, a venture capital firm focused on life sciences and healthcare investment, since 2007 and has over 30 years of experience in the biotechnology industry. From 2003 to 2007 he served as Senior Vice President of Business Development at Alnylam Pharmaceuticals, Inc. (NASDAQ: ALNY), and from 1997 to 2004 he served as a Vice President at Millennium Pharmaceuticals, Inc. Prior to that, Dr. Miles served as Director of the Office of Technology Transfer at the Dana-Farber Cancer Institute from 1996 to 1997, and as vice president of various research and development and business functions at RiboGene, Inc. (a predecessor of Questcor Pharmaceuticals (NASDAQ: QCOR), which was acquired by Mallinckrodt (NYSE: MNK) in 2014) from 1992 to 1996, and Pharmacia P-L Biochemicals Inc. from 1986 to 1992. Dr. Miles serves on the board of directors of Hydra Biosciences Inc., Magellan Diagnostics, Inc., Dynex Technologies, Inc., Avillon Development 1 Ltd. and Bond 1 Development GP Ltd., and also served on the boards of Dicerna Pharmaceuticals, Inc. (NASDAQ: DRNA) from 2013 to 2014 and PrimeraDx, Inc. from 2008 to 2014. Dr. Miles received his B.Sc. and Ph.D. from University College London. We believe Dr. Miles s scientific and business experience serving as an executive officer, director and venture capital investor in biopharmaceutical companies qualifies him to serve on our board. Dr. Miles has indicated to us his intention to resign from our board of directors upon the closing of this offering.

Scott Minick joined our board of directors in October 2007. From January 2010 to March 2015, Mr. Minick served as President and Chief Executive Officer of BIND Therapeutics, Inc. (NASDAQ: BIND), a biopharmaceutical company, or BIND. From 1998 to 2010, Mr. Minick was Managing Director of ARCH Venture Partners and was instrumental in the startup, development and financing of numerous ARCH portfolio companies, including BIND and Chiasma. From 1995 to 1998, Mr. Minick was Director, President and Chief Operating Officer of SEQUUS Pharmaceuticals, Inc. (NASDAQ:SEQU), a biopharmaceutical company that was acquired by ALZA Corporation. Mr. Minick was formerly an executive at Baxter International, Inc. and Eli Lilly & Company. He serves as a member of the board of directors of BIND and Alzheon, Inc., and is a trustee of Beth Israel Deaconess Medical Center. Mr. Minick received his postgraduate training in neurobiology at the Salk Institute, an M.B.A. from Northwestern University, and a B.A. from the University of California, San Diego. We believe Mr. Minick s extensive knowledge of Chiasma s business as a company director since October 2007 and extensive experience in the biopharmaceutical industry and as a venture capitalist and senior executive qualify him to serve on our board.

John A. Scarlett, M.D. joined our board of directors in February 2015. Dr. Scarlett has been Chief Executive Officer and director of Geron Corporation (NASDAQ: GERN), a biotechnology company, since September 2011 and President since January 2012. Previously, he was the President and Chief Executive Officer of Proteolix, Inc., a biotechnology company that merged with Onyx Pharmaceuticals, Inc. (NASDAQ: ONXX) in October 2009, and a founder and Chief Executive Officer of Tercica, Inc. (NASDAQ: TRCA), which was acquired by Ipsen S.A. in 2008. From 1993 to 2001, Dr. Scarlett was also the founder and Chief Executive Officer of Sensus Drug Development Corporation, which was acquired by Pharmacia Corporation in 2001, and co-founded Covance Biotechnology Services, Inc., a contract biologics manufacturing and process development business that was acquired by Akzo Nobel s Diosynth Division in 2001. Earlier in his career, he worked for McNeil Pharmaceutical, a subsidiary of Johnson & Johnson, and Novo Nordisk Inc. He received his B.A. from Earlham College and his M.D. from the

University of Chicago, Pritzker School of Medicine. He completed his training in Internal Medicine at the Hospital of the University of Pennsylvania and his fellowship in Endocrinology and

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Metabolism at the University of Colorado Health Sciences Center. We believe Dr. Scarlett s experience as chief executive officer of two publicly traded biotechnology companies, as well as experience developing life sciences companies, qualifies him to serve on our board.

In addition to the individual attributes of each of our directors listed above, we highly value the collective qualifications and experiences of our board members. We believe the collective viewpoints and perspectives of our directors results in a board that is dedicated to advancing the interests of our stockholders.

Board Composition and Election of Directors

Board Composition

Our board of directors currently consists of nine members, all of whom were elected pursuant to the board composition provisions of our stockholders voting agreement, which is described under Certain Relationships and Related Party Transactions Stockholders Voting Agreement in this prospectus. The board composition provisions in our voting agreement will terminate immediately prior to the consummation of this offering. Upon the termination of these provisions, there will be no further contractual obligations regarding the election of our directors. Our nominating and governance committee and board of directors may therefore consider a broad range of factors relating to the qualifications and background of nominees, which may include diversity and is not limited to race, gender or national origin. We have no formal policy regarding board diversity. Our nominating and governance committee s and board of directors priority in selecting board members is identification of persons who will further the interests of our stockholders through his or her established record of professional accomplishment, the ability to contribute positively to the collaborative culture among board members, knowledge of our business, understanding of the competitive landscape and professional and personal experiences and expertise relevant to our growth strategy. Our directors hold office until their successors have been elected and qualified or until the earlier of their resignation or removal.

Our amended and restated certificate of incorporation and amended and restated bylaws that will become effective upon the completion of this offering also provide that our directors may be removed only for cause by the affirmative vote of the holders of at least 75% of the votes that all our stockholders would be entitled to cast in an annual election of directors, and that any vacancy on our board of directors, including a vacancy resulting from an enlargement of our board of directors, may be filled only by vote of a majority of our directors then in office.

Director Independence

Our common stock will be listed on The NASDAQ Global Select Market. Applicable NASDAQ rules require a majority of a listed company s board of directors to be comprised of independent directors within one year of listing. In addition, the NASDAQ rules require that, (i) on the date of the completion of the offering, at least one member of each of a listed company s audit, compensation and nominating and corporate governance committees be independent, (ii) within 90 days of the date of the completion of the offering, a majority of the members of such committees be independent and (iii) within one year of the date of the completion of the offering, all the members of such committees be independent. Audit committee members must also satisfy the independence criteria set forth in Rule 10A-3 under the Securities Exchange Act of 1934, as amended. Under applicable NASDAQ rules, a director will only qualify as an independent director if, in the opinion of the listed company s board of directors, that person does not have a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director.

In order to be considered independent for purposes of Rule 10A-3, a member of an audit committee of a listed company may not, other than in his or her capacity as a member of the audit committee, the board of directors, or any

other board committee, accept, directly or indirectly, any consulting, advisory, or other compensatory fee from the listed company or any of its subsidiaries or otherwise be an affiliated person of the listed company or any of its subsidiaries.

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In June 2015, our board of directors undertook a review of the composition of our board of directors and its committees and the independence of each director. Based upon information requested from and provided by each director concerning his or her background, employment and affiliations, including family relationships, our board of directors has determined that all directors other than Mr. Leuchtenberger are independent directors as defined under applicable NASDAQ rules. In making such determination, our board of directors considered the relationships that each such non-employee director has with our company and all other facts and circumstances that our board of directors deemed relevant in determining his or her independence, including the beneficial ownership of our capital stock by each non-employee director. Mr. Brandwein and Dr. Miles, currently members of our board of directors, have indicated to us their intention to resign from our board of directors upon the closing of this offering.

There are no family relationships among any of our directors or executive officers.

Staggered Board

In accordance with the terms of our amended and restated certificate of incorporation and amended and restated bylaws that will become effective upon the completion of this offering, our board of directors will be divided into three classes, Class I, Class II and Class III, with each class serving staggered three-year terms. Upon the expiration of the term of a class of directors, directors in that class will be eligible to be elected for a new three-year term at the annual meeting of stockholders in the year in which their term expires.

Our Class I directors will be Mr. Leuchtenberger, Mr. Stack, and Dr. Scarlett;

Our Class II directors will be Mr. Foley, Dr. Gadicke, and Dr. Geesaman; and

Our Class III directors will be Mr. Minick.

Mr. Brandwein and Dr. Miles, currently members of our board of directors, have indicated to us their intention to resign from our board of directors upon the closing of this offering.

Our amended and restated certificate of incorporation and amended and restated bylaws that will become effective upon the completion of this offering provide that the authorized number of directors may be changed only by resolution of the board of directors. Any additional directorships resulting from an increase in the number of directors will be distributed among the three classes so that, as nearly as possible, each class shall consist of one third of the board of directors.

The division of our board of directors into three classes with staggered three-year terms may delay or prevent stockholder efforts to effect a change of our management or a change in control.

Board Committees

Effective upon the completion of this offering, our board of directors will have three standing committees: the audit committee, the compensation committee and the nominating and corporate governance committee. Our board of directors may establish other committees from time to time. Each of these committees will operate under a charter that has been approved by our board of directors. The composition of all of our committees will comply with all applicable requirements of the Sarbanes-Oxley Act of 2002, The NASDAQ Stock Market, or NASDAQ and Securities and

Exchange Commission, or SEC, rules and regulations.

Audit Committee

Upon completion of this offering, our audit committee will consist of Mr. Minick, Dr. Scarlett and Dr. Geesaman, with Mr. Minick serving as chairman of the committee. Our board of directors has determined that each of the directors serving on our audit committee, other than Dr. Geesaman, meets the independence requirements of Rule 10A-3 under the Exchange Act and the applicable listing standards of NASDAQ. Our board of directors has determined that Mr. Minick is an audit committee financial expert within the meaning of the

SEC regulations and applicable listing standards of NASDAQ. In making this determination, our board has considered the formal education and nature and scope of his previous experience, coupled with past and present service on various audit committees. Our board has also determined that Dr. Geesaman does not satisfy independence requirements under applicable SEC and NASDAQ Stock Market rules for service on the audit committee. The transition rules of The NASDAQ Stock Market provide that two members of the audit committee may be exempt from independence requirements for 90 days after the effectiveness of this registration statement, and one member may be exempt for one year after the effectiveness of this registration statement. Our board of directors intends to cause our audit committee to comply with the transition rules within the applicable time periods. Our audit committee assists our board of directors in its oversight of our accounting and financial reporting process and the audits of our financial statements. The audit committee s responsibilities upon completion of this offering will include:

appointing, approving the compensation of, reviewing the performance of, and assessing the independence of our independent registered public accounting firm;

pre-approving audit and permissible non-audit services, and the terms of such services, to be provided by our independent registered public accounting firm;

reviewing the internal audit plan with the independent registered public accounting firm and members of management responsible for preparing our financial statements;

reviewing and discussing with management and the independent registered public accounting firm our annual and quarterly financial statements and related disclosures as well as critical accounting policies and practices used by us;

reviewing the adequacy of our internal control over financial reporting;

establishing policies and procedures for the receipt and retention of accounting-related complaints and concerns;

recommending, based upon its review and discussions with management and the independent registered public accounting firm, whether our audited consolidated financial statements shall be included in our Annual Report on Form 10-K;

preparing the audit committee report required by the rules of the SEC to be included in our annual proxy statement;

reviewing all related party transactions for potential conflict of interest situations and approving all such transactions; and

reviewing policies related to risk assessment and risk management; and establishing, maintaining and overseeing our Code of Business Conduct and Ethics.

All audit services to be provided to us and all non-audit services, other than *de minimis* non-audit services, to be provided to us by our independent registered public accounting firm must be approved in advance by our audit committee.

Compensation Committee

Upon completion of this offering, our compensation committee will consist of Dr. Scarlett, Mr. Foley and Mr. Stack, with Dr. Scarlett serving as chairman of the committee. Our board of directors has determined that each member of the compensation committee is independent as defined under the applicable listing standards of NASDAQ. Our compensation committee assists our board of directors in the discharge of its responsibilities relating to the compensation of our executive officers. The compensation committee s responsibilities upon completion of this offering will include:

annually reviewing and recommending for approval by the independent directors of the board individual and corporate goals and objectives relevant to the compensation of our executive officers;

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evaluating the performance of our executive officers in light of such individual and corporate goals and objectives and determining the compensation of our executive officers;

appointing, compensating and overseeing the work of any compensation consultant, legal counsel or other advisor retained by the compensation committee;

conducting the independence assessment outlined in NASDAQ rules with respect to any compensation consultant, legal counsel or other advisor retained by the compensation committee;

annually reviewing and reassessing the adequacy of the committee charter in its compliance with the listing requirements of NASDAQ;

overseeing and administering our compensation and similar plans;

reviewing and approving our policies and procedures for the grant of equity-based awards;

reviewing and making recommendations to the board of directors with respect to director compensation;

reviewing and approving stock option grants, and making recommendations to the board of directors with respect to stock option grants made to directors, executive officers, senior vice presidents or anyone reporting directly to our chief executive officer;

reviewing and discussing with management the compensation discussion and analysis, if any, to be included in our annual proxy statement; and

reviewing and discussing with the board of directors corporate succession plans for the chief executive officer and other senior management positions.

Nominating and Corporate Governance Committee

Upon completion of this offering, our nominating and corporate governance committee will consist of Mr. Stack, Mr. Minick and Mr. Foley, with Mr. Stack serving as chairman of the committee. Our board of directors has determined that each member of the nominating and corporate governance committee is independent as defined under the applicable listing standards of NASDAQ. Following this offering, the nominating and corporate governance committee s responsibilities will include:

developing and recommending to the board of directors criteria for board and committee membership;

establishing procedures for identifying and evaluating board of director candidates, including nominees recommended by stockholders;

identifying individuals qualified to become members of the board of directors;

recommending to the board of directors the persons to be nominated for election as directors and to each of the board s committees; and

developing and recommending to the board of directors a set of corporate governance principles.

Compensation Committee Interlocks and Insider Participation

None of our executive officers serves as a member of the board of directors or compensation committee, or other committee serving an equivalent function, of any other entity that has one or more of its executive officers serving as a member of our board of directors or compensation committee. None of the members of our compensation committee has ever been employed by us. For a description of transactions between us and members of our compensation committee and affiliates of such members, please see the section of this prospectus titled Certain Relationships and Related Party Transactions.

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Code of Business Conduct and Ethics

We have adopted a written code of business conduct and ethics that applies to all of our employees, officers and directors, including those officers responsible for financial reporting. Our code of business conduct and ethics is posted on the Corporate Governance section of our website, which is located at www.chiasmapharma.com. We intend to disclose amendments to the code, or any waivers of its requirements, on our website or in a current report on Form 8-K as may be required by SEC or NASDAQ rules.

Board Leadership Structure and Board s Role in Risk Oversight

The positions of our chairman of the board and chief executive officer are separated. Separating these positions allows our chief executive officer to focus on our day-to-day business, while allowing the chairman of the board to lead the board of directors in its fundamental role of providing advice to and independent oversight of management. Our board of directors recognizes the time, effort and energy that the chief executive officer must devote to his position in the current business environment, as well as the commitment required to serve as our chairman, particularly as the board of directors oversight responsibilities continue to grow. Our board of directors also believes that this structure ensures a greater role for the independent directors in the oversight of our company and active participation of the independent directors in setting agendas and establishing priorities and procedures for the work of our board of directors. This leadership structure is also preferred by a significant number of our stockholders. Our board of directors believes its administration of its risk oversight function has not affected its leadership structure.

Although our bylaws that will be in effect upon the completion of this offering will not require our chairman and chief executive officer positions to be separate, our board of directors believes that having separate positions is the appropriate leadership structure for us at this time and demonstrates our commitment to good corporate governance.

Risk is inherent with every business, and how well a business manages risk can ultimately determine its success. We face a number of risks, including those described under the section titled Risk Factors. Our board of directors is actively involved in oversight of risks that could affect us. This oversight is conducted primarily by our full board of directors, which has responsibility for general oversight of risks.

Following the completion of this offering, our board of directors will satisfy this responsibility through full reports by each committee chair regarding the committee s considerations and actions, as well as through regular reports directly from officers responsible for oversight of particular risks within our company. Our board of directors believes that full and open communication between management and the board of directors is essential for effective risk management and oversight.

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EXECUTIVE COMPENSATION

Overview

Historically, our executive compensation program has reflected our growth and development-oriented corporate culture. Compensation for our executive officers consists of a combination of base salary, bonuses, long-term incentive compensation in the form of stock options and benefits programs. As we transition from a private company to a publicly traded company, we will evaluate our compensation values and philosophy and compensation plans and arrangements as circumstances require. At a minimum, we expect to review executive compensation annually with input from a compensation consultant. As part of this review process, we expect the board of directors and the compensation committee to apply our values and philosophy, while considering the compensation levels needed to ensure our executive compensation program remains competitive. We will also review whether we are meeting our retention objectives and the potential cost of replacing a key employee.

The compensation provided to our named executive officers for 2014 is detailed in the 2014 Summary Compensation Table and accompanying footnotes and narrative that follow this section. Our named executive officers in 2014 were:

Roni Mamluk Ph.D., our former Chief Executive Officer and our current Chief Development Officer; and

Chaime Orlev, our Vice President, Finance and Administration.

In addition, Mark Leuchtenberger joined us as our President and Chief Executive Officer in March 2015 and Mark J. Fitzpatrick joined us as our Chief Financial Officer in June 2015.

2014 Summary Compensation Table

The following table sets forth information regarding compensation awarded to, earned by or paid to each of our named executive officers during the year ended December 31, 2014.

Name and Principal Position	Year	Salary ($)[2]	Bonus ($)[2][3]	Option Awards ($)[4]	All Other Compensation ($)[2]	Total ($)
Roni Mamluk, Ph.D.[1]						
Former President and Chief Executive Officer; Chief Development Officer	2014	302,351	122,729	850,662[5]	58,204[7]	1,333,946
Chaime Orlev						
Vice President, Finance and Administration	2014	145,288	53,117	154,490[6]	54,616[8]	407,511

(1) Dr. Mamluk resigned as Chief Executive Officer effective March 16, 2015 and, since that time, has served as our Chief Development Officer.

(2) Amounts reported in the Salary, Bonus and All Other Compensation columns have been converted to U.S. dollars from Israeli Shekels, or NIS, using the exchange rate on the date of payment.

(3) Represents discretionary bonuses paid to the named executive officers with respect to the year ended December 31, 2014.

(4) Amounts reflect the grant date fair value of option awards granted or modified in 2014 in accordance with the Financial Accounting Standards Board Accounting Standards Codification Topic 718, or ASC 718. Such grant date fair value does not take into account any estimated forfeitures related to service-vesting conditions. For information regarding assumptions underlying the valuation of equity awards, see Note 11 to our financial statements and the discussion under Management s Discussion and Analysis of Financial Condition and Results of Operations Critical Accounting Policies and Use of Estimates Stock-based Compensation included elsewhere in this prospectus. These amounts do not correspond to the actual value that may be recognized by the named executive officers upon vesting of applicable awards.

(5) The amount reported includes $260,743 attributable to the incremental fair value associated with the modification of three stock options held by Dr. Mamluk, in each case to reduce the per share exercise price of the stock option to $0.09 per share. The modified options cover an aggregate of 242,881 shares of common stock.

(6) The amount reported includes $45,437 attributable to the incremental fair value associated with the modification of four stock options held by Mr. Orlev, in each case to reduce the per share exercise price of the stock option to $0.09 per share. The modified options cover an aggregate of 41,720 shares of common stock.

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(7) The amount reported represents $15,945 in automobile expense reimbursement, $16,727 in company contributions to the severance plan and other fringe benefits.
(8) The amount reported represents $20,460 in automobile expense reimbursement, $12,264 in company contributions to the severance plan and other fringe benefits.

2014 Outstanding Equity Awards at Fiscal Year-End

The following table sets forth information concerning outstanding equity awards for each of our named executive officers as of December 31, 2014. All equity awards granted to our named executive officers were made pursuant to our 2008 Stock Incentive Plan, as amended, or the 2008 Plan.

Name	Vesting Start Date	Number of Securities Underlying Unexercised Options (#) Exercisable	Number of Securities Underlying Unexercised Options (#) Unexercisable	Option Exercise Price ($)	Option Expiration Date
Roni Mamluk, Ph.D.	10/16/2008(1)	9,556		0.09(4)	10/14/2018
	9/7/2011(2)	122,800	28,339	0.09(5)	9/4/2021
	9/12/2012(2)	46,229	35,957	0.09(5)	9/10/2022
	10/21/2014(3)	9,403	216,286	3.29	10/18/2024
Chaime Orlev	7/20/2010(2)	3,185		0.09(4)	7/17/2020
	9/7/2011(2)	15,439	3,563	0.09(5)	9/4/2021
	12/13/2011(2)	4,106	1,369	0.09(5)	12/10/2021
	9/12/2012(2)	7,908	6,150	0.09(5)	9/10/2022
	10/21/2014(3)	1,738	39,983	3.29	10/18/2024

(1) The shares underlying this stock option vested as follows: (i) 25% of the shares vested on the vesting start date, (ii) 25% of the shares vested on March 24, 2009 and (iii) the remaining 50% of the shares vested in equal monthly installments over the following two years.
(2) The shares underlying these stock options vest as follows: (i) 25% of the shares vested on the first anniversary of the vesting start date and (ii) the remaining 75% of the shares vest in equal quarterly installments over the following three years.
(3) The shares underlying these stock options vest in equal monthly installments over the four-year period following the vesting start date; provided, however, that 50% of the then-unvested shares shall vest upon approval by the FDA of an NDA for oral octreotide.
(4) On May 5, 2014, the board of directors approved a reduction in the per share exercise price of these stock options from $5.48 to $0.09.
(5) On May 5, 2014, the board of directors approved a reduction in the per share exercise price of these stock options from $1.92 to $0.09.

Employment Agreements with Our Named Executive Officers and Our Chief Executive Officer

Mark Leuchtenberger. On May 29, 2015, we entered into an amended and restated employment agreement with Mr. Leuchtenberger for the position of President and Chief Executive Officer. Mr. Leuchtenberger currently receives a base salary of $435,000, which is subject to periodic review and adjustment. Mr. Leuchtenberger is also eligible for an annual performance bonus targeted at 50% of his base salary. Mr. Leuchtenberger is eligible to participate in the

employee benefit plans generally available to full-time employees, subject to the terms of those plans. In connection with his employment, Mr. Leuchtenberger was granted an option to purchase 703,407 shares of our common stock on April 14, 2015, which was equal to 3% of our issued and outstanding common stock on the date of grant, subject to vesting over four years, with 25% of the shares underlying such option vesting on the one-year anniversary of his employment start date and the remaining 75% of the shares vesting in equal monthly installments over the following 36 months. In the event that Mr. Leuchtenberger s employment is terminated by us without cause (as defined in his employment agreement) or Mr. Leuchtenberger terminates his employment with us for good reason (as defined in his employment agreement), Mr. Leuchtenberger will be entitled to receive: (i) base salary continuation for 12 months following termination and (ii) continuation of group health plan benefits until the earlier of 12 months following the date of termination or the date he becomes eligible for health benefits through another employer or otherwise becomes ineligible for COBRA, with the cost of the premium for such benefits shared by Mr. Leuchtenberger and us in the same proportion as in effect on the date of termination. However, in the event that Mr. Leuchtenberger s employment is terminated by us without cause, or Mr. Leuchtenberger terminates his employment with us for good reason, in either case within 12 months following the occurrence of the first event constituting a change in control (as defined in his employment

agreement), in lieu of the severance payments and benefits described in the preceding sentence, Mr. Leuchtenberger will be entitled to receive: (i) base salary continuation for 18 months following termination, (ii) payment of his target bonus for the year in which the change in control occurs, (iii) continuation of group health plan benefits until the earlier of 18 months following the date of termination or the date he becomes eligible for health benefits through another employer or otherwise becomes ineligible for COBRA, with the cost of the premium for such benefits shared by Mr. Leuchtenberger and us in the same proportion as in effect on the date of termination, and (iv) full and immediate vesting and exercisability of the unvested shares underlying his new hire stock option. Receipt of the severance payments and benefits described above is conditioned upon Mr. Leuchtenberger entering into and not revoking a separation agreement with us, including a general release of claims, resigning all positions held with us and our affiliates and returning all company property. In addition, Mr. Leuchtenberger has entered into a Non-Competition, Non-Solicitation, Confidentiality and Assignment Agreement that contains, among other things, non-competition and non-solicitation provisions that apply during the term of Mr. Leuchtenberger s employment and for 12 months thereafter.

Roni Mamluk, Ph.D. On December 16, 2014, Dr. Mamluk entered into an employment agreement with our subsidiary Chiasma (Israel) Ltd., or the Israeli Subsidiary. Dr. Mamluk currently receives a base salary of $285,000 (which is payable in NIS at a conversion rate of $1.00 to 3.84 NIS) and is eligible for an annual performance bonus targeted at 30% of her base salary. Pursuant to the terms of her employment agreement, we furnish Dr. Mamluk with a cellular telephone and an automobile and pay expenses related to such automobile, including gas and insurance. In addition, on a monthly basis we have agreed to make the following contributions on behalf of Dr. Mamluk: (i) an amount equal to 8.33% of her salary towards severance pay, (ii) an amount equal to up to 6% of her salary towards a fund for life insurance and pension and (iii) an amount towards disability insurance equal to 2.5% of her salary. In addition, we pay, on a monthly basis, an amount equal to 7.5% of Dr. Mamluk s salary toward a study fund chosen by her. In the event that Dr. Mamluk s employment is terminated for cause (as defined in her employment agreement), she will not be entitled to the amounts accrued in the study fund. Pursuant to the terms of her employment agreement, in the event that Dr. Mamluk s employment is terminated due to her death or disability, she or her estate will be entitled to receive: (i) salary payments through the end of the month in which the termination occurs, (ii) any earned but unpaid bonus for the year prior to the year of termination, or the Prior Year Bonus, and (iii) a pro-rated bonus for the year of termination. If Dr. Mamluk resigns without good reason (as defined in her employment agreement) within 60 days following the earlier of (a) approval by the FDA of an NDA for oral octreotide or (b) September 16, 2016, subject to her execution of a release of claims, Dr. Mamluk will be entitled to: (i) full vesting of any outstanding stock options held by her, (ii) an amount equal to 12 months of her then-current salary, (iii) the Prior Year Bonus and (iv) any statutory severance amount. In the event that Dr. Mamluk s employment is terminated by us without cause or by her for good reason, provided she executes a release of claims, she will be entitled to (i) 1.5 times (or 0.75 times in the event that such termination occurs in connection with a bankruptcy, liquidation or other wind down of our company that is not a change in control) her then-current annual salary, (ii) the Prior Year Bonus and (iii) 1.5 times (or 0.75 times in the event that such termination occurs in connection with a bankruptcy, liquidation or other wind down of our company that is not a change in control) the bonus earned by Dr. Mamluk in the year of termination. In the event that such termination occurs within 12 months following a change in control (as defined in her employment agreement), Dr. Mamluk s target bonus will be used rather than her earned bonus for purposes of clause (iii) of the preceding sentence. Dr. Mamluk has also entered into a Confidentiality, Non-Competition, Non-Solicitation and Intellectual Property Assignment Agreement that contains, among other things, non-competition and non-solicitation provisions that apply during Dr. Malmuk s employment and for 12 months thereafter.

Mark J. Fitzpatrick. On May 8, 2015, we entered into an employment agreement with Mr. Fitzpatrick for the position of Chief Financial Officer. Mr. Fitzpatrick currently receives a base salary of $350,000, which is subject to periodic review and adjustment. Mr. Fitzpatrick is also eligible for an annual performance bonus targeted at 35% of his base salary. Mr. Fitzpatrick is eligible to participate in the employee benefit plans generally available to full-time

employees, subject to the terms of those plans. In connection with his employment, Mr. Fitzpatrick will receive a sign-on bonus of $25,000 no later than 30 days after his start date. In the event that Mr. Fitzpatrick s employment is

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terminated prior to the one-year anniversary of his start date for any reason other than (i) by us without cause (as defined in his employment agreement), (ii) death, (iii) disability (as defined in his employment agreement) or (iv) a change in control termination (as defined in his employment agreement), Mr. Fitzpatrick must repay the net after-tax amount of the sign-on bonus to us within 30 days of termination of his employment. In addition, on June 14, 2015, Mr. Fitzpatrick was granted an option to purchase a number of shares of our common stock on equal to 1.25% of our issued and outstanding common stock on the date of grant (calculated on an as-converted, fully-diluted basis), subject to vesting over four years, with 25% of the shares underlying such option vesting on the one-year anniversary of his employment start date and the remaining 75% of the shares vesting in equal monthly installments over the following 36 months. In the event that Mr. Fitzpatrick s employment is terminated by us without cause, he will be entitled to receive: (i) base salary continuation for 12 months following termination and (ii) continuation of group health plan benefits until the earlier of 12 months following the date of termination or the date he becomes eligible for health benefits through another employer or otherwise becomes ineligible for COBRA, with the cost of the premium for such benefits shared by Mr. Fitzpatrick and us in the same proportion as in effect on the date of termination. However, in the event that Mr. Fitzpatrick s employment is terminated by us without cause, or Mr. Fitzpatrick terminates his employment with us for good reason (as defined in his employment agreement), in either case within 12 months following the occurrence of the first event constituting a change in control (as defined in his employment agreement), in lieu of the severance payments and benefits described in the preceding sentence, Mr. Fitzpatrick will be entitled to receive: (i) base salary continuation for 12 months following termination, (ii) payment of his target bonus for the year in which the change in control occurs, (iii) continuation of group health plan benefits until the earlier of 12 months following the date of termination or the date he becomes eligible for health benefits through another employer or otherwise becomes ineligible for COBRA, with the cost of the premium for such benefits shared by Mr. Fitzpatrick and us in the same proportion as in effect on the date of termination, and (iv) full and immediate vesting and exercisability of the unvested shares underlying his new hire stock option. Receipt of the severance payments and benefits described above is conditioned upon Mr. Fitzpatrick entering into and not revoking a separation agreement with us, including a general release of claims, resigning all positions held with us and our affiliates and returning all company property. In addition, Mr. Fitzpatrick has entered into a Non-Competition, Non-Solicitation, Confidentiality and Assignment Agreement that contains, among other things, non-competition and non-solicitation provisions that apply during the term of Mr. Fitzpatrick s employment and for 12 months thereafter.

Chaime Orlev. On June 22, 2010, Mr. Orlev entered into an employment agreement with the Israeli Subsidiary, for the position of Director of Finance. Mr. Orlev currently receives a base salary of NIS 570,000 (equivalent to $146,875 based on a conversion rate of $1.00 to NIS 3.889). Pursuant to the terms of his employment agreement, Mr. Orlev is entitled to a company-paid automobile and we will pay, on a monthly basis: (i) an amount equal to 8.33% of Mr. Orlev s salary towards severance pay, (ii) an amount equal to 5% of his salary towards a fund for life insurance and pension and (iii) an amount towards disability insurance equal to the lower of (a) an amount that will provide Mr. Orlev 75% of his salary or (b) an amount equal to 2.5% of his salary. In addition, we pay, on a monthly basis, an amount equal to 7.5% of Mr. Orlev s salary toward a study fund chosen by him. In the event that Mr. Orlev s employment is terminated for cause (as defined in his employment agreement), he will not be entitled to the amounts accrued in the study fund. Our monthly contribution of an amount equal to 8.33% of Mr. Orlev s salary towards severance pay is in lieu of any employee severance that he may otherwise be entitled to receive. Pursuant to the terms of his employment agreement, either Mr. Orlev or the Israeli Subsidiary may terminate his employment upon 60 days prior written notice. Mr. Orlev has also entered into a Confidentiality, Non-Competition, Non-Solicitation and Intellectual Property Assignment Agreement that contains, among other things, non-competition and non-solicitation provisions that apply during Mr. Orlev s employment and for 12 months thereafter.

We believe the benefits provided to our executives located in Israel are reasonable and customary for similarly situated employees in Israel.

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2014 Director Compensation

In the year ended December 31, 2014, other than as set forth below, we did not pay any compensation, make any equity awards or non-equity awards to, or pay any other compensation to any of the non-employee members of our board of directors. We did not maintain any standard fee arrangements for the non-employee members of our board of directors for their service as a director in 2014.

Name	Option Awards ($)[1]	Total ($)
David Stack	240,953	240,953
Dror Brandwein		
Todd Foley		
Ansbert Gadicke, M.D.		
Bard Geesaman, M.D., Ph.D.		
Vincent Miles, Ph.D.		
Scott Minick		
John A. Scarlett, M.D.		

(1) Amounts reflect the grant date fair value of option awards granted in 2014 in accordance with ASC Topic 718. Such grant-date fair value does not take into account any estimated forfeitures related to service-vesting conditions. For information regarding assumptions underlying the valuation of equity awards, see Note 11 to our consolidated financial statements and the discussion under Management s Discussion and Analysis of Financial Condition and Results of Operations Critical Accounting Policies and Use of Estimates Stock-based Compensation included elsewhere in this prospectus. These amounts do not correspond to the actual value that may be recognized by the directors upon vesting.

As of December 31, 2014, Mr. Stack held an unexercised stock option covering 91,954 shares of our common stock. None of our other non-employee directors held unexercised or unvested equity awards as of such date.

Non-Employee Director Compensation Policy

Our board of directors has adopted a non-employee director compensation policy, effective as of the completion of this offering, that is designed to enable us to attract and retain, on a long-term basis, highly qualified non-employee directors. Under the policy, each director who is not an employee will be paid cash compensation from and after the completion of this offering, as set forth below:

	Annual Retainer
Board of Directors:	
All non-employee members	$ 35,000
Additional retainer for chair	25,000
Audit Committee:	
Members	7,500
Chair	15,000

Compensation Committee:	
Members	5,000
Chair	10,000
Nominating and Corporate Governance Committee:	
Members	4,000
Chair	8,000

In addition, each non-employee director will be granted a non-qualified stock option to purchase 20,000 shares of common stock on the date of such director s election or appointment to the board of directors, which will vest in equal annual installments over the three years following the grant date, subject to continued service as a director; provided that, if not already vested, such stock option shall vest and become fully exercisable on the date of the

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third annual meeting of stockholders following the grant date. On the date of each annual meeting of stockholders of our company, each continuing non-employee director who has served as a director for the previous six months will be granted a non-qualified stock option to purchase 10,000 shares of common stock, which will vest and become fully exercisable upon the earlier to occur of the first anniversary of the grant date or the date of the next annual meeting of stockholders following the date of grant, subject to continued service as a director through such date.

Compensation Risk Assessment

We believe that, although a portion of the compensation provided to our executive officers and other employees is performance-based, our executive compensation program does not encourage excessive or unnecessary risk taking. This is primarily due to the fact that our compensation programs are designed to encourage our executive officers and other employees to remain focused on both short-term and long-term strategic goals, in particular in connection with our pay-for-performance compensation philosophy. As a result, we do not believe that our compensation programs are reasonably likely to have a material adverse effect on us.

Employee Share Plans

The equity incentive plans described in this section are our 2003 Israeli Stock Option Plan, or the 2003 Plan, the 2008 Plan, our 2008 Stock Incentive Plan Sub-Plan for Participants in Israel, or the Israel Sub-Plan, the Chiasma, Inc. 2015 Stock Option and Incentive Plan, or the 2015 Plan and the Israeli Addendum to the 2015 Plan, or the Israeli Addendum, and the 2015 Employee Stock Purchase Plan, or the ESPP. Prior to this offering, we granted awards to eligible participants under the 2008 Plan and the Israel Sub-Plan. Following the closing of this offering, we expect to grant awards to eligible participants only under the 2015 Plan.

2003 Stock Incentive Plan

Our 2003 Plan was approved by our board of directors and stockholders on November 26, 2003. The 2003 Plan was most recently amended on November 14, 2006, with the approval of both our board of directors and our stockholders. Under the 2003 Plan, we have reserved for issuance an aggregate of 17,980 shares of our common stock. The number of shares of common stock reserved for issuance is subject to adjustment in the event of a stock split, combination or reclassification of shares, as well as any distribution of bonus shares.

The shares of common stock underlying options that are terminated, expire or are canceled prior to exercise or relinquishment in full are added back to the shares of common stock available for issuance under the 2003 Plan.

Our board of directors has acted as administrator of the 2003 Plan. The administrator has full power to designate, from among the individuals eligible for options, the individuals to whom options will be granted, and to determine the specific terms and conditions of each option, subject to the provisions of the 2003 Plan. Persons eligible to participate in the 2003 Plan are those employees, holders of control, as defined in the 1961 Israeli Income Tax Ordinance [New Version] 1961, or the Ordinance, consultants and other services providers to the company, as selected from time to time by the administrator in its discretion.

The 2003 Plan permits the granting of (1) options to purchase common stock to employees through a trustee pursuant to Section 102(b) of the Ordinance, (2) options to purchase common stock to employees not held in trust by a trustee pursuant to Section 102(c) of the Ordinance and (3) options to purchase common stock to grantees who are not employees and not held in trust by a trustee pursuant to Section 3(i) of the Ordinance. The per share option exercise price of each option will be determined by the administrator but may not be less than the par value of the shares of common stock. The term of each option will be fixed by the administrator and may not exceed ten years from the date

of grant. Unless otherwise determined by the administrator, each option will vest over four years with 25% vesting on the one-year anniversary of the grantee s start date and the remainder vesting in 36 equal monthly installments thereafter.

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The 2003 Plan provides that upon the occurrence of a merger transaction, as defined in the 2003 Plan, the acquiring or successor corporation may either assume or substitute outstanding options under the 2003 Plan. If the acquiring or successor corporation does not assume or substitute all of the outstanding options, then each grantee will have a period of 15 days, from the date designated by us in a written notice given to the grantee, to exercise the vested options. All options, whether vested or not, which are neither assumed or substituted nor exercised by the end of the 15-day period, will expire and terminate as of the date of the consummation of the merger transaction.

The administrator may prescribe, amend, modify, rescind or terminate the 2003 Plan at any time, subject to stockholder approval where such approval is required by applicable law. The administrator of the 2003 Plan may also amend, modify or cancel any outstanding option, provided that no amendment to an option may materially and adversely affect a grantee s rights without his or her consent.

The 2003 Plan provides that it will continue in effect until the earlier of (1) its termination by our board of directors or (2) the date on which all of the shares available for issuance under the 2003 Plan have been issued and all restrictions on these shares and agreements evidencing options granted under the 2003 Plan have lapsed. On May 6, 2008, the board of directors resolved that no further stock options or other equity based awards would be granted under the 2003 Plan.

2008 Stock Incentive Plan

Our 2008 Plan was approved by our board of directors on May 6, 2008 and was subsequently approved by our stockholders on May 12, 2008. The 2008 Plan was most recently amended in April 2015 with the approval of both our board of directors and our stockholders. Under the 2008 Plan, we have reserved for issuance an aggregate of 4,186,375 shares of our common stock. The number of shares of common stock reserved for issuance is subject to adjustment in the event of a stock split, stock dividend, recapitalization, combination of shares, reclassification of shares, spin-off or other similar change in our capitalization.

The shares of common stock underlying awards that are terminated, surrendered or canceled without having been fully exercised or are forfeited or repurchased or result in shares of common stock not being issued under the 2008 Plan are added back to the shares of common stock available for issuance under the 2008 Plan. In addition, shares of common stock tendered to us by a participant to exercise an award are added back to the shares available for grant under the 2008 Plan.

Our board of directors has acted as administrator of the 2008 Plan. The administrator has full power to select, from among the individuals eligible for awards, the individuals to whom awards will be granted, and to determine the specific terms and conditions of each award, subject to the provisions of the 2008 Plan. Persons eligible to participate in the 2008 Plan are those employees, officers and directors of, and consultants and advisors to, the company as selected from time to time by the administrator in its discretion.

The 2008 Plan permits the granting of (1) options to purchase common stock intended to qualify as incentive stock options under Section 422 of the Code and (2) options that do not so qualify. The per share option exercise price of each option will be determined by the administrator but may not be less than 100% of the fair market value of the common stock on the date of grant. The term of each option will be fixed by the administrator. The administrator will determine at what time or times each option may be exercised. In addition, the 2008 Plan permits the granting of restricted shares of common stock, restricted stock units and other stock-based awards.

The 2008 Plan provides that upon the occurrence of a reorganization event, as defined in the 2008 Plan, our board of directors may take one or more of the following actions as to some or all awards outstanding under the 2008 Plan:

(1) provide that outstanding awards shall be assumed or substituted by the acquiring or successor corporation,
(2) upon written notice to holders of outstanding awards, provide that unexercised awards will terminate immediately prior to the consummation of the reorganization event unless exercised by the participant

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(to the extent exercisable) within a specified period following the date of such notice, (3) provide that all awards will become exercisable, realizable or deliverable, or restrictions applicable to an award will lapse, in whole or in part, prior to or upon the reorganization event, (4) in the event of a reorganization event in which the holders of common stock will receive a cash payment for each share surrendered, make or provide for a per share cash payment to holders of awards in an amount equal to the difference between the per share cash consideration in the reorganization event and the per share exercise price of the outstanding award, (5) provide that, in connection with a liquidation or dissolution of the company, awards will convert into the right to receive liquidation proceeds or (6) any combination of the foregoing.

Upon the occurrence of a reorganization event other than a liquidation or dissolution of our company, our repurchase and other rights under each restricted stock award will inure to the benefit of our successor, and will apply to the cash, securities or other property which the common stock was converted into or exchanged for pursuant to the reorganization event. Upon the occurrence of a reorganization event involving the liquidation or dissolution of our company, except to the extent provided to the contrary in the instrument evidencing the restricted stock award or any other agreement between the holder of restricted stock and us, all restrictions and conditions on outstanding restricted stock awards will automatically be deemed terminated or satisfied.

The administrator may amend, suspend or terminate the 2008 Plan at any time, subject to stockholder approval where such approval is required by applicable law. The administrator of the 2008 Plan may also amend, modify or terminate any outstanding award, provided that no amendment to an award may materially and adversely affect a participant s rights without his or her consent.

Our board of directors has also adopted the Israel Sub-Plan to apply to grants made to employees, directors, consultants and advisors of the company or its parent or subsidiary entities who are subject to taxation by the Israeli Income Tax, or the Israeli Service Providers. The Israel Sub-Plan allows us to grant awards to the Israeli Service Providers under the 2008 Plan under similar terms to those in the 2008 Plan, and such awards may qualify for tax-favorable treatment pursuant to Section 102 of the Ordinance.

The 2008 Plan will terminate automatically upon the earlier of 10 years from the date on which the Plan was adopted by our board of directors or the date the Plan was approved by our stockholders. Our board of directors has determined not to make any further awards under the 2008 Plan following the closing of this offering.

2015 Stock Option and Incentive Plan

Our 2015 Plan was adopted by our board of directors in June 2015 and approved by our stockholders in June 2015 and became effective on July 15, 2015. The 2015 Plan will replace the 2008 Plan as our board of directors has determined not to make additional awards under the 2008 Plan following the closing of our initial public offering. The 2015 Plan allows the compensation committee to make equity-based and cash-based incentive awards to our officers, employees, directors and other key persons (including consultants).

We have initially reserved 2,200,000 shares of our common stock for the issuance of awards under the 2015 Plan, plus the shares of common stock remaining available for issuance under the 2008 Plan, collectively, the Initial Limit. The 2015 Plan provides that the number of shares reserved and available for issuance under the plan will automatically increase each January 1, beginning on January 1, 2016, by 4% of the outstanding number of shares of our common stock on the immediately preceding December 31 or such lesser number of shares as determined by our compensation committee, or the Annual Increase. The number of shares reserved under the 2015 Plan is subject to adjustment in the event of a stock split, stock dividend or other change in our capitalization.

The shares we issue under the 2015 Plan will be authorized but unissued shares or shares that we reacquire. The shares of common stock underlying any awards that are forfeited, cancelled, held back upon exercise or settlement of an award to satisfy the exercise price or tax withholding, reacquired by us prior to vesting, satisfied without the issuance of stock, expire or are otherwise terminated (other than by exercise) under the 2015 Plan and the 2008 Plan will be added back to the shares of common stock available for issuance under the 2015 Plan.

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Stock options and stock appreciation rights with respect to no more than 2,000,000 shares of common stock may be granted to any one individual in any one calendar year. The maximum number of shares that may be issued as incentive stock options may not exceed the Initial Limit cumulatively increased on January 1, 2016 and on each January 1 thereafter by the lesser of the Annual Increase or 1,500,000 shares. The value of all awards made under the 2015 Plan and all other cash compensation paid by us to any non-employee director in any calendar year shall not exceed $2,000,000.

The 2015 Plan will be administered by our compensation committee. Our compensation committee has full power to select, from among the individuals eligible for awards, the individuals to whom awards will be granted, to make any combination of awards to participants, and to determine the specific terms and conditions of each award, subject to the provisions of the 2015 Plan. Persons eligible to participate in the 2015 Plan will be those full or part-time officers, employees, non-employee directors and other key persons (including consultants) as selected from time to time by our compensation committee in its discretion.

The 2015 Plan permits the granting of both options to purchase common stock intended to qualify as incentive stock options under Section 422 of the Code and options that do not so qualify. The option exercise price of each option will be determined by our compensation committee but may not be less than 100% of the fair market value of our common stock on the date of grant. The term of each option will be fixed by our compensation committee and may not exceed 10 years from the date of grant. Our compensation committee will determine at what time or times each option may be exercised.

Our compensation committee may award stock appreciation rights subject to such conditions and restrictions as it may determine. Stock appreciation rights entitle the recipient to shares of common stock equal to the value of the appreciation in our stock price over the exercise price. The exercise price may not be less than 100% of the fair market value of our common stock on the date of grant. The term of each stock appreciation right will be fixed by our compensation committee and may not exceed 10 years from the date of grant. Our compensation committee will determine at what time or times each stock appreciation right may be exercised.

Our compensation committee may award restricted shares of common stock and restricted stock units to participants subject to such conditions and restrictions as it may determine. These conditions and restrictions may include the achievement of certain performance goals and/or continued employment with us through a specified vesting period. Our compensation committee may also grant shares of common stock that are free from any restrictions under the 2015 Plan. Unrestricted stock may be granted to participants in recognition of past services or for other valid consideration and may be issued in lieu of cash compensation due to such participant.

Our compensation committee may grant performance share awards to participants that entitle the recipient to receive awards of common stock upon the achievement of certain performance goals and such other conditions as our compensation committee shall determine. Our compensation committee may grant dividend equivalent rights to participants that entitle the recipient to receive credits for dividends that would be paid if the recipient had held a specified number of shares of common stock.

Our compensation committee may grant cash bonuses under the 2015 Plan to participants, subject to the achievement of certain performance goals.

Our compensation committee may grant awards of restricted stock, restricted stock units, performance share awards or cash-based awards under the 2015 Plan that are intended to qualify as performance-based compensation under Section 162(m) of the Code. Such awards will only vest or become payable upon the attainment of performance goals that are established by our compensation committee and related to one or more performance criteria. The performance

criteria that could be used with respect to any such awards include: cash flow (including, but not limited to, operating cash flow and free cash flow); sales or revenue; corporate revenue; earnings before interest, taxes, depreciation and amortization; net income (loss) (either before or after interest, taxes, depreciation and/or amortization); changes in the market price of our common stock; economic value-

added; development, clinical, regulatory or commercial milestones; acquisitions or strategic transactions, partnerships or joint ventures; operating income (loss); return on capital, assets, equity, or investment; stockholder returns; return on sales; gross or net profit levels; productivity; expense efficiency; margins; operating efficiency; customer satisfaction; working capital; earnings (loss) per share of our common stock; sales or market shares; number of customers; operating income and/or other strategic, financial or operational objectives, any of which may be measured either in absolute terms or as compared to any incremental increase or as compared to results of a peer group. From and after the time that we become subject to Section 162(m) of the Code, the maximum award that is intended to qualify as performance-based compensation under Section 162(m) of the Code that may be made to certain of our officers during any one calendar year period is 4,000,000 shares of common stock with respect to a share-based award and $6,000,000 with respect to a cash-based award.

The 2015 Plan provides that upon the effectiveness of a sale event, as defined in the 2015 Plan, an acquirer or successor entity may assume, continue or substitute for the outstanding awards under the 2015 Plan. To the extent that awards granted under the 2015 Plan are not assumed or continued or substituted by the successor entity, all options and stock appreciation rights that are not exercisable immediately prior to the effective time of the sale event shall become fully exercisable as of the effective time of the sale event, all other awards with time-based vesting, conditions or restrictions, shall become fully vested and nonforfeitable as of the effective time of the sale event and all awards with conditions and restrictions relating to the attainment of performance goals may become vested and nonforfeitable in the discretion of our compensation committee. Upon the effective time of the sale event, all outstanding awards granted under the 2015 Plan shall terminate. In the event of such termination, individuals holding options and stock appreciation rights will be permitted to exercise such options and stock appreciation rights (to the extent exercisable) prior to the sale event. In addition, in connection with the termination of outstanding awards upon a sale event, we may make or provide for a cash payment to participants holding vested and exercisable options and stock appreciation rights equal to the difference between the per share cash consideration payable to stockholders in the sale event and the exercise price of the options or stock appreciation rights.

Our board of directors may amend or discontinue the 2015 Plan and our compensation committee may amend or cancel outstanding awards for purposes of satisfying changes in law or any other lawful purpose, but no such action may adversely affect rights under an award without the holder s consent. Certain amendments to the 2015 Plan require the approval of our stockholders.

Our board of directors has also adopted the Israeli Addendum to the 2015 Plan to apply to grants made to Israeli Service Providers. The Israeli Addendum allows us to grant awards to the Israeli Service Providers under the 2015 Plan under similar terms to those in the 2015 Plan, and such awards may qualify for favorable tax treatment pursuant to Section 102 of the Ordinance.

No awards may be granted under the 2015 Plan after the date that is 10 years from the effective date of the 2015 Plan. No awards under the 2015 Plan have been made prior to the date hereof.

Employee Stock Purchase Plan

In June 2015, our board of directors and stockholders adopted and approved the ESPP. The ESPP is intended to qualify as an employee stock purchase plan within the meaning of Section 423 of the Code. The ESPP initially reserves and authorizes the issuance of up to a total of 260,000 shares of common stock to participating employees. The ESPP provides that the number of shares reserved and available for issuance will automatically increase each January 1, beginning on January 1, 2016, by the lesser of (i) 520,000 shares of common stock, (ii) 1% of the outstanding number of shares of our common stock on the immediately preceding December 31 or (iii) such lesser number of shares as determined by the ESPP administrator. The number of shares reserved under the ESPP is subject

to adjustment in the event of a stock split, stock dividend or other change in our capitalization.

All employees whose customary employment is for more than 20 hours per week are eligible to participate in the ESPP. However, any employee who owns 5% or more of the total combined voting power or value of all classes of stock is not eligible to purchase shares under the ESPP.

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We will make one or more offerings each year to our employees to purchase shares under the ESPP. Offerings will usually begin on each January 1 and July 1 and will continue for six-month periods, referred to as offering periods. Each eligible employee may elect to participate in any offering by submitting an enrollment form at least 15 days before the relevant offering date.

Each employee who is a participant in the ESPP may purchase shares by authorizing payroll deductions of up to 10% of his or her base compensation during an offering period. Unless the participating employee has previously withdrawn from the offering, his or her accumulated payroll deductions will be used to purchase shares on the last business day of the offering period at a price equal to 85% of the fair market value of the shares on the first business day or the last business day of the offering period, whichever is lower. Under applicable tax rules, an employee may purchase no more than $25,000 worth of shares of common stock, valued at the start of the purchase period, under the ESPP in any calendar year.

The accumulated payroll deductions of any employee who is not a participant on the last day of an offering period will be refunded. An employee s rights under the ESPP terminate upon voluntary withdrawal from the plan or when the employee ceases employment with us for any reason.

The ESPP may be terminated or amended by our board of directors at any time. An amendment that increases the number of shares of common stock authorized under the ESPP and certain other amendments require the approval of our stockholders.

Senior Executive Cash Incentive Bonus Plan

In June 2015, our board of directors adopted the Senior Executive Cash Incentive Bonus Plan, or the Bonus Plan. The Bonus Plan provides for cash bonus payments based upon the attainment of performance targets established by our compensation committee. The payment targets will be related to financial and operational measures or objectives with respect to our company, or Corporate Performance Goals, as well as individual performance objectives.

Our compensation committee may select Corporate Performance Goals from among the following: cash flow (including, but not limited to, operating cash flow and free cash flow); sales or revenue; corporate revenue; earnings before interest, taxes, depreciation and amortization; net income (loss) (either before or after interest, taxes, depreciation and/or amortization); changes in the market price of our common stock; economic value-added; development, clinical, regulatory or commercial milestones; acquisitions or strategic transactions, partnerships or joint ventures; operating income (loss); return on capital, assets, equity, or investment; stockholder returns; return on sales; gross or net profit levels; productivity; expense efficiency; margins; operating efficiency; customer satisfaction; working capital; earnings (loss) per share of our common stock; sales or market shares; number of customers; operating income and/or other strategic, financial or operational objectives, any of which may be measured in absolute terms, as compared to any incremental increase, in terms of growth, as compared to results of a peer group, against the market as a whole, compared to applicable market indices and/or measured on a pre-tax or post-tax basis.

Each executive officer who is selected to participate in the Bonus Plan will have a target bonus opportunity set for each performance period. The bonus formulas will be adopted in each performance period by the compensation committee and communicated to each executive. The Corporate Performance Goals will be measured at the end of each performance period after our financial reports have been published or such other appropriate time as the compensation committee determines. If the Corporate Performance Goals and individual performance objectives are met, payments will be made as soon as practicable following the end of each performance period. The Bonus Plan also permits the compensation committee to approve additional bonuses to executive officers in its sole discretion.

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401(k) Plan

Currently, we do not maintain any retirement plans for our employees in the United States but we intend to adopt a 401(k) retirement plan that is intended to qualify under Sections 401(a) and 501(a) of the Code in 2015.

Benefits to Israeli Employees

We are obligated to make pension and severance liability contributions for the benefit of all Israeli employees based on labor laws in Israel, subject to certain conditions. Our liability is provided for by regular deposits to funds administered by financial institutions and by an accrual for the amount of the liability which has not yet been deposited.

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CERTAIN RELATIONSHIPS AND RELATED PARTY TRANSACTIONS

Other than compensation arrangements, during our last three fiscal years, we have engaged in the following transactions with our directors and executive officers and holders of more than 5% of our voting securities and affiliates of our directors, executive officers and such 5% stockholders. We believe that all of the transactions described below were made on terms no less favorable to us than could have been obtained from unaffiliated third parties.

Sales and Purchases of Securities

Series C Financing

On April 17, 2012, we issued and sold to investors an aggregate of 3,038,331 shares of Series C Convertible Preferred Stock, or Series C Preferred Stock, at a price per share of $1.00, for aggregate cash consideration of $3,038,331, pursuant to a stock purchase agreement initially entered into with investors on June 24, 2011, as amended on April 17, 2012.

The following table summarizes the participation in the April 17, 2012 closing of the Series C Preferred Stock financing by any of our directors, executive officers, holders of more than 5% of our voting securities, or any member of the immediate family of the foregoing persons.

Name	Shares of Series C Preferred Stock
ARCH Venture Fund VI, L.P.(1)	381,334
Affiliates of MPM Capital(2)	1,644,446
7 Med Health Ventures LP(3)	500,001

(1) ARCH Venture Fund, VI, L.P. is a holder of more than 5% of our voting securities. Scott Minick, is a venture partner of ARCH Venture Partners, of which ARCH Venture Fund VI, L.P. is an affiliated fund, and is a member of our board of directors.
(2) Includes 1,041,379 shares of Series C Convertible Preferred Stock to MPM BioVentures IV-QP, L.P., 40,121 shares of Series C Convertible Preferred Stock to MPM BioVentures IV GmbH & Co., 29,612 shares of Series C Convertible Preferred Stock to MPM Asset Management Investors BV4 LLC and 533,334 shares of Series C Convertible Preferred Stock to MPM Bio IV NVS Strategic Fund, L.P. These entities collectively hold more than 5% of our voting securities. Bard Geesaman, David Stack, Todd Foley and Ansbert Gadicke are Managing Directors of MPM Asset Management LLC and are members of our board of directors.
(3) 7 Med Health Ventures LP is a holder of more than 5% of our voting securities.

Bridge Financing

On June 1, 2012, we entered into a Second Amendment to Series C Convertible Preferred Stock Purchase Agreement, pursuant to which we sold an aggregate of $3,038,335 in subordinated convertible promissory notes to investors, or the Bridge Financing. Pursuant to the promissory notes, interest accrued at a rate of 8% per annum on all amounts outstanding, and the loans matured on September 5, 2012. The convertible promissory notes were also subject to a subordination agreement. Amounts outstanding were converted into shares of Series D Convertible Preferred Stock, or

Series D Preferred Stock, on June 1, 2012 at the initial closing of the Series D Preferred Stock financing, further described below.

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The following table summarizes the participation in the Bridge Financing by any of our directors, executive officers, holders of more than 5% of our voting securities, or any member of the immediate family of the foregoing persons.

Name	Principal Amount of Convertible Promissory Notes
ARCH Venture Fund VI, L.P.(1)	$ 381,334
Affiliates of MPM Capital(2)	$ 1,644,449
7 Med Health Ventures L.P.(3)	$ 500,001

(1) ARCH Venture Fund, VI, L.P. is a holder of more than 5% of our voting securities. Scott Minick, is a venture partner of ARCH Venture Partners, of which ARCH Venture Fund VI, L.P. is an affiliated fund, and is a member of our board of directors.
(2) Includes $1,541,245 in principal to MPM BioVentures IV-QP, L.P., $59,378 in principal to MPM BioVentures IV GmbH & Co. Beteiligungs KG and $43,826 in principal to MPM Asset Management Investors BV4 LLC. These entities collectively hold more than 5% of our voting securities. Bard Geesaman, David Stack, Todd Foley and Ansbert Gadicke are Managing Directors of MPM Asset Management LLC and are members of our board of directors.
(3) 7 Med Health Ventures LP is a holder of more than 5% of our voting securities.

Series D Financing

On July 11, 2012, October 22, 2012 and March 28, 2013, we issued and sold to investors an aggregate of 38,504,439 shares of Series D Convertible Preferred Stock, or Series D Preferred Stock, along with warrants to purchase up to 1,698,066 shares of common stock, at a price per share of $1.00 for aggregate cash consideration of $35,466,104 and the conversion of certain convertible promissory notes, pursuant to a securities purchase agreement entered into with investors on July 11, 2012, as amended on March 28, 2013. The warrants have an exercise price of $0.09 per share of common stock.

The following table summarizes the participation in the Series D Preferred Stock financing by any of our directors, executive officers, holders of more than 5% of our voting securities, or any member of the immediate family of the foregoing persons.

Name	Shares of Series D Preferred Stock	Warrants to Purchase Common Stock
Abingworth Bioventures V LP(1)	15,000,000	410,642
ARCH Venture Fund VI, L.P.(2)	762,668	0
Affiliates of MPM Capital(3)	16,066,669	1,026,562
7 Med Health Ventures L.P.(4)	4,700,000	222,168

(1)

Abingworth Bioventures V LP is a holder of more than 5% of our voting securities. Vincent Miles, is a partner at Abingworth, of which Abingworth Bioventures V LP is an affiliated fund, and is a member of our board of directors. Dr. Miles has indicated to us his intention to resign from our board of directors upon the closing of this offering.

(2) ARCH Venture Fund VI, L.P. is a holder of more than 5% of our voting securities. Scott Minick, is a venture partner of ARCH Venture Partners, of which ARCH Venture Fund VI, L.P. is an affiliated fund, and is a member of our board of directors.

(3) Includes 14,058,587 shares of Series D Convertible Preferred Stock and warrants to purchase 962,136 shares of common stock to MPM BioVentures IV-QP, L.P., 541,646 shares of Series D Convertible Preferred Stock and warrants to purchase 37,068 shares of common stock to MPM BioVentures IV GmbH & Co. Beteiligungs KG, 399,767 shares of Series D Convertible Preferred Stock and warrants to purchase 27,358 shares of common stock to MPM Asset Management Investors, and 1,066,669 shares of Series D Convertible Preferred Stock to MPM Bio IV NVS Strategic Fund, L.P. These entities collectively hold more than 5% of our voting securities. Bard Geesaman, David Stack, Todd Foley and Ansbert Gadicke are Managing Directors of MPM Asset Management LLC and are members of our board of directors.

(4) 7 Med Health Ventures LP is a holder of more than 5% of our voting securities.

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Exchange of Previously Outstanding Preferred Stock

On March 28, 2013, and in connection with the execution of our license agreement with Roche and the receipt of upfront payment pursuant thereto, we initiated a redemption of all of our then-outstanding Series D Preferred Stock, Series C Preferred Stock, and Series B1 Convertible Preferred Stock, or Series B1 Preferred Stock and together with the Series D Preferred Stock and Series C Preferred Stock, the Original Preferred Stock, in exchange for an initial cash payment, shares of Series D Convertible Preferred Stock, Series C Convertible Preferred Stock and Series B1 Convertible Preferred Stock, or collectively, the Prime Stock, and rights to receive future contingent payments under the Roche agreement, which rights were terminated upon termination of the Roche agreement. The Prime Stock has substantially similar terms and was issued on a one-for-one basis for shares of the respective Original Preferred Stock. On March 29, 2013 and May 13, 2013, we completed the redemption.

The following table summarizes the participation in the redemption by any of our directors, officers, holders of more than 5% of our voting securities, or any member of the immediate family of the foregoing persons.

Name	Shares of Series B1 Convertible Preferred Stock Issued Upon Redemption of Series B1 Preferred Stock	Shares of Series C Convertible Preferred Stock Issued Upon Redemption of Series C Preferred Stock	Shares of Series D Convertible Preferred Stock Issued Upon Redemption of Series D Preferred Stock	Cash Payment Upon Redemption of All Shares
Abingworth Bioventures V LP(1)	0	0	15,000,000	$ 21,408,451
ARCH Venture Fund VI, L.P.(2)	468,684	5,697,615	762,668	$ 1,088,503
Affiliates of MPM Capital(3)	95,225	22,721,988	16,066,669	$ 22,930,833
Globeways Holdings Limited(4)	0	0	333,334	$ 475,744
7 Med Health Ventures LP(5)	112,665	6,946,314	4,700,000	$ 6,707,981

(1) Abingworth BioVentures V LP is a holder of more than 5% of our voting securities. Vincent Miles, is a partner at Abingworth, of which Abingworth Bioventures V LP is an affiliated fund, and is a member of our board of directors. Dr. Miles has indicated to us his intention to resign from our board of directors upon the closing of this offering.

(2) ARCH Venture Fund VI, L.P. is a holder of more than 5% of our voting securities. Scott Minick, is a venture partner of ARCH Venture Partners, of which ARCH Venture Fund VI, L.P. is an affiliated fund, and is a member of our board of directors.

(3) Includes 2,538 shares of Series B1 Convertible Preferred Stock, 384,295 shares of Series C Convertible Preferred Stock, 399,767 shares of Series D Convertible Preferred Stock issued to and a cash payment of $570,559 to MPM Asset Management Investors BV4 LLC; 3,438 shares of B1 Convertible Preferred Stock, 520,674 shares of Series C Convertible Preferred Stock, 541,646 shares of Series D Convertible Preferred issued to and a cash payment of $773,053 to MPM BioVentures IV GmbH & Co., Beteiligungs KG; 89,249 shares of Series B1 Convertible Preferred Stock, 13,514,544 shares of Series C Convertible Preferred Stock 14,058,587 shares of Series D Convertible Preferred Stock issued to and a cash payment of $20,064,838 to MPM BioVentures IV-QP, L.P.; and

8,302,475 shares of Series C Convertible Preferred Stock, 1,066,669 shares of Series D Convertible Preferred Stock issued to and a cash payment of $1,522,382 to MPM Bio IV NVS Strategic Fund, L.P. These entities collectively hold more than 5% of our voting securities. Bard Geesaman, David Stack, Todd Foley and Ansbert Gadicke are Managing Directors of MPM Asset Management LLC and are members of our board of directors.

(4) Globeways Holdings Limited is an affiliate of F2 Capital I 2014 Limited. F2 Capital I 2014 Limited is a holder of more than 5% of our voting securities.

(5) 7 Med Health Ventures L.P. is a holder of more than 5% of our voting securities.

Series E Financing

On December 16, 2014 and February 26, 2015, we issued and sold to investors an aggregate of 69,722,786 shares of Series E Convertible Preferred Stock, or Series E Preferred Stock, along with warrants to purchase up to 1,908,738 shares of common stock, at a price per share of $1.00, for aggregate consideration of $69,722,786. The warrants have an exercise price of $9.13 per share of common stock.

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The following table summarizes the participation in the Series E Preferred Stock financing by any of our directors, executive officers, holders of more than 5% of our voting securities, or any member of the immediate family of the foregoing persons.

Name	Shares of Series E Preferred Stock	Warrants to Purchase Common Stock
Abingworth Bioventures V LP(1)	4,000,000	109,504
ARCH Venture Fund VI, L.P.(2)	4,000,000	109,504
Affiliates of Fidelity Securities(3)	19,948,328	546,107
Affiliates of MPM Capital(4)	13,000,000	355,889
Affiliates of F2 Capital I 2014 Limited(5)	13,584,458	371,891
Affiliates of 7 Med Health Ventures L.P.(6)	5,500,000	150,568
Minick Family Trust(7)	250,000	6,844

(1) Abingworth Bioventures V LP is a holder of more than 5% of our voting securities. Vincent Miles, is a partner at Abingworth, of which Abingworth Bioventures V LP is an affiliated fund, and is a member of our board of directors. Dr. Miles has indicated to us his intention to resign from our board of directors upon the closing of this offering.

(2) ARCH Venture Fund VI, L.P. is a holder of more than 5% of our voting securities. Scott Minick, is a venture partner of ARCH Venture Partners, of which ARCH Venture Fund VI, L.P. is an affiliated fund, and is a member of our board of directors.

(3) Includes 13,978,670 shares of Series E Convertible Preferred Stock and a warrant to purchase 382,683 shares of common stock to Fidelity Select Portfolios: Biotechnology Portfolio, 2,023,348 shares of Series E Convertible Preferred Stock and a warrant to purchase 23,784 shares of Common Stock to Fidelity Securities Fund: Fidelity Blue Chip Growth Fund, 2,969,660 shares of Series E Convertible Preferred Stock and a warrant to purchase 81,298 shares of common stock to Fidelity Advisor Series VII: Fidelity Advisor Biotechnology Fund, 868,819 shares of Series E Convertible Preferred Stock and a warrant to purchase 55,391 shares of common stock to Fidelity Securities Fund: Fidelity Series Blue Chip Growth Fund, and 107,831 shares of Series E Convertible Preferred Stock and a warrant to purchase 2,951 shares of common stock to Pyramis Lifecycle Blue Chip Growth Comingled Pool. Fidelity Select Portfolios: Biotechnology Portfolio is a holder of more than 5% of our voting securities.

(4) Includes 8,575,756 shares of Series E Preferred Stock and a warrant to purchase 234,722 shares of common stock to MPM BioVentures IV-QP, L.P., 330,387 shares of Series E Preferred Stock and a warrant to purchase 9,044 shares of common stock to MPM BioVentures IV GmbH & Co. Beteiligungs KG, 243,857 shares of Series E Preferred Stock and a warrant to purchase 6,675 shares of common stock to MPM Asset Management Investors BV4 LLC and 3,850,000 shares of Series E Preferred Stock and a warrant to purchase 105,398 to MPM Bio IV NVS Strategic Fund, L.P. These entities collectively hold more than 5% of our voting securities. Bard Geesaman, David Stack, Todd Foley and Ansbert Gadicke are Managing Directors of MPM Asset Management LLC and are members of our board of directors.

(5) Includes 13,500,000 shares of Series E Convertible Preferred Stock and a warrant to purchase 369,579 shares of common stock to F2 Capital I 2014 Limited and 84,458 shares of Series E Convertible Preferred Stock and a warrant to purchase 2,312 shares of common stock to Globeways Holdings Limited. F2 Capital I 2014 Limited is a holder of more than 5% of our voting securities. Globeways Holdings Limited is an affiliate of F2 Capital I 2014 Limited.

(6) Includes 3,000,000 shares of Series E Convertible Preferred Stock and a warrant to purchase 82,128 shares of common stock to 7 Med Health Ventures L.P. and 2,500,000 shares of Series E Convertible Preferred Stock and a warrant to purchase 68,440 shares of common stock to Ruth Wertheimer. 7 Med Health Ventures L.P. is a holder of more than 5% of our voting securities. Ruth Wertheimer is an affiliate of 7 Med Health Ventures L.P.

(7) Scott Minick, an affiliate of the Minick Family Trust, is a member of our board of directors.

Indemnification Agreements

We intend to enter into agreements to indemnify our directors and executive officers to the maximum extent allowed under Delaware law. Subject to the provisions of these agreements, these agreements will, among other things, indemnify these individuals for certain expenses (including attorneys fees), judgments, fines and settlement amounts reasonably incurred by such person in any action or proceeding, including any action by or in our right, on account of any services undertaken by such person on behalf of us or that person s status as a member of our board of directors.

Agreements with our Stockholders

In connection with our preferred stock financings, we entered into an investor rights agreement, a right of first refusal and co-sale agreement, and stockholders voting agreement, in each case, with the purchasers of our preferred stock and certain holders of our common stock. Our amended and restated right of first refusal and co-

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sale agreement, or ROFR Agreement, provides for rights of first refusal, co-sale and drag along rights in respect of sales by certain holders of our capital stock. Our amended and restated stockholders voting agreement, or Voting Agreement, contains provisions with respect to the election of our board of directors and its composition.

Our amended and restated investor rights agreement, or Investor Rights Agreement, provides certain holders of our preferred stock with a participation right to purchase their *pro rata* share of new securities that we may propose to sell and issue, subject to certain exceptions. The Investor Rights Agreement further provides certain holders of our capital stock with the right to demand that we file a registration statement, subject to certain limitations, and to request that their shares be covered by a registration statement that we are otherwise filing. See Description of Capital Stock Registration Rights for additional information regarding such registration rights.

The rights under each of the ROFR Agreement, Voting Agreement and Investor Rights Agreement will terminate upon the closing of this offering, other than certain registration rights for certain holders of our preferred stock as provided for in the Investor Rights Agreement and described below in Description of Capital Stock Registration Rights.

Services and Consulting Agreement

In August 2014, we entered into a services agreement with MPM Asset Management LLC, or MPM, and Gary Patou, M.D., our Senior Medical Advisor. Pursuant to the terms of the services agreement, Dr. Patou agreed to devote 50% of his business time to us. The services agreement specifically tasks him with filing drug applications, clinical development and product development. Pursuant to the services agreement, we have agreed to pay MPM a services fee of $26,600 per month. In addition, we have agreed to pay Dr. Patou a bonus in the event of a change of control transaction. We also granted Dr. Patou options to purchase 122,605 shares of our common stock. The services agreement may be terminated by either MPM or Dr. Patou upon 30 days notice or by us immediately upon written notice. Dr. Patou is a Managing Director at MPM Capital, affiliates of which hold more than 5% of our outstanding stock.

On December 1, 2014, we entered into a consulting agreement with Waterloo Holdings Limited, an affiliate of F2 Capital, affiliates of which hold more than 5% of our outstanding stock. Pursuant to the terms of the consulting agreement, Morana-Jovan Embiricos, Ph.D., as a representative of Waterloo Holdings Limited, agreed to provide us with certain financial and consulting services as requested, up to a maximum of commitment of 20 hours per month. For so long as Dr. Embiricos is providing consulting services to us, we will pay Waterloo Holdings Limited $62,500 a month, with such number to increase to $83,333 per month from and after the date of this offering. The term of the consulting agreement shall expire upon the earlier to occur of (i) December 31, 2016 and (ii) termination of the consulting agreement with 10 days notice and the approval of at least 75% of our board of directors.

Participation in this Offering

Certain of our existing stockholders, including certain affiliates of our directors, are purchasing an aggregate of 1,681,250 shares of our common stock in this offering at the initial public offering price.

Related Person Transactions Policy

Our board of directors reviews and approves transactions with directors, officers and holders of 5% or more of our voting securities and their affiliates, or each, a related party. Prior to this offering, the material facts as to the related party s relationship or interest in the transaction are disclosed to our board of directors prior to their consideration of such transaction, and the transaction is not considered approved by our board of directors unless a majority of the

directors who are not interested in the transaction approve the transaction. Further, when stockholders are entitled to vote on a transaction with a related party, the material facts of the related party s

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relationship or interest in the transaction are disclosed to the stockholders, who must approve the transaction in good faith.

We have adopted a written related party transactions policy that such transactions must be approved by our audit committee or another independent body of our board of directors.

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PRINCIPAL STOCKHOLDERS

The following table sets forth information relating to the beneficial ownership of our common stock as of June 30, 2015 by: each person, or group of affiliated persons, known by us to beneficially own more than 5% of our outstanding shares of common stock; each of our directors; each of our named executive officers; and all directors and executive officers as a group.

The number of shares beneficially owned by each entity, person, director or executive officer is determined in accordance with the rules of the SEC, and the information is not necessarily indicative of beneficial ownership for any other purpose. Under such rules, beneficial ownership includes any shares over which the individual has sole or shared voting power or investment power as well as any shares that the individual has the right to acquire within 60 days of June 30, 2015 through the exercise of any stock options or other rights. Except as otherwise indicated, and subject to applicable community property laws, the persons named in the table have sole voting and investment power with respect to all shares of common stock held by that person.

The percentage of shares beneficially owned before the offering is computed on the basis of 16,609,642 shares of our common stock outstanding as of June 30, 2015, which reflects the assumed conversion of all 149,792,472 of our outstanding shares of preferred stock into an aggregate of 16,403,011 shares of common stock. The percentage of shares beneficially owned after the offering is computed on the basis of 22,974,642 shares of our common stock outstanding as of June 30, 2015, which reflects the assumed conversion of all 149,792,472 shares of our outstanding shares of preferred stock into an aggregate of 16,403,011 shares of common stock and 6,365,000 shares of our common stock sold in the offering. Certain of our existing stockholders, including certain affiliates of our directors are purchasing an aggregate of 1,681,250 shares of our common stock in this offering at the initial public offering price. The information set forth in the table below does not reflect any purchase of any shares in this offering by such parties.

Shares of our common stock that a person has the right to acquire within 60 days of June 30, 2015 are deemed outstanding for purposes of computing the percentage ownership of the person holding such rights, but are not deemed outstanding for purposes of computing the percentage ownership of any other person, except with respect to the percentage ownership of all directors and executive officers as a group. Unless otherwise indicated below, the address for each beneficial owner listed is c/o Chiasma, Inc., 60 Wells Avenue, Suite 102, Newton, MA 02459.

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Name and address of beneficial owner	Number of shares beneficially owned	Percentage of shares beneficially owned: Before offering	Percentage of shares beneficially owned: After offering
5% or greater stockholders:			
Affiliates of MPM Capital(1)	7,118,747	39.4%	29.2%
Affiliates of Fidelity Securities(2)	2,730,547	15.9	11.6
Abingworth Bioventures V LP(3)	2,600,741	15.2	11.1
Affiliates of 7 Med Health Ventures LP(4)	2,262,680	13.3	9.7
Affiliates of F2 Capital(5)	1,895,959	11.2	8.1
ARCH Venture Fund VI, L.P.(6)	1,306,280	7.8	5.7
Directors and executive officers:			
Mark Leuchtenberger		*	*
Roni Mamluk, Ph.D.(7)	287,130	1.7	1.2
Mark J. Fitzpatrick		*	*
Chaime Orlev (8)	49,303	*	*
David Stack(1)(9)	23,297	*	*
Dror Brandwein(10)		*	*
Todd Foley(1)		*	*
Ansbert Gadicke(1)		*	*
Bard Geesaman, M.D., Ph.D.(1)		*	*
Vincent Miles, Ph.D.(10)		*	*
Scott Minick(11)	96,751	*	*
John Scarlett, M.D.(12)	61,322	*	*
All executive officers and directors as a group (12 persons)(13)	517,803	3.1	2.2

* Represents beneficial ownership of less than one percent of our outstanding common stock.

(1) Consists of (i) 277 shares of common stock issuable upon conversion of the Series B1 Preferred Stock, 42,083 shares of common stock issuable upon conversion of the Series C Preferred Stock, 43,776 shares of common stock issuable upon conversion of the Series D Preferred Stock, 26,704 shares of common stock issuable upon conversion of the Series E Preferred Stock and warrants to purchase 35,492 shares of common stock exercisable within 60 days of June 30, 2015, in each case held by MPM Asset Management Investors BV4, LLC, (ii) 376 shares of common stock issuable upon conversion of the Series B1 Preferred Stock, 57,016 shares of common stock issuable upon conversion of the Series C Preferred Stock, 59,313 shares of common stock issuable upon conversion of the Series D Preferred Stock, 36,179 shares of common stock issuable upon conversion of the Series E Preferred Stock and warrants to purchase 48,089 shares of common stock exercisable within 60 days of June 30, 2015, in each case held by MPM BioVentures IV GmbH & Co. Beteiligungs KG, (iii) 9,773 shares of common stock issuable upon conversion of the Series B1 Preferred Stock, 1,479,910 shares of common stock issuable upon conversion of the Series C Preferred Stock, 1,539,486 shares of common stock issuable upon conversion of the Series D Preferred Stock, 939,089 shares of common stock issuable upon conversion of the Series E Preferred Stock and warrants to purchase 1,248,224 shares of common stock exercisable within 60 days of June 30, 2015, in each case held by MPM BioVentures IV-QP, L.P. and (iv) 909,162 shares of common stock issuable upon conversion of the Series C Preferred Stock, 116,806 shares of common stock issuable upon conversion of the

Series D Preferred Stock, 421,594 shares of common stock issuable upon conversion of the Series E Preferred Stock and warrants to purchase 105,398 shares of common stock exercisable within 60 days of June 30, 2015, in each case held by MPM Bio IV NVS Strategic Fund, L.P. MPM BioVentures IV LLC is the Managing Member of MPM BioVentures IV GP LLC, which is the General Partner of MPM BioVentures IV-QP, LP and MPM Bio IV NVS Strategic Fund, L.P. and the Managing Limited Partner of MPM BioVentures IV GmbH & Co. Beteiligungs KG. MPM BioVentures IV LLC is the Manager of MPM Asset Management Investors BV4 LLC. MPM BioVentures IV LLC is the Managing Member of MPM BioVentures IV GP LLC, which is the General Partner of MPM BioVentures IV-QP, LP and MPM Bio IV NVS Strategic Fund, L.P. and the Managing Limited Partner of MPM BioVentures IV GmbH & Co. Beteiligungs KG. MPM BioVentures IV LLC is the Manager of MPM Asset Management Investors

BV4 LLC. David Stack, Todd Foley, Ansbert Gadicke and Bard Geesaman, each of whom is a member of our board of directors, are Managing Directors of MPM Asset Management LLC, which is the Management Company of MPM BioVentures IV LLC. Todd Foley, Ansbert Gadicke Luke Evnin, Jim Scopa and Vaughn Kailian are the members of MPM BioVentures IV LLC. Investment and voting decisions with respect to the shares held by MPM Asset Management Investors BV4, LLC, MPM BioVentures IV GmbH & Co. Beteiligungs KG, MPM BioVentures IV-QP, L.P. and MPM Bio IV NVS Strategic Fund, L.P. are made by the members of MPM BioVentures IV LLC. MPM s address is 450 Kendall Street, Cambridge, MA 02142.

(2) Consists of (i) 1,530,734 shares of common stock issuable upon conversion of the Series E Preferred Stock and warrants to purchase 382,683 shares of common stock exercisable within 60 days of June 30, 2015, in each case held by Fidelity Select Portfolios: Biotechnology Portfolio, (ii) 325,192 shares of common stock issuable upon conversion of Series E Preferred Stock and warrants to purchase 81,298 shares of common stock exercisable within 60 days of June 30, 2015, in each case held by Fidelity Advisor Series VII: Fidelity Advisor Biotechnology Fund, (iii) 11,808 shares of common stock issuable upon conversion of the Series E Preferred Stock and warrants to purchase 2,951 shares of common stock exercisable within 60 days of June 30, 2015, in each case held by Pyramis Lifecycle Blue Chip Growth Commingled Pool, (iv) 95,140 shares of common stock issuable upon conversion of the Series E Preferred Stock and warrants to purchase 23,784 shares of common stock exercisable within 60 days of June 30, 2015, in each case held by Fidelity Securities Fund: Fidelity Securities Blue Chip Growth Fund and (v) 221,566 shares of common stock issuable upon conversion of the Series E Preferred Stock and warrants to purchase 55,391 shares of common stock exercisable within 60 days of June 30, 2015, in each case held by Fidelity Securities Fund: Fidelity Blue Chip Growth Fund. These entities are managed by direct or indirect subsidiaries of FMR LLC. Edward C. Johnson 3d is a Director and the Chairman of FMR LLC and Abigail P. Johnson is a Director, the Vice Chairman and the President of FMR LLC. Members of the family of Edward C. Johnson 3d, including Abigail P. Johnson, are the predominant owners, directly or through trusts, of Series B voting common shares of FMR LLC, representing 49% of the voting power of FMR LLC. The Johnson family group and all other Series B stockholders have entered into a stockholders voting agreement under which all Series B voting common shares will be voted in accordance with the majority vote of Series B voting common shares. Accordingly, through their ownership of voting common shares and the execution of the stockholders voting agreement, members of the Johnson family may be deemed, under the Investment Company Act of 1940, to form a controlling group with respect to FMR LLC. Neither FMR LLC nor Edward C. Johnson 3d nor Abigail P. Johnson has the sole power to vote or direct the voting of the shares owned directly by the various investment companies registered under the Investment Company Act, or the Fidelity Funds, advised by Fidelity Management & Research Company, a wholly owned subsidiary of FMR LLC, which power resides with the Fidelity Funds Boards of Trustees. Fidelity Management & Research Company carries out the voting of the shares under written guidelines established by the Fidelity Funds Boards of Trustees. The address of entities and individuals affiliated with Fidelity Select Portfolios: Biotechnology Portfolio, Pyramis Lifecycle Blue Chip Growth Commingled Pool, Fidelity Securities Fund: Fidelity Securities Blue Chip Growth Fund and Fidelity Securities Fund: Fidelity Blue Chip Growth Fund is Brown Brothers Harriman & Co., 525 Washington Blvd., 15th Floor, Jersey City, NJ 07310, Attn: Michael Lerman and entities and individuals affiliated with Fidelity Advisor Series VII: Fidelity Advisor Biotechnology Fund is State Street Bank & Trust, PO Box 5756, Boston, MA 02206, Attn: Bangle & Co fbo Fidelity Advisor Series VII: Fidelity Advisor Biotechnology Fund.

(3) Consists of 1,642,575 shares of common stock issuable upon conversion of the Series D Preferred Stock, 438,020 shares of common stock issuable upon conversion of the Series E Preferred Stock and warrants to purchase 520,146 shares of common stock exercisable within 60 days of June 30, 2015. Abingworth LLP is the manager of Abingworth Bioventures V, LP and may be deemed to beneficially own the shares held by Abingworth Bioventures V, LP. An investment committee, comprised of Joseph Anderson, Michael F. Bigham, Stephen W. Bunting, Timothy J. Haines and Genghis Lloyd-Harris, approves investment and voting decisions by a majority vote, and no individual member has the sole control or voting power over the shares held by Abingworth Bioventures V, LP. Each of Abingworth LLP, Joseph Anderson, Michael F. Bigham, Stephen W. Bunting,

Timothy J. Haines and Genghis Lloyd-Harris disclaims the beneficial ownership of such shares, except to the extent of its or his pecuniary interest therein. The address of Abingworth Bioventures V, LP is 38 Jermyn Street, London SW1Y 6DN, United Kingdom.

(4) Consists of (i) 12,337 shares of common stock issuable upon conversion of the Series B1 Preferred Stock, 760,656 shares of common stock issuable upon conversion of the Series C Preferred Stock, 514,674 shares of common stock issuable upon conversion of the Series D Preferred Stock, 328,515 shares of common stock issuable upon conversion of the Series E Preferred Stock and warrants to purchase 304,296 shares of common stock exercisable within 60 days of June 30, 2015, in each case held by 7 Med Health Ventures LP and (ii) 273,762 shares of common stock issuable upon conversion of the Series E Preferred Stock and warrants to purchase 68,440 shares of common stock exercisable within 60 days of June 30, 2015, in each case held by Ruth Wertheimer. 7 Med Ltd., an Israeli company, is the general partner of 7 Med Health Ventures LP. Ruth Wertheimer owns 100% of the membership interests of 7 Med Ltd. The address for all entities and individuals affiliated with 7 Med Health Ventures LP is 16B Shenkar Street, P.O.B. 12327, Herzliya Pituach, 46733 Israel.

(5) Consists of (i) 1,478,318 shares of common stock issuable upon conversion of the Series E Preferred Stock and warrants to purchase 369,579 shares of common stock exercisable within 60 days of June 30, 2015, in each case held by F2 Capital I 2014 Limited, and (ii) 36,501 shares of common stock issuable upon conversion of the Series D Preferred Stock, 9,249 shares of common stock issuable upon conversion of the Series E Preferred Stock and warrants to purchase 2,312 shares of common stock exercisable within 60 days of June 30, 2015, in each case held by Globeways Holdings Limited. Globeways Holdings Limited is a member of F2 Capital 1 2014 Limited and has sole power to vote upon the acquisition, holding and disposal of all shares and warrants held by F2 Capital 1 2014 Limited. LJSJ Skye Trustees Ltd. has the sole power to vote upon the acquisition, holding and disposal of all shares and warrants held by Globeways Holdings Limited. The directors of LJSJ Skye Trustees Ltd. are Mark Vale, Robert James, Stanley Burton and Paul John Quirk. The address of LJSJ Skye Trustees Ltd. is Commerce House, 1 Bowring Road, Ramsey, Isle of Man IM8 2LQ, British Isles.

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(6) Consists of 51,323 shares of common stock issuable upon conversion of the Series B1 Preferred Stock, 623,917 shares of common stock issuable upon conversion of the Series C Preferred Stock, 83,516 shares of common stock issuable upon conversion of the Series D Preferred Stock, 438,020 shares of common stock issuable upon conversion of the Series E Preferred Stock and warrants to purchase 109,504 shares of common stock exercisable within 60 days of June 30, 2015. ARCH Venture Partners VI, L.P. is the sole general partner of ARCH Venture Fund VI, L.P. ARCH Venture Partners VI, L.P., as the sole general partner of ARCH Venture Fund VI, L.P. may be deemed to beneficially own certain of the shares held of record by ARCH Venture Fund VI, L.P. ARCH Venture Partners VI, LLC disclaims beneficial ownership of all shares held of record of ARCH Venture Fund VI, L.P. in which it does not have an actual pecuniary interest. Keith Crandell, Clinton Bybee and Robert Nelson are the managing directors of ARCH Venture Partners VI, LLC, and may be deemed to beneficially own certain of the shares held of record by ARCH Venture Fund VI, L.P. The managing directors disclaim beneficial ownership of all shares held of record by ARCH Venture Fund VI, L.P. in which they do not have an actual pecuniary interest. The address for all entities and individuals affiliated with ARCH Venture Fund VI, L.P. is 8725 W. Higging Road, Suite 290, Chicago, IL 60631.

(7) Consists of options to purchase 287,130 shares of common stock presently exercisable or exercisable within sixty (60) days of June 30, 2015.

(8) Consists of options to purchase 49,303 shares of common stock presently exercisable or exercisable within sixty (60) days of June 30, 2015.

(9) Consists of options to purchase 23,297 shares of common stock presently exercisable or exercisable within sixty (60) days of June 30, 2015.

(10) Each of Dr. Miles and Mr. Brandwein has indicated his intention to resign from our board of directors upon the closing of this offering.

(11) Consists of (i) 1,209 shares of common stock issuable upon conversion of the Series B1 Preferred Stock and 61,322 shares of common stock, of which 56,212 shares are subject to our right of repurchase as of June 30, 2015, in each case held by Scott Minick and (ii) 27,376 shares of common stock issuable upon conversion of the Series E Preferred Stock and warrants to purchase 6,844 shares of common stock presently exercisable or exercisable within 60 days of June 30, 2015, in each case held by Minick Family Trust. Mr. Minick is a trustee of the Minick Family Trust.

(12) Consists of 61,322 shares of common stock, of which 56,212 shares are subject to our right of repurchase as of June 30, 2015.

(13) Consists of 1,209 shares of common stock issuable upon conversion of the Series B1 Preferred Stock, 27,376 shares of common stock issuable upon conversion of the Series E Preferred Stock, 122,644 shares of common stock, of which 112,424 shares are subject to our right of repurchase as of June 30, 2015, options to purchase 359,730 shares of common stock presently exercisable or exercisable within 60 days of June 30, 2015 and warrants to purchase 6,844 shares of common stock presently exercisable or exercisable within 60 days of June 30, 2015.

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DESCRIPTION OF CAPITAL STOCK

The following descriptions are summaries of the material terms of our amended and restated certificate of incorporation and amended and restated bylaws, which will be effective upon consummation of this offering. The descriptions of the common stock and preferred stock give effect to changes to our capital structure that will occur immediately prior to the closing of this offering. We refer in this section to our amended and restated certificate of incorporation as our certificate of incorporation, and we refer to our amended and restated bylaws as our bylaws.

General

Upon completion of this offering, our authorized capital stock will consist of 125,000,000 shares of common stock, par value $0.01 per share, and 5,000,000 shares of preferred stock, par value $0.01 per share, all of which shares of preferred stock will be undesignated.

As of June 30, 2015, 16,609,642 shares of our common stock were outstanding and held by 51 stockholders of record. This amount assumes the conversion of all outstanding shares of our preferred stock into common stock, which will occur immediately prior to the consummation of this offering. In addition, as of June 30, 2015, we had outstanding options to purchase 3,632,210 shares of our common stock, at a weighted average exercise price of $4.56 per share, 874,516 of which were exercisable and outstanding warrants to purchase 3,624,012 shares of our common stock, at a weighted average exercise price of $4.85 per share.

Common Stock

The holders of our common stock are entitled to one vote for each share held on all matters submitted to a vote of the stockholders. The holders of our common stock do not have any cumulative voting rights. Holders of our common stock are entitled to receive ratably any dividends declared by the board of directors out of funds legally available for that purpose, subject to any preferential dividend rights of any outstanding preferred stock. Our common stock has no preemptive rights, conversion rights or other subscription rights or redemption or sinking fund provisions.

In the event of our liquidation, dissolution or winding up, holders of our common stock will be entitled to share ratably in all assets remaining after payment of all debts and other liabilities and any liquidation preference of any outstanding preferred stock. The shares to be issued by us in this offering will be, when issued and paid for, validly issued, fully paid and non-assessable.

Preferred Stock

Immediately prior to the consummation of this offering, all outstanding shares of our preferred stock will be converted into shares of our common stock. Immediately prior to the consummation of this offering, our amended and restated certificate of incorporation will be amended and restated to delete all references to such shares of preferred stock. Upon the consummation of this offering, our board of directors will have the authority, without further action by our stockholders, to issue up to 5,000,000 shares of preferred stock in one or more series and to fix the rights, preferences, privileges and restrictions thereof. These rights, preferences and privileges could include dividend rights, conversion rights, voting rights, terms of redemption, liquidation preferences, sinking fund terms and the number of shares constituting, or the designation of, such series, any or all of which may be greater than the rights of common stock. The issuance of our preferred stock could adversely affect the voting power of holders of common stock and the likelihood that such holders will receive dividend payments and payments upon our liquidation. In addition, the issuance of preferred stock could have the effect of delaying, deferring or preventing a change in control of our company or other corporate action. Immediately after consummation of this offering, no shares of preferred stock will

be outstanding, and we have no present plans to issue any shares of preferred stock.

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Registration Rights

Upon the closing of this offering, the holders of our registrable shares, as described in the Investor Rights Agreement, are entitled to rights with respect to the registration of these shares under the Securities Act as hereinafter described. These rights are provided under the terms of the Investor Rights Agreement, and include demand registration rights, short-form registration rights and piggyback registration rights. All fees, costs and expenses of underwritten registrations will be borne by us and all selling expenses, including underwriting discounts and selling commissions, will be borne by the holders of the shares being registered.

Demand Registration Rights

Upon the closing of this offering, certain holders of shares of our common stock, including shares issuable upon the conversion of preferred stock or their permitted transferees, are entitled to demand registration rights. Under the terms of the Investor Rights Agreement, we will be required, upon the written request of holders of at least 25% of the shares of our common stock issued upon conversion of our Series E Preferred Stock upon the consummation of this offering, to use our best efforts to effect the registration of our common shares issued upon conversion of our preferred stock upon consummation of this offering, subject to certain exceptions. We are required to effect only two registrations pursuant to this provision of the Investor Rights Agreement. A demand for registration may not be made until 180 days after the closing of this offering. An aggregate of 16,543,995 shares of common stock and 3,624,012 shares of our common stock issuable upon the exercise of outstanding warrants are entitled to these demand registration rights.

Form S-3 Registration Rights

Upon the closing of this offering, certain holders of shares of our common stock issued upon the conversion of our preferred stock or their permitted transferees are also entitled to short form registration rights. If we are eligible to file a registration statement on Form S-3, upon the written request of certain holders of our common stock issued upon conversion of our preferred stock upon consummation of this offering to register shares with an anticipated aggregate offering price of at least $3,000,000, we will be required to use our best efforts to effect a registration of such shares, subject to certain exceptions. An aggregate of 16,543,995 shares of common stock and 3,624,012 shares of our common stock issuable upon the exercise of outstanding warrants are entitled to these Form S-3 registration rights.

Piggyback Registration Rights

Upon the closing of this offering, certain holders of shares of our common stock issued upon the conversion of our preferred stock or their permitted transferees are entitled to piggyback registration rights. If we propose to register any of our securities, either for our own account or for the account of other security holders, the holders of these shares are entitled to include their shares in the registration, and if such holders exercise their right to be included in such registration, we will b required to use our best efforts to include them in the registration. Subject to certain exceptions, the managing underwriter may limit the number of shares included in the underwritten offering if it concludes that marketing factors require such a limitation. An aggregate of 16,544,027 shares of common stock and 3,624,012 shares of our common stock issuable upon the exercise of outstanding warrants are entitled to these piggyback registration rights.

Indemnification

Our Investor Rights Agreement contains customary cross-indemnification provisions, under which we are obligated to indemnify holders of registrable securities in the event of material misstatements or omissions in the registration

statement attributable to us, and they are obligated to indemnify us for material misstatements or omissions attributable to them.

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Expiration of Registration Rights

The registration rights granted under the Investor Rights Agreement will terminate on the earliest of (i) the fifth anniversary of the closing of this offering, (ii) the date on which no stockholder party to the Investor Rights Agreement holds any Registrable Shares (as defined therein) or (iii) a Company Sale (as defined therein).

Anti-Takeover Effects of Our Certificate of Incorporation and Our Bylaws

Our certificate of incorporation and bylaws will contain certain provisions that are intended to enhance the likelihood of continuity and stability in the composition of the board of directors and which may have the effect of delaying, deferring or preventing a future takeover or change in control of the company unless such takeover or change in control is approved by the board of directors.

These provisions include:

Classified Board. Our certificate of incorporation will provide that our board of directors will be divided into three classes of directors, with the classes as nearly equal in number as possible. As a result, approximately one-third of our board of directors will be elected each year. The classification of directors will have the effect of making it more difficult for stockholders to change the composition of our board. Our certificate of incorporation will also provide that, subject to any rights of holders of preferred stock to elect additional directors under specified circumstances, the number of directors will be fixed exclusively pursuant to a resolution adopted by our board of directors. Upon completion of this offering, we expect that our board of directors will have seven members.

Action by Written Consent; Special Meetings of Stockholders. Our certificate of incorporation will provide that stockholder action can be taken only at an annual or special meeting of stockholders and cannot be taken by written consent in lieu of a meeting. Our certificate of incorporation and the bylaws will also provide that, except as otherwise required by law, special meetings of the stockholders can be called only by or at the direction of the board of directors pursuant to a resolution adopted by a majority of the total number of directors. Stockholders will not be permitted to call a special meeting or to require the board of directors to call a special meeting.

Removal of Directors. Our certificate of incorporation will provide that our directors may be removed only for cause by the affirmative vote of at least 75% of the votes that all our stockholders would be entitled to cast in an annual election of directors, voting together as a single class, at a meeting of the stockholders called for that purpose. This requirement of a supermajority vote to remove directors could enable a minority of our stockholders to prevent a change in the composition of our board.

Advance Notice Procedures. Our bylaws will establish an advance notice procedure for stockholder proposals to be brought before an annual meeting of our stockholders, including proposed nominations of persons for election to the board of directors. Stockholders at an annual meeting will only be able to consider proposals or nominations specified in the notice of meeting or brought before the meeting by or at the direction of the board of directors or by a stockholder who was a stockholder of record on the record date for the meeting, who is entitled to vote at the meeting and who has given our Secretary timely written notice, in proper form, of the stockholder s intention to bring that business before the meeting. Although the bylaws will not give the board of directors the power to approve or disapprove stockholder nominations of candidates or proposals regarding other business to be conducted at a special or annual meeting, the bylaws may have the effect of precluding the conduct of certain business at a meeting if the proper procedures are not followed or may discourage or deter a potential acquirer from conducting a solicitation of proxies to elect its own slate of directors or otherwise attempting to obtain control of the company.

Super Majority Approval Requirements. The Delaware General Corporation Law generally provides that the affirmative vote of a majority of the shares entitled to vote on any matter is required to amend a corporation s certificate of incorporation or bylaws, unless either a corporation s certificate of incorporation or bylaws requires

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a greater percentage. A majority vote of our board of directors or the affirmative vote of holders of at least 75% of the total votes of the outstanding shares of our capital stock entitled to vote with respect thereto, voting together as a single class, will be required to amend, alter, change or repeal the bylaws. In addition, the affirmative vote of the holders of at least 75% of the total votes of the outstanding shares of our capital stock entitled to vote with respect thereto, voting together as a single class, will be required to amend, alter, change or repeal, or to adopt any provisions inconsistent with, any of the provisions in our certificate of incorporation relating to amendments to our certificate of incorporation and bylaws and as described under Action by Written Consent; Special Meetings of Stockholders , Classified Board and Removal of Directors above. This requirement of a supermajority vote to approve amendments to our bylaws and certificate of incorporation could enable a minority of our stockholders to exercise veto power over any such amendments.

Authorized but Unissued Shares. Our authorized but unissued shares of common stock and preferred stock will be available for future issuance without stockholder approval. These additional shares may be utilized for a variety of corporate purposes, including future public offerings to raise additional capital and corporate acquisitions. The existence of authorized but unissued shares of common stock and preferred stock could render more difficult or discourage an attempt to obtain control of a majority of our common stock by means of a proxy contest, tender offer, merger or otherwise.

Exclusive Forum. Our certificate of incorporation will provide that, subject to limited exceptions, the state or federal courts located in the State of Delaware will be the sole and exclusive forum for (i) any derivative action or proceeding brought on our behalf, (ii) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers or other employees to us or our stockholders, (iii) any action asserting a claim against us arising pursuant to any provision of the Delaware General Corporation Law, our certificate of incorporation or our bylaws, or (iv) any other action asserting a claim against us that is governed by the internal affairs doctrine. Any person or entity purchasing or otherwise acquiring any interest in shares of our capital stock shall be deemed to have notice of and to have consented to the provisions of our certificate of incorporation described above. Although we believe these provisions benefit us by providing increased consistency in the application of Delaware law for the specified types of actions and proceedings, the provisions may have the effect of discouraging lawsuits against our directors and officers. The enforceability of similar choice of forum provisions in other companies certificates of incorporation has been challenged in legal proceedings, and it is possible that, in connection with one or more actions or proceedings described above, a court could find the choice of forum provisions contained in our certificate of incorporation to be inapplicable or unenforceable.

Section 203 of the Delaware General Corporation Law

Upon completion of this offering, we will be subject to the provisions of Section 203 of the Delaware General Corporation Law. In general, Section 203 prohibits a publicly-held Delaware corporation from engaging in a business combination with an interested stockholder for a three-year period following the time that this stockholder becomes an interested stockholder, unless the business combination is approved in a prescribed manner. A business combination includes, among other things, a merger, asset or stock sale or other transaction resulting in a financial benefit to the interested stockholder. An interested stockholder is a person who, together with affiliates and associates, owns, or did own within three years prior to the determination of interested stockholder status, 15% or more of the corporation s voting stock.

Under Section 203, a business combination between a corporation and an interested stockholder is prohibited unless it satisfies one of the following conditions: before the stockholder became interested, the board of directors approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder; upon consummation of the transaction which resulted in the stockholder becoming an interested

stockholder, the interested stockholder owned at least 75% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the voting stock outstanding, shares owned by persons who are directors and also officers, and employee stock plans, in some instances; or at or after the time the stockholder became interested, the business combination was approved by

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the board of directors of the corporation and authorized at an annual or special meeting of the stockholders by the affirmative vote of at least two-thirds of the outstanding voting stock which is not owned by the interested stockholder.

A Delaware corporation may opt out of these provisions with an express provision in its original certificate of incorporation or an express provision in its certificate of incorporation or bylaws resulting from a stockholders amendment approved by at least a majority of the outstanding voting shares. We have not opted out of these provisions. As a result, mergers or other takeover or change in control attempts of us may be discouraged or prevented.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is American Stock Transfer & Trust Company, LLC. The transfer agent and registrar s address is 59 Maiden Lane, New York, NY 10038, and its telephone number is (212) 936-5100.

Listing

Our common stock has been approved for listing on The NASDAQ Global Select Market under the symbol CHMA .

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SHARES ELIGIBLE FOR FUTURE SALE

Prior to this offering, there has been no public market for our common stock. Future sales of our common stock, including shares issued upon the exercise of outstanding options and warrants, in the public market after this offering, or the perception that those sales may occur, could cause the prevailing market price for our common stock to fall or impair our ability to raise equity capital at a time and price we deem appropriate. As described below, only a limited number of shares of our common stock will be available for sale in the public market for a period of several months after completion of this offering due to contractual and legal restrictions on resale described below.

Based on the number of shares of our common stock outstanding as of June 30, 2015, upon the closing of this offering and assuming (1) the conversion of our outstanding preferred stock into common stock, (2) no exercise of the underwriters option to purchase additional shares of common stock, and (3) no exercise of outstanding options and warrants, we would have had outstanding an aggregate of approximately 22,974,642 shares of common stock. Of these shares, all of the shares of common stock to be sold in this offering, and any shares sold upon exercise of the underwriters option to purchase additional shares, will be freely tradable in the public market without restriction or further registration under the Securities Act, unless the shares are held by any of our affiliates as such term is defined in Rule 144 of the Securities Act.

Rule 144

In general, a person who has beneficially owned restricted stock for at least six months would be entitled to sell their securities provided that (i) such person is not deemed to have been one of our affiliates at the time of, or at any time during the 90 days preceding, a sale and (ii) we are subject to the Securities Exchange Act of 1934, as amended, or the Exchange Act, periodic reporting requirements for at least 90 days before the sale. Persons who have beneficially owned restricted shares for at least six months but who are our affiliates at the time of, or any time during the 90 days preceding, a sale, would be subject to additional restrictions, by which such person would be entitled to sell within any three-month period only a number of securities that does not exceed the greater of either of the following:

- 1% of the number of shares then outstanding, which will equal approximately 229,746 shares immediately after this offering assuming no exercise of the underwriters option to purchase additional shares, based on the number of shares outstanding as of June 30, 2015; or
- the average weekly trading volume of our common stock on The NASDAQ Global Select Market during the four calendar weeks preceding the filing of a notice on Form 144 with respect to the sale.

Provided, in each case, that we are subject to the Exchange Act periodic reporting requirements for at least 90 days before the sale. Such sales both by affiliates and by non-affiliates must also comply with the manner of sale, current public information and notice provisions of Rule 144.

Rule 701

Rule 701 under the Securities Act, as in effect on the date of this prospectus, permits resales of shares in reliance upon Rule 144 but without compliance with certain restrictions of Rule 144, including the holding period requirement. Most of our employees, executive officers or directors who purchased shares under a written compensatory plan or contract may be entitled to rely on the resale provisions of Rule 701, but all holders of Rule 701 shares are required to wait until 90 days after the date of this prospectus before selling their shares. However, substantially all Rule 701 shares

are subject to lock-up agreements as described below in the section titled Underwriting included elsewhere in this prospectus and will become eligible for sale upon the expiration of the restrictions set forth in those agreements.

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Lock-up Agreements

All of our directors and executive officers and certain holders of our shares, who collectively held 16,374,307 shares of common stock as of June 30, 2015, have signed a lock-up agreement which prevents them from selling any of our common stock or any securities convertible into or exercisable or exchangeable for common stock for a period of not less than 180 days from the date of this prospectus, subject to certain exceptions, without the prior written consent of Barclays Capital Inc. and Cowen and Company, LLC, as representatives of the underwriters. The representatives may in their sole discretion and at any time without notice release some or all of the shares subject to lock-up agreements prior to the expiration of the 180-day period. When determining whether or not to release shares from the lock-up agreements, Barclays Capital Inc. and Cowen and Company, LLC will consider, among other factors, the stockholder s reasons for requesting the release, the number of shares for which the release is being requested and market conditions at the time.

Registration Rights

Upon completion of this offering, the holders of 16,544,027 shares of common stock or their transferees will be entitled to various rights with respect to registration of these shares under the Securities Act. Registration of these shares under the Securities Act would result in these shares becoming fully tradable without restriction under the Securities Act immediately upon the effectiveness of the registration. See the section titled Description of Capital Stock Registration Rights for additional information.

Stock Option Plans

We intend to file one or more registration statements on Form S-8 under the Securities Act to register our shares issued or reserved for issuance under our stock option plans. The first such registration statement is expected to be filed soon after the date of this prospectus and will automatically become effective upon filing with the Securities and Exchange Commission. Accordingly, shares registered under such registration statement will be available for sale in the open market, unless such shares are subject to vesting restrictions with us or the lock-up restrictions described above. As of June 30, 2015, we estimate that such registration statement on Form S-8 will cover approximately 6,234,493 shares.

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MATERIAL UNITED STATES FEDERAL INCOME TAX CONSIDERATIONS

FOR NON-U.S. HOLDERS

The following is a general discussion of the material U.S. federal income and estate tax considerations applicable to non-U.S. holders (as defined below) with respect to their ownership and disposition of shares of our common stock issued pursuant to this offering. For purposes of this discussion, a non-U.S. holder means a beneficial owner of our common stock that is not a United States person or a partnership for U.S. federal income tax purposes. A United States person is any of the following:

- an individual citizen or resident (for U.S. federal income tax purposes) of the United States;
- a corporation (or other entity treated as a corporation for U.S. federal income tax purposes) created or organized under the laws of the United States, any state thereof or the District of Columbia;
- an estate, the income of which is subject to U.S. federal income tax regardless of its source; or
- a trust (1) whose administration is subject to the primary supervision of a U.S. court and which has one or more United States persons who have the authority to control all substantial decisions of the trust, or (2) that has a valid election in effect under applicable Treasury regulations to be treated as a United States person for U.S. federal income tax purposes.

This discussion does not address the tax treatment of partnerships or other entities that are pass-through entities for U.S. federal income tax purposes or persons that hold their common stock through partnerships or other pass-through entities. A partner in a partnership or other pass-through entity that will hold our common stock should consult his, her or its own tax advisor regarding the tax consequences of acquiring, holding and disposing of our common stock through a partnership or other pass-through entity, as applicable.

An individual may be treated as a resident instead of a nonresident of the United States in any calendar year for U.S. federal income tax purposes if the individual was present in the United States for at least 31 days in that calendar year and for an aggregate of at least 183 days during the three-year period ending with the current calendar year. For purposes of this calculation, all of the days present in the current year, one-third of the days present in the immediately preceding year and one-sixth of the days present in the second preceding year are counted, subject to certain exceptions not discussed herein. The tax treatment of U.S. citizens and residents (including individuals who meet the foregoing substantial presence test) who hold shares of our common stock is not discussed in this summary.

This discussion is based on current provisions of the U.S. Internal Revenue Code of 1986, as amended, which we refer to as the Code, existing and proposed U.S. Treasury Regulations promulgated thereunder, current administrative rulings and judicial decisions, all as in effect as of the date of this prospectus, all of which are subject to change or to differing interpretation, possibly with retroactive effect. Any change could alter the tax consequences to non-U.S. holders described in this prospectus. There can be no assurance that the Internal Revenue Service, which we refer to as the IRS, will not challenge one or more of the tax consequences described herein. We assume in this discussion that a non-U.S. holder holds shares of our common stock as a capital asset, generally property held for investment.

This discussion does not address all aspects of U.S. federal income and estate taxation that may be relevant to a particular non-U.S. holder in light of that non-U.S. holder s individual circumstances nor does it address any aspects of U.S. state, local or non-U.S. taxes, the alternative minimum tax, or gift tax.

This discussion also does not consider any specific facts or circumstances that may apply to a non-U.S. holder and does not address the special tax rules applicable to particular non-U.S. holders, including without limitation:

insurance companies;

tax-exempt organizations;

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financial institutions;

brokers or dealers in securities or currencies;

pension plans;

controlled foreign corporations;

passive foreign investment companies;

persons that have a functional currency other than the U.S. dollar;

owners deemed to sell our common stock under the constructive sale provisions of the Code;

corporations that accumulate earnings to avoid U.S. federal income tax;

owners in special situations, such as those who have elected to mark securities to market, or those that hold our common stock as part of a straddle, hedge, conversion transaction, synthetic security or other integrated investment; and

certain U.S. expatriates.

This discussion is for general information only and is not tax advice. Accordingly, all prospective non-U.S. holders of our common stock should consult their own tax advisors with respect to the U.S. federal, state, local and non-U.S. tax consequences of the purchase, ownership and disposition of our common stock.

Distributions on Our Common Stock

Distributions, if any, on our common stock generally will constitute dividends for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. If a distribution exceeds our current and accumulated earnings and profits, the excess will be allocated ratably among each share of common stock with respect to which the distribution is paid and treated as a tax-free return of the non-U.S. holder s investment, up to such holder s adjusted tax basis in the common stock. A holder s adjusted tax basis in a share of our common stock is generally the purchase price of such share, reduced by the amount of any such tax-free returns of capital. Any remaining excess will be treated as capital gain, subject to the tax treatment described below in Gain on sale, exchange or other disposition of our common stock. Any such distributions will also be subject to the discussion below under the section titled Withholding and Information Reporting Requirements FATCA.

Dividends paid to a non-U.S. holder generally will be subject to withholding of U.S. federal income tax at a 30% rate or such lower rate as may be specified by an applicable income tax treaty between the United States and such holder s country of residence.

Dividends that are treated as effectively connected with a trade or business conducted by a non-U.S. holder within the United States and, if an applicable income tax treaty so provides, that are attributable to a permanent establishment or a fixed base maintained by the non-U.S. holder within the United States, are generally exempt from the 30% withholding tax if the non-U.S. holder satisfies applicable certification and disclosure requirements, including delivery of a properly executed IRS Form W-8ECI. However, such U.S. effectively connected income, net of specified deductions and credits, is taxed at the same graduated U.S. federal income tax rates applicable to United States persons. Any U.S. effectively connected income received by a non-U.S. holder that is a corporation may also, under certain circumstances, be subject to an additional branch profits tax at a 30% rate or such lower rate as may be specified by an applicable income tax treaty between the United States and such holder s country of residence.

A non-U.S. holder of our common stock who claims the benefit of an applicable income tax treaty between the United States and such holder s country of residence generally will be required to (i) provide a properly executed IRS Form W-8BEN or W-8BEN-E (or successor form) and certify under penalties of perjury that such holder is

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not a United States person and is eligible for treaty benefits, or (ii) if our common stock is held through certain foreign intermediaries, satisfy applicable certification and other requirements. Special certification and other requirements apply to certain non-U.S. holders that act as intermediaries (including partnerships). Non-U.S. holders are urged to consult their tax advisors regarding their entitlement to benefits under a relevant income tax treaty.

A non-U.S. holder that is eligible for a reduced rate of U.S. withholding tax under an income tax treaty may obtain a refund or credit of any excess amounts withheld by timely filing a U.S. tax return with the IRS.

Gain on Sale, Exchange or Other Disposition of Our Common Stock

Subject to the discussion below regarding backup withholding and FATCA, in general, a non-U.S. holder will not be subject to any U.S. federal income tax on any gain realized upon such holder s sale, exchange or other disposition of shares of our common stock unless:

the gain is effectively connected with the non-U.S. holder s conduct of a U.S. trade or business and, if an applicable income tax treaty so provides, is attributable to a permanent establishment or a fixed-base maintained by such non-U.S. holder in the United States, in which case the non-U.S. holder generally will be taxed on a net income basis at the graduated U.S. federal income tax rates applicable to United States persons and, if the non-U.S. holder is a foreign corporation, the branch profits tax described above in Distributions on Our Common Stock also may apply;

the non-U.S. holder is a nonresident alien individual who is present in the United States for 183 days or more in the taxable year of the disposition and certain other conditions are met, in which case the non-U.S. holder will be subject to U.S. federal income tax at a rate of 30% (or such lower rate as may be specified by an applicable income tax treaty between the United States and such holder s country of residence) on the net gain derived from the disposition, which may be offset by certain U.S. source capital losses (not including any capital loss carryovers) of the non-U.S. holder, if any (even though the individual is not considered a resident of the United States), provided that the non-U.S. holder has timely filed U.S. federal income tax returns with respect to such disposition and capital losses; or

we are, or have been, at any time during the five-year period preceding such disposition (or the non-U.S. holder s holding period, if shorter) a U.S. real property holding corporation, unless our common stock is regularly traded on an established securities market and the non-U.S. holder holds no more than 5% of our outstanding common stock, actually or constructively, during the shorter of the 5-year period ending on the date of the disposition or the period that the non-U.S. holder held our common stock. If we are determined to be a U.S. real property holding corporation and the foregoing exception does not apply, then a purchaser may withhold 10% of the proceeds payable to a non-U.S. holder from a sale of our common stock and the non-U.S. holder generally will be taxed on its net gain derived from the disposition at the graduated U.S. federal income tax rates applicable to United States persons. Generally, a corporation is a U.S. real property holding corporation only if the fair market value of its U.S. real property interests equals or exceeds 50% of the sum of the fair market value of its worldwide real property interests plus its other assets used or held for use in a trade or business. Although there can be no assurance, we do not believe that we are, or have been, a U.S. real property holding corporation, or that we are likely to become one in the future. No assurance can be provided that our common stock will be regularly traded on an established securities market for purposes of

the rules described above.

Backup Withholding and Information Reporting

We must report annually to the IRS and to each non-U.S. holder the gross amount of the distributions on our common stock paid to such holder and the tax withheld, if any, with respect to such distributions. Non-U.S. holders may have to comply with specific certification procedures to establish that the holder is not a United States person (as defined in the Code) in order to avoid backup withholding at the applicable rate with respect to

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dividends on our common stock. Dividends paid to non-U.S. holders subject to withholding of U.S. federal income tax, as described above in Distributions on Our Common Stock, generally will be exempt from U.S. backup withholding.

Information reporting and backup withholding will generally apply to the proceeds of a disposition of our common stock by a non-U.S. holder effected by or through the U.S. office of any broker, U.S. or foreign, unless the holder certifies its status as a non-U.S. holder (usually on IRS Form W-8BEN or W-8BEN-E) and satisfies certain other requirements, or otherwise establishes an exemption. Generally, information reporting and backup withholding will not apply to a payment of disposition proceeds to a non-U.S. holder where the transaction is effected outside the United States through a non-U.S. office of a broker. However, for information reporting purposes, dispositions effected through a non-U.S. office of a broker with substantial U.S. ownership or operations generally will be treated in a manner similar to dispositions effected through a U.S. office of a broker. Non-U.S. holders should consult their own tax advisors regarding the application of the information reporting and backup withholding rules to them.

Copies of information returns may be made available to the tax authorities of the country in which the non-U.S. holder resides or is incorporated under the provisions of a specific treaty or agreement.

Backup withholding is not an additional tax. Any amounts withheld under the backup withholding rules from a payment to a non-U.S. holder can be refunded or credited against the non-U.S. holder s U.S. federal income tax liability, if any, provided that an appropriate claim is filed with the IRS in a timely manner.

Withholding and Information Reporting Requirements FATCA

The Foreign Account Tax Compliance Act, or FATCA, generally imposes a U.S. federal withholding tax at a rate of 30% on payments of dividends on, or gross proceeds from the sale or other disposition of, our common stock paid to a foreign entity unless (i) if the foreign entity is a foreign financial institution, such foreign entity undertakes certain due diligence, reporting, withholding, and certification obligations, (ii) if the foreign entity is not a foreign financial institution, such foreign entity identifies certain of its U.S. investors, if any, or (iii) the foreign entity is otherwise exempt under FATCA. Under applicable U.S. Treasury regulations, withholding under FATCA currently applies to payments of dividends on our common stock, and will apply to payments of gross proceeds from a sale or other disposition of our common stock made after December 31, 2016. Under certain circumstances, a non-U.S. holder may be eligible for refunds or credits of the tax. An intergovernmental agreement between the United States and an applicable foreign country may modify the requirements described in this paragraph. Non-U.S. holders should consult their own tax advisors regarding the possible implications of this legislation on their investment in our common stock and the entities through which they hold our common stock.

United States Federal Estate Tax

Shares of our common stock that are owned or treated as owned at the time of death by an individual who is not a citizen or resident of the United States, as specifically defined for U.S. federal estate tax purposes, are considered U.S. situs assets and will be included in the individual s gross estate for U.S. federal estate tax purposes. Such shares, therefore, may be subject to U.S. federal estate tax, unless an applicable estate tax or other treaty provides otherwise.

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UNDERWRITING

Barclays Capital Inc. and Cowen and Company, LLC are acting as the representatives of the underwriters and the joint book-running managers of this offering. Under the terms of an underwriting agreement, each of the underwriters named below has severally agreed to purchase from us the respective number of shares of common stock shown opposite its name below:

Underwriters	Number of Shares
Barclays Capital Inc.	2,546,000
Cowen and Company, LLC	2,100,450
William Blair & Company, L.L.C.	1,082,050
Oppenheimer & Co. Inc.	636,500
Total	6,365,000

The underwriting agreement provides that the underwriters obligation to purchase shares of common stock depends on the satisfaction of the conditions contained in the underwriting agreement, including:

- the obligation to purchase all of the shares of common stock offered hereby (other than those shares of common stock covered by their option to purchase additional shares as described below), if any of the shares are purchased;
- the representations and warranties made by us to the underwriters are true;
- there is no material change in our business or the financial markets; and
- we deliver customary closing documents to the underwriters.

The underwriters have informed us that they do not expect to sell more than 5% of the common stock in the aggregate to accounts over which they exercise discretionary authority.

Commissions and Expenses

The following table summarizes the underwriting discounts and commissions we will pay to the underwriters. These amounts are shown assuming both no exercise and full exercise of the underwriters option to purchase additional shares. The underwriting fee is the difference between the initial price to the public and the amount the underwriters pay to us for the shares.

	No Exercise	Full Exercise

Per Share	$ 1.12	$ 1.12
Total	$ 7,128,800	$ 8,198,120

Certain of our existing stockholders, including certain affiliates of our directors, are purchasing an aggregate of 1,681,250 shares of our common stock in this offering at the initial public offering price. Such purchases will be made on the same terms as shares that are sold to the public generally and not pursuant to any pre-existing contractual rights or obligations. Such purchases did not affect the underwriters commitment to purchase the common shares offered by us.

The representatives have advised us that the underwriters propose to offer the shares of common stock directly to the public at the public offering price set forth on the cover of this prospectus and to selected dealers, which may include the underwriters, at such offering price less a selling concession not in excess of $0.672 per share. After the offering, the representatives may change the offering price and other selling terms.

The expenses of the offering that are payable by us are estimated to be approximately $2,500,000 (excluding underwriting discounts and commissions). We have also agreed to reimburse the underwriters for certain of their expenses in an amount up to $30,000 as set forth in the underwriting agreement.

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Option to Purchase Additional Shares

We have granted the underwriters an option exercisable for 30 days after the date of this prospectus to purchase, from time to time, in whole or in part, up to an aggregate of 954,750 additional shares of common stock from us at the public offering price less underwriting discounts and commissions. To the extent that this option is exercised, each underwriter will be obligated, subject to certain conditions, to purchase its pro rata portion of these additional shares based on the underwriter s percentage underwriting commitment in the offering as indicated in the table at the beginning of this Underwriting section.

Lock-Up Agreements

We, all of our directors and executive officers and holders of substantially all of our outstanding stock have agreed that, for a period of 180 days after the date of this prospectus subject to certain limited exceptions as described below, we and they will not directly or indirectly, without the prior written consent of each of Barclays Capital Inc. and Cowen and Company, LLC, (1) offer for sale, sell, pledge, or otherwise dispose of (or enter into any transaction or device that is designed to, or could be expected to, result in the disposition by any person at any time in the future of) any shares of common stock (including, without limitation, shares of common stock that may be deemed to be beneficially owned by us or them in accordance with the rules and regulations of the SEC and shares of common stock that may be issued upon exercise of any options or warrants) or securities convertible into or exercisable or exchangeable for common stock (other than the stock and shares issued pursuant to employee benefit plans, qualified stock option plans, or other employee compensation plans existing on the date of this prospectus or pursuant to currently outstanding options, warrants or rights not issued under one of those plans), or sell or grant options, rights or warrants with respect to any shares of common stock or securities convertible into or exchangeable for common stock (other than the grant of options pursuant to option plans existing on the date of this prospectus), (2) enter into any swap or other derivatives transaction that transfers to another, in whole or in part, any of the economic benefits or risks of ownership of shares of common stock, whether any such transaction described in clause (1) or (2) above is to be settled by delivery of common stock or other securities, in cash or otherwise, (3) make any demand for or exercise any right or file or cause to be filed a registration statement, including any amendments thereto, with respect to the registration of any shares of common stock or securities convertible, exercisable or exchangeable into common stock or any of our other securities (other than any registration statement on Form S-8), or (4) publicly disclose the intention to do any of the foregoing.

The restrictions above do not apply to:

transactions relating to shares of our common stock or other securities acquired in this offering, other than purchases by our officers and directors, or in the open market after the completion of this offering;

bona fide gifts, sales or other dispositions of shares of any class of our capital stock, in each case that are made exclusively between and among us and them or members of our or their family, or affiliates of us or them, including its partners (if a partnership) or members (if a limited liability company);

bona fide gifts of shares of any class of our capital stock to charities or educational institutions;

the exercise of warrants or the exercise of stock options granted pursuant to our stock option/incentive plans or otherwise outstanding on the date of the agreement referenced above (provided, that the restrictions shall apply to shares of the common stock issued upon such exercise or conversion);

transfers by a corporation, partnership, limited liability company, trust or other business entity to another corporation, partnership, limited liability company, trust or other business entity that is an affiliate (including, a fund managed by the same manager or managing member or general partners or management company or by an entity controlling, controlled by, or under common control with such manager or managing member or general partner or management company as the undersigned or who shares a common investment advisor with the undersigned) or as part of a distribution without consideration by the undersigned to its stockholders, partners, members or other equity holders, provided that such transfer shall not involve a disposition for value;

transfers by will or intestate succession upon death;

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transfers in connection with the net or cashless exercise or settlement of stock options, restricted stock units or other equity awards (including any transfer for the payment of taxes due as a result of such vesting or exercise whether by means of a net settlement or otherwise) pursuant to an employee benefit plan disclosed in this prospectus;

transfers (A) following the commencement of a tender or exchange offer made to all holders of our capital stock involving a change of control or (B) upon the consummation of a merger or sale of us, regardless of how such a transaction is structured;

the conversion of the outstanding preferred into shares of our common stock;

transfers by operation of law, such as pursuant to a qualified domestic order or in connection with a divorce settlement;

the establishment of any contract, instruction or plan that meets the requirements of Rule 10b5-1, or a Rule 10b5-1 Plan, under the Exchange Act (provided, however, that no sales of the common stock or securities convertible into, or exchangeable or exercisable for, the common stock, shall be made pursuant to a Rule 10b5-1 Plan prior to the expiration of the 180-day restricted period); and

any demands or requests for, exercise any right with respect to, or take any action in preparation of, our registration under the Securities Act of our or their shares of the common stock.

Barclays Capital Inc. and Cowen and Company, LLC, in their sole discretion, may release the common stock and other securities subject to the lock-up agreements described above in whole or in part at any time. When determining whether or not to release common stock and other securities from lock-up agreements, Barclays Capital Inc. and Cowen and Company, LLC will consider, among other factors, the holder s reasons for requesting the release, the number of shares of common stock and other securities for which the release is being requested and market conditions at the time. At least three business days before the effectiveness of any release or waiver of any of the restrictions described above with respect to an officer or director of our company, Barclays Capital Inc. and Cowen and Company, LLC will notify us of the impending release or waiver and we have agreed to announce the impending release or waiver by press release through a major news service at least two business days before the effective date of the release or waiver, except where the release or waiver is effected solely to permit a transfer of common stock that is not for consideration and where the transferee has agreed in writing to be bound by the same terms as the lock-up agreements described above to the extent and for the duration that such terms remain in effect at the time of transfer.

Offering Price Determination

Prior to this offering, there has been no public market for our common stock. The initial public offering price was negotiated between the representatives and us. In determining the initial public offering price of our common stock, the representatives considered:

the history and prospects for the industry in which we compete;

our financial information;

the ability of our management and our business potential and earning prospects;

the prevailing securities markets at the time of this offering; and

the recent market prices of, and the demand for, publicly traded shares of generally comparable companies.

Indemnification

We have agreed to indemnify the underwriters against certain liabilities, including liabilities under the Securities Act, and to contribute to payments that the underwriters may be required to make for these liabilities.

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Stabilization, Short Positions and Penalty Bids

The representatives may engage in stabilizing transactions, short sales and purchases to cover positions created by short sales, and penalty bids or purchases for the purpose of pegging, fixing or maintaining the price of the common stock, in accordance with Regulation M under the Exchange Act:

- Stabilizing transactions permit bids to purchase the underlying security so long as the stabilizing bids do not exceed a specified maximum.

- A short position involves a sale by the underwriters of shares in excess of the number of shares the underwriters are obligated to purchase in the offering, which creates the syndicate short position. This short position may be either a covered short position or a naked short position. In a covered short position, the number of shares involved in the sales made by the underwriters in excess of the number of shares they are obligated to purchase is not greater than the number of shares that they may purchase by exercising their option to purchase additional shares. In a naked short position, the number of shares involved is greater than the number of shares in their option to purchase additional shares. The underwriters may close out any short position by either exercising their option to purchase additional shares and/or purchasing shares in the open market. In determining the source of shares to close out the short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which they may purchase shares through their option to purchase additional shares. A naked short position is more likely to be created if the underwriters are concerned that there could be downward pressure on the price of the shares in the open market after pricing that could adversely affect investors who purchase in the offering.

- Syndicate covering transactions involve purchases of the common stock in the open market after the distribution has been completed in order to cover syndicate short positions.

- Penalty bids permit the representatives to reclaim a selling concession from a syndicate member when the common stock originally sold by the syndicate member is purchased in a stabilizing or syndicate covering transaction to cover syndicate short positions.

These stabilizing transactions, syndicate covering transactions and penalty bids may have the effect of raising or maintaining the market price of our common stock or preventing or retarding a decline in the market price of the common stock. As a result, the price of the common stock may be higher than the price that might otherwise exist in the open market. These transactions may be effected on The NASDAQ Global Select Market or otherwise and, if commenced, may be discontinued at any time.

Neither we nor any of the underwriters make any representation or prediction as to the direction or magnitude of any effect that the transactions described above may have on the price of the common stock. In addition, neither we nor any of the underwriters make any representation that the representatives will engage in these stabilizing transactions or that any transaction, once commenced, will not be discontinued without notice.

Electronic Distribution

A prospectus in electronic format may be made available on the Internet sites or through other online services maintained by one or more of the underwriters and/or selling group members participating in this offering, or by their affiliates. In those cases, prospective investors may view offering terms online and, depending upon the particular underwriter or selling group member, prospective investors may be allowed to place orders online. The underwriters may agree with us to allocate a specific number of shares for sale to online brokerage account holders. Any such allocation for online distributions will be made by the representatives on the same basis as other allocations.

Other than the prospectus in electronic format, the information on any underwriter s or selling group member s web site and any information contained in any other web site maintained by an underwriter or selling group

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member is not part of the prospectus or the registration statement of which this prospectus forms a part, has not been approved and/or endorsed by us or any underwriter or selling group member in its capacity as underwriter or selling group member and should not be relied upon by investors.

Listing on The NASDAQ Global Select Market

Our common stock has been approved for listing on The NASDAQ Global Select Market under the symbol CHMA.

Stamp Taxes

If you purchase shares of common stock offered in this prospectus, you may be required to pay stamp taxes and other charges under the laws and practices of the country of purchase, in addition to the offering price listed on the cover page of this prospectus.

Other Relationships

The underwriters and certain of their affiliates are full service financial institutions engaged in various activities, which may include securities trading, commercial and investment banking, financial advisory, investment management, investment research, principal investment, hedging, financing and brokerage activities. The underwriters and certain of their affiliates have, from time to time, performed, and may in the future perform, various commercial and investment banking and financial advisory services for the issuer and its affiliates, for which they received or may in the future receive customary fees and expenses.

In the ordinary course of their various business activities, the underwriters and certain of their affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (including bank loans) for their own account and for the accounts of their customers, and such investment and securities activities may involve securities and/or instruments of the issuer or its affiliates. If the underwriters or their affiliates have a lending relationship with us, they routinely hedge their credit exposure to us consistent with their customary risk management policies. Typically, the underwriters and their affiliates would hedge such exposure by entering into transactions which consist of either the purchase of credit default swaps or the creation of short positions in our securities or the securities of our affiliates, including potentially the shares of common stock offered hereby. Any such credit default swaps or short positions could adversely affect future trading prices of the shares of common stock offered hereby. The underwriters and certain of their affiliates may also communicate independent investment recommendations, market color or trading ideas and/or publish or express independent research views in respect of such securities or instruments and may at any time hold, or recommend to clients that they acquire, long and/or short positions in such securities and instruments.

Selling Restrictions

This prospectus does not constitute an offer to sell to, or a solicitation of an offer to buy from, anyone in any country or jurisdiction (i) in which such an offer or solicitation is not authorized, (ii) in which any person making such offer or solicitation is not qualified to do so or (iii) in which any such offer or solicitation would otherwise be unlawful. No action has been taken that would, or is intended to, permit a public offer of the shares of common stock or possession or distribution of this prospectus or any other offering or publicity material relating to the shares of common stock in any country or jurisdiction (other than the United States) where any such action for that purpose is required. Accordingly, each underwriter has undertaken that it will not, directly or indirectly, offer or sell any shares of common stock or have in its possession, distribute or publish any prospectus, form of application, advertisement or other document or information in any country or jurisdiction except under circumstances that will, to the best of its

knowledge and belief, result in compliance with any applicable laws and regulations and all offers and sales of shares of common stock by it will be made on the same terms.

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European Economic Area

In relation to each Member State of the European Economic Area which has implemented the Prospectus Directive (each, a Relevant Member State) an offer to the public of any common stock which are the subject of the offering contemplated herein may not be made in that Relevant Member State, except that an offer to the public in that Relevant Member State of any common stock may be made at any time under the following exemptions under the Prospectus Directive, if they have been implemented in that Relevant Member State:

- to legal entities which are qualified investors as defined under the Prospectus Directive;
- by the underwriters to fewer than 100, or, if the Relevant Member State has implemented the relevant provisions of the 2010 PD Amending Directive, 150, natural or legal persons (other than qualified investors as defined in the Prospectus Directive), as permitted under the Prospectus Directive, subject to obtaining the prior consent of the representatives of the underwriters for any such offer; or
- in any other circumstances falling within Article 3(2) of the Prospectus Directive,

provided that no such offer of common stock shall result in a requirement for us or any underwriter to publish a prospectus pursuant to Article 3 of the Prospectus Directive or supplement a prospectus pursuant to Article 16 of the Prospectus Directive.

Each person in a Relevant Member State who receives any communication in respect of, or who acquires any common stock under, the offers contemplated here in this prospectus will be deemed to have represented, warranted and agreed to and with each underwriter and us that:

- it is a qualified investor as defined under the Prospectus Directive; and
- in the case of any common stock acquired by it as a financial intermediary, as that term is used in Article 3(2) of the Prospectus Directive, (i) the common stock acquired by it in the offering have not been acquired on behalf of, nor have they been acquired with a view to their offer or resale to, persons in any Relevant Member State other than qualified investors, as that term is defined in the Prospectus Directive, or in the circumstances in which the prior consent of the representatives of the underwriters has been given to the offer or resale or (ii) where common stock have been acquired by it on behalf of persons in any Relevant Member State other than qualified investors, the offer of such common stock to it is not treated under the Prospectus Directive as having been made to such persons.

For the purposes of this representation and the provision above, the expression an offer of common stock to the public in relation to any common stock in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and any common stock to be offered so as to enable an investor to decide to purchase or subscribe for the common stock, as the same may be varied in that Relevant Member State by any measure implementing the Prospectus Directive in that Relevant Member State, the expression Prospectus Directive means Directive 2003/71/EC (and amendments thereto, including the 2010 PD Amending Directive, to the extent implemented in the Relevant Member State), and includes any relevant implementing measure

in each Relevant Member State and the expression 2010 PD Amending Directive means Directive 2010/73/EU.

United Kingdom

This prospectus has only been communicated or caused to have been communicated and will only be communicated or caused to be communicated as an invitation or inducement to engage in investment activity (within the meaning of Section 21 of the Financial Services and Markets Act of 2000 (the FSMA)) as received in connection with the issue or sale of the common stock in circumstances in which Section 21(1) of the FSMA does not apply to us. All applicable provisions of the FSMA will be complied with in respect to anything done in relation to the common stock in, from or otherwise involving the United Kingdom.

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Notice to Investors in Israel

This document does not constitute a prospectus under the Israeli Securities Law, 5728-1968, and has not been filed with or approved by the Israel Securities Authority. In Israel, this prospectus is being distributed only to, and is directed only at, investors listed in the first addendum, or the Addendum, to the Israeli Securities Law, consisting primarily of joint investment in trust funds, provident funds, insurance companies, banks, portfolio managers, investment advisors, members of the Tel Aviv Stock Exchange Ltd., underwriters, each purchasing for their own account, venture capital funds, entities with shareholders equity in excess of NIS 50 million and qualified individuals , each as defined in the Addendum (as it may be amended from time to time). Such individuals are collectively referred to as qualified investors. Qualified investors shall be required to submit written confirmation that they fall within the scope of the Addendum.

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LEGAL MATTERS

The validity of the common stock offered in this prospectus will be passed upon for us by Goodwin Procter LLP, Boston, Massachusetts. Cooley LLP, New York, New York is serving as counsel to the underwriters.

EXPERTS

The consolidated financial statements of Chiasma, Inc. at December 31, 2013 and 2014, and for each of the two years in the period ended December 31, 2014, included in this prospectus and Registration Statement have been audited by Kost, Forer, Gabbay & Kasierer, a member of Ernst & Young Global, independent registered public accounting firm, as set forth in their report thereon appearing elsewhere herein, and are included in reliance upon such report given on the authority of such firm as experts in accounting and auditing. The offices of Kost, Forer, Gabbay & Kasierer are located at 3 Aminadav St., Tel Aviv, 6706703 Israel.

WHERE YOU CAN FIND MORE INFORMATION

We have filed with the SEC a registration statement on Form S-1 (File Number 333-204949) under the Securities Act with respect to the shares of common stock offered hereby. This prospectus, which constitutes a part of the registration statement, does not contain all of the information set forth in the registration statement or the exhibits and schedules filed therewith. For further information with respect to us and the common stock offered hereby, reference is made to the registration statement and the exhibits and schedules filed therewith. Statements contained in this prospectus regarding the contents of any contract or any other document that is filed as an exhibit to the registration statement are not necessarily complete, and each such statement is qualified in all respects by reference to the full text of such contract or other document filed as an exhibit to the registration statement. A copy of the registration statement and the exhibits and schedules filed therewith may be inspected without charge at the public reference room maintained by the SEC, located at 100 F Street N.E., Washington, D.C. 20549, and copies of all or any part of the registration statement may be obtained from such offices upon the payment of the fees prescribed by the SEC. Please call the SEC at 1-800-SEC-0330 for further information about the public reference room. The SEC also maintains a website that contains reports, proxy and information statements and other information regarding registrants that file electronically with the SEC. The address is www.sec.gov.

Upon completion of this offering, we will become subject to the information and periodic reporting requirements of the Exchange Act and, in accordance therewith, will file periodic reports, proxy statements and other information with the SEC. Such periodic reports, proxy statements and other information will be available for inspection and copying at the public reference room and website of the SEC referred to above.

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CHIASMA, INC.

CONDENSED CONSOLIDATED BALANCE SHEETS

	December 31, 2014 (audited)	March 31, 2015 (unaudited)	Pro Forma Stockholders Equity March 31, 2015 (unaudited)
ASSETS			
Current assets:			
Cash	$ 40,160,435	$ 70,871,768	
Prepaid expenses and other current assets	311,299	445,078	
Total current assets	40,471,734	71,316,846	
Property and equipment, net	615,242	562,377	
Other assets	311,730	758,895	
Total assets	$ 41,398,706	$ 72,638,118	
LIABILITIES, REDEEMABLE CONVERTIBLE PREFERRED STOCK, AND STOCKHOLDERS (DEFICIT) EQUITY			
Current liabilities:			
Accounts payable	$ 317,994	$ 1,035,457	
Accrued expenses and other current liabilities	4,000,294	2,739,893	
Total current liabilities	4,318,288	3,775,350	
Long-term liabilities	4,612,450	4,724,276	
Total liabilities	8,930,738	8,499,626	
Redeemable convertible preferred stock, $0.01 par value:			
Series B1 preferred, 1,134,997 shares authorized, issued and outstanding at December 31, 2014 and March 31, 2015; no shares issued and outstanding pro forma (unaudited); aggregate liquidation preference and redemption value of $7,218,438 at March 31, 2015	9,143,823	9,143,823	$
Series C preferred, 40,719,409 shares authorized; 40,430,250 shares issued and outstanding at December 31, 2014 and March 31, 2015; no shares issued and outstanding pro forma (unaudited); aggregate liquidation preference and redemption value of $40,430,250 at March 31, 2015	40,430,250	40,430,250	
Series D preferred, 38,504,439 shares authorized, issued and outstanding at December 31, 2014 and March 31, 2015; no	22,054,186	22,054,186	

shares issued and outstanding pro forma (unaudited); aggregate liquidation preference and redemption value of $22,054,186 at March 31, 2015			
Series E preferred, 45,000,000 and 80,774,458 shares authorized at December 31, 2014 and March 31, 2015, respectively; 33,774,763 and 69,722,786 shares issued and outstanding at December 31, 2014 and March 31, 2015, respectively; no shares issued and outstanding pro forma (unaudited); aggregate liquidation preference and redemption value of $69,722,786 at March 31, 2015	32,857,713	67,168,201	
Total redeemable convertible preferred stock	104,485,972	138,796,460	
Stockholders (deficit) equity:			
Common stock, $0.01 par value, 175,000,000 and 250,000,000 shares authorized at December 31, 2014 and March 31, 2015, respectively; 44,326 and 81,870 shares issued and outstanding at December 31, 2014 and March 31, 2015, respectively; 16,484,881 shares issued and outstanding pro forma (unaudited)	443	818	164,848
Additional paid-in capital	9,489,627	11,093,496	149,725,926
Accumulated deficit	(81,508,074)	(85,752,282)	(85,752,282)
Total stockholders (deficit) equity	(72,018,004)	(74,657,968)	$ 64,138,492
Total liabilities, redeemable convertible preferred stock, and stockholders equity	$ 41,398,706	$ 72,638,118	

See accompanying notes to unaudited condensed consolidated financial statements.

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CHIASMA, INC.

CONDENSED CONSOLIDATED STATEMENTS OF OPERATIONS

(unaudited)

	Three Months Ended March 31,	
	2014	**2015**
Revenue from license agreement	$ 4,573,478	$
Operating expenses:		
Research and development	1,649,545	2,218,786
Marketing, general and administrative	954,318	1,931,210
Total operating expenses	2,603,863	4,149,996
Income (loss) from operations	1,969,615	(4,149,996)
Other expenses, net	24,839	89,482
Income (loss) before provision for income taxes	1,944,776	(4,239,478)
Provision for income taxes	(129,259)	4,730
Net income (loss)	2,074,035	(4,244,208)
Accretion of redeemable convertible preferred stock	(339,744)	(97,521)
Net income (loss) attributable to common stockholders	$ 1,734,291	$ (4,341,729)
Net income (loss) per share attributable to common stockholders, basic	$ 39.82	$ (59.73)
Weighted average common shares outstanding, basic	43,558	72,693
Net income (loss) per share attributable to common stockholders, diluted	$ 0.19	$ (59.73)
Weighted average common shares outstanding, diluted	11,130,865	72,693
Pro forma net loss per share attributable to common stockholders, basic and diluted		$ (0.30)
Pro forma weighted average common shares outstanding, basic and diluted		13,982,593

See accompanying notes to unaudited condensed consolidated financial statements.

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CHIASMA, INC.

CONDENSED CONSOLIDATED STATEMENT OF REDEEMABLE CONVERTIBLE PREFERRED STOCK

AND STOCKHOLDERS DEFICIT

	Redeemable Convertible Preferred Stock							Common Stock		
d	Series C Preferred Shares	Amount	Series D Preferred Shares	Amount	Series E Preferred Shares	Amount	Total Amount	Shares	Amount	Additi Paid Capi
3	40,430,250	$ 40,430,250	38,504,439	$ 22,054,186	33,774,763	$ 32,857,713	$ 104,485,972	44,326	$ 443	$ 9,48
										22
								37,544	375	
					35,948,023	34,212,967	34,212,967			1,47
						97,521	97,521			(9
3	40,430,250	$ 40,430,250	38,504,439	$ 22,054,186	69,722,786	$ 67,168,201	$ 138,796,460	81,870	$ 818	$ 11,09

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CHIASMA, INC.

CONDENSED CONSOLIDATED STATEMENTS OF CASH FLOWS

(unaudited)

	Three Months Ended March 31,	
	2014	**2015**
CASH FLOWS FROM OPERATING ACTIVITIES:		
Net income (loss)	$ 2,074,035	$ (4,244,208)
Adjustments to reconcile net income (loss) to net cash provided by (used in) operating activities:		
Depreciation and amortization	71,402	50,986
Stock-based compensation	128,697	220,958
Loss (gain) on sale of property and equipment	190	(4,286)
Changes in operating assets and liabilities:		
Deferred income taxes	(192,604)	(27,014)
Prepaid expenses and other current assets	2,194	(106,814)
Accounts payable	(996,313)	717,463
Accrued expenses and other current liabilities	(3,285,894)	(1,648,749)
Deferred revenue and customer advances, net	4,409,022	
Other assets	1,207	6,614
Long-term liabilities	17,992	111,825
Net cash provided by (used in) operating activities	2,229,928	(4,923,225)
CASH FLOWS FROM INVESTING ACTIVITIES:		
Decrease in value of other assets	10,401	
Proceeds from sale of property and equipment	417	11,500
Purchases of property and equipment		(5,335)
Net cash provided by investing activities	10,818	6,165
CASH FLOWS FROM FINANCING ACTIVITIES:		
Proceeds from issuance of Series E redeemable convertible preferred stock and warrants for common stock, net		35,690,345
Deferred offering costs.		(65,381)
Exercise of warrants		3,429
Net cash provided by financing activities		35,628,393
NET INCREASE IN CASH	2,240,746	30,711,333
Cash, beginning of period	12,849,579	40,160,435
Cash, end of period	$ 15,090,325	$ 70,871,768

SUPPLEMENTAL NON-CASH FINANCING ACTIVITIES:		
Deferred offering costs	$	$ 388,348
SUPPLEMENTAL DISCLOSURES OF CASH FLOW INFORMATION:		
Cash paid for interest		
Cash paid for income taxes	$ 6,037	$ 10,035

See accompanying notes to unaudited condensed consolidated financial statements.

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CHIASMA, INC.

NOTES TO UNAUDITED CONDENSED CONSOLIDATED FINANCIAL STATEMENTS

1. Nature of Business and Summary of Significant Accounting Policies

Nature of business

Chiasma, Inc. is a late-stage biopharmaceutical company incorporated in 2001 under the laws of the State of Delaware. The Company is dedicated to improving the lives of patients suffering from orphan diseases by developing and commercializing novel oral therapies that are available only as injections. The Company has completed a multinational Phase 3 clinical trial of its most advanced Transient Permeability Enhancer platform-based product candidate, oral octreotide, for the treatment of acromegaly. Since its inception, the Company has devoted substantially all of its efforts to business planning, research and development, recruiting management and technical staff, and raising capital, and has financed its operations through the issuance of redeemable convertible preferred stock, long-term debt, and proceeds from a license agreement.

Chiasma, Inc. is headquartered in Massachusetts and has a wholly owned subsidiary; Chiasma (Israel) Ltd. Chiasma, Inc. and Chiasma (Israel) Ltd. are herein collectively referred to as the Company. The Company s product development facilities are in Israel.

The Company is subject to risks common to companies in the biopharmaceutical development industry. There can be no assurance that the Company s research and development will be successfully completed, that adequate protection for the Company s intellectual property will be obtained, that any products developed will obtain required regulatory approval or that any approved products will be commercially viable. Even if the Company s development efforts are successful, it is uncertain when, if ever, the Company will generate significant product sales. The Company operates in an environment of rapid technological change and substantial competition from pharmaceutical and biotechnology companies.

Basis of presentation

The Company has prepared the accompanying unaudited condensed consolidated financial statements pursuant to the rules and regulations of the U.S. Securities and Exchange Commission (SEC) regarding interim financial reporting. Accordingly, they do not include all of the information and footnotes required by accounting principles generally accepted in the United States of America (U.S. GAAP) for complete financial statements and should be read in conjunction with the Company s audited consolidated financial statements as of and for the years ended December 31, 2013 and 2014.

In the opinion of management, the Company has prepared the accompanying unaudited condensed consolidated financial statements on the same basis as its audited financial statements, and these financial statements include all adjustments, consisting only of normal recurring adjustments, necessary for a fair presentation of the results of the interim periods presented. The operating results for the interim periods presented are not necessarily indicative of the results expected for the full year 2015.

Unaudited pro forma financial information

The unaudited pro forma consolidated balance sheet information at March 31, 2015 has been prepared to reflect the automatic conversion of all shares of redeemable convertible preferred stock outstanding at March 31, 2015 into

16,403,011 shares of common stock as if a proposed initial public offering had occurred on March 31, 2015. For purposes of pro forma basic and diluted net loss per share attributable to common stockholders, all shares of redeemable convertible preferred stock have been treated as if they have been converted to common stock in all periods in which such shares were outstanding. Accordingly, the pro forma basic and diluted loss per share attributable to common stockholders does not include the effects of the accretion of redeemable convertible preferred stock to redemption value.

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Use of Estimates

The preparation of consolidated financial statements in conformity with GAAP requires us to make estimates and assumptions that affect the amounts reported and disclosed in the financial statements and the accompanying notes. Actual results could differ materially from these estimates. On an ongoing basis, we evaluate our estimates, including those related to the accounts receivable and sales allowances, fair values of financial instruments, useful lives of property and equipment, income taxes, and contingent liabilities, among others. We base our estimates on historical experience and on various other assumptions that are believed to be reasonable, the results of which form the basis for making judgments about the carrying values of assets and liabilities.

Recently issued accounting pronouncements

In May 2014, FASB issued Accounting Standards Update (ASU) No. 2014-09, *Revenue from Contracts with Customers* (ASU 2014-09), which amends the guidance for revenue recognition to replace numerous industry-specific requirements. ASU 2014-09 implements a five-step process for customer contract revenue recognition that focuses on transfer of control, as opposed to transfer of risk and rewards. ASU 2014-09 also requires enhanced disclosures regarding the nature, amount, timing, and uncertainty of revenues and cash flows from contracts with customers. Other major provisions include ensuring the time value of money is considered in the transaction price, and allowing estimates of variable consideration to be recognized before contingencies are resolved in certain circumstances. The amendments in ASU 2014-09 are effective for reporting periods beginning after December 15, 2016, and early adoption is not permitted. Entities can transition to the standard either retrospectively or as a cumulative-effect adjustment as of the date of adoption. The Company is currently in the process of evaluating the effect the adoption of ASU 2014-09 may have on its consolidated financial statements.

In August 2014, the FASB issued ASU No. 2014-15, *Disclosure of Uncertainties about an Entity s Ability to Continue as a Going Concern* (ASU 2014-15). ASU 2014-15 requires management to assess an entity s ability to continue as a going concern and to provide related disclosures in certain circumstances. The requirements of ASU 2014-15 will be effective for the annual financial statement period beginning after December 15, 2016, with early adoption permitted. The Company is currently in the process of evaluating the impact of adopting ASU 2014-15.

2. Net Loss per Share Attributable to Common Stockholders

Basic net income (loss) per share attributable to common stockholders is computed by dividing the net income (loss) attributable to common stockholder by the weighted-average common shares outstanding for the period. Because the Company has reported net loss attributable to common stockholders for the three months ended March 31, 2015, basic and diluted net loss per share attributable to common stockholders are the same as basic net loss per share attributable to common stockholders for this period.

All redeemable convertible preferred stock, common stock warrants, and stock options have been excluded from the computation of diluted weighted-average shares outstanding because such securities would have an anti-dilutive impact due to net losses reported during three months ended March 31, 2015.

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The following table sets forth the computation of basic and diluted earnings per share:

	Three Months Ended March 31, 2014	Three Months Ended March 31, 2015
Numerator		
Net income (loss) attributable to common stockholders, basic	$ 1,734,291	$ (4,341,729)
Accretion of redeemable convertible preferred stock	339,744	
Net income (loss) attributable to common stockholders, diluted	$ 2,074,035	$ (4,341,729)
Denominator		
Weighted average common shares outstanding, basic	43,558	72,693
Effects of dilutive securities		
Warrants to purchase common stock	1,722,067	
Options to employees	597,216	
Preferred Shares	8,768,024	
Weighted average common shares outstanding, diluted	11,130,865	72,693
Net income (loss) per share attributable to common stockholders, basic	$ 39.82	$ (59.73)
Net income (loss) per share attributable to common stockholders, diluted	$ 0.19	$ (59.73)

For the three months ended March 31, 2014, 70,103 options have been excluded from the calculation of the diluted income per share since their effect was anti-dilutive.

For the three months ended March 31, 2015, all outstanding options and warrants have been excluded from the calculation of the diluted net loss per share since their effect was anti-dilutive.

The pro forma basic and diluted net loss per share attributable to common stockholders for the three months ended March 31, 2015 has been computed using the weighted-average common shares outstanding after giving pro forma effect to the automatic conversion of all shares of redeemable convertible preferred stock into shares of common stock as if such conversions had occurred at the beginning of 2015 or the date of original issuance, if later.

Pro forma basic and diluted net loss per share attributable to common stockholders is computed as follows:

	Three Months Ended March 31, 2015

Numerator Net loss attributable to common stockholders, basic and diluted	$ (4,244,208)
Denominator:	
Weighted-average common shares outstanding, basic and diluted	72,693
Adjustment for assumed effect of conversion of redeemable convertible preferred stock	13,909,900
Pro forma weighted average common shares outstanding, basic and diluted	13,982,593
Pro forma net loss per share, basic and diluted	$ (0.30)

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3. Accrued Expenses and Other Current Liabilities

Accrued expenses and other current liabilities consist of the following:

	December 31, 2014	March 31, 2015
Accrued professional fees	$ 373,727	$ 724,678
Accrued research and development expenses	3,028,389	1,668,569
Accrued payroll and employee benefits	598,178	346,646
Total accrued expenses and other current liabilities	$ 4,000,294	$ 2,739,893

4. License Agreement

In December 2012, the Company signed a license agreement with F. Hoffmann-La Roche Ltd. and Hoffmann-La Roche Inc. (collectively Roche), which was effective in January 2013, and granted Roche an exclusive, non-transferable license to the Company s intellectual property related to the oral octreotide. Under the terms of the agreement, Roche obtained worldwide rights to research, develop, make, import, export, sell, market or distribute the commercial product. The Company retained certain research and development activities under a joint development plan. The Company retained all rights to the intellectual property contained in the agreement. The agreement provided for an upfront payment of $65,000,000, future consideration of up to $530,000,000 in development and commercial milestones, and the right to receive tiered, double-digit royalties on net sales of oral octreotide.

The Company s total service obligations of $85,000,000 were recognized over the expected service period using the proportional performance method of revenue recognition. During the three months ended March 31, 2014, the Company recognized $4,573,478 in revenue for services rendered. In July 2014, Roche terminated the license agreement and returned all rights and documentation granted under the agreement to the Company. The Company was relieved of further obligations under the agreement. There was no remaining revenue to be recognized in the three months ended March 31, 2015.

Subsequent to the termination of the Roche agreement, the Company purchased from Roche active pharmaceutical ingredient (API) supplies to continue the development and manufacturing of oral octreotide as well as Roche s proposed trade name for oral octreotide for an aggregate amount of $5,100,000 payable in three equal annual installments of $1,700,000 in January 2016, January 2017 and January 2018. The difference between the aggregate purchase price and the present value of the installment payments represents the interest component of the financing arrangement and is being recorded as interest expense over the payment term. Other than these payments, the Company has no other financial and operational obligations to Roche. Following the termination of the license agreement, the Company is not entitled to further payments from Roche, Roche has no remaining rights to oral octreotide and the Company retains all rights to oral octreotide and all related intellectual property.

5. Redeemable Convertible Preferred Stock

In February 2015, the Company increased the number of authorized shares of Series E redeemable convertible preferred stock (Series E preferred stock) to a total of 80,774,458 shares and subsequently sold and issued an aggregate of 35,948,023 shares of Series E preferred at $1.00 per share for gross proceeds of $35,948,023, net of issuance costs of $257,680. In connection with the issuance of Series E preferred, the Company issued holders of

Series E preferred warrants to purchase 984,116 shares of the Company s common stock, with an exercise price of $9.13 per share, which is accounted for as a discount on the issuance of Series E preferred.

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6. Warrants

A summary of warrant activity is as follows:

	Three Months Ended March 31,	
	2014	2015
Warrants outstanding, beginning of period	1,752,818	2,677,440
Exercised		(37,544)
Issuances		984,116
Warrants outstanding, end of period	1,752,818	3,624,012

In connection with the issuance of Series E preferred in February 2015, the Company issued to holders of Series E preferred warrants to purchase 984,116 shares of the Company s common stock, with an exercise price of $9.13 per share, which is accounted for as a discount on the issuance of Series E preferred. These common stock warrants were classified as a component of stockholders equity because they are free standing financial instruments that are legally detachable and separately exercisable from the redeemable convertible preferred stock, are contingently exercisable, do not embody an obligation for the Company to repurchase its own shares, and permit the holders to receive a fixed number of common shares upon exercise. In addition, the common stock warrants require physical settlement and do not provide any guarantee of value or return. Common stock warrants were initially recorded at their relative fair value and were not subsequently remeasured. Common stock warrants were valued using a Black-Scholes option-pricing model (Black-Scholes) (level 3) based on the following assumptions:

Expected volatility	7.5%
Expected term (years)	1.75
Risk-free interest rate	0.47%
Expected dividend yield	0%

7. Stock Compensation

In February 2015, the board of directors approved the grant of options to purchase an aggregate of 122,644 shares of common stock, at an exercise price of $3.29 per share, to directors. The options will vest over a period of four years, and have a 10 year term.

The fair value of each of the stock options granted, estimated at the date of grant using Black-Scholes, was $2.65.

Stock-based compensation expense is classified in the consolidated statements of operations as follows:

	Three Months Ended March 31,	
	2014	2015
Research and development	$ 45,890	$ 136,206

General and administrative	82,807	84,753
Total	$ 128,697	$ 220,959

8. Income Taxes

Provision for income taxes was $(129,259) and $4,730 for the three months ended March 31, 2014 and 2015, respectively.

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The effective rate of (6.64%) for the three months ended March 31, 2014 and (0.11%) for the three months ended March 31, 2015 differs from the U.S. federal statutory income tax rate of 34% primarily due to a full valuation allowance against the Company s U.S. deferred tax asset.

As of March 31, 2014 and 2015, the Company had provided a liability for $111,342 and $266,906, respectively, for uncertain tax positions related to various income tax matters which was classified as other long-term liabilities. For the three months ended March 31, 2014 and 2015, the Company had provided for accrued interest related to uncertain tax positions of $3,354 and $7,386, respectively. These uncertain tax positions would impact the Company s effective tax rate, if recognized. The Company does not expect that the amounts of uncertain tax positions will change significantly within the next 12 months.

The Company files U.S. federal, various state and Israeli income tax returns. The associated tax filings remain subject to examination by applicable tax authorities for a certain length of time following the tax year to which those filings relate. In the United States and Israel, the 2011 and subsequent tax years remain subject to examination by the applicable taxing authorities as of March 31, 2015. However, U.S. tax attributes that were generated prior to 2011 may still be adjusted upon examination by federal, state or local tax authorities if they either have been or will be used in a future period.

9. Subsequent events

In April 2015, the board of directors approved the grant of options to purchase an aggregate of 1,507,234 shares of common stock to certain officers, directors and employees.

During April and May 2015, 124,761 options were exercised by directors and former employees into 124,761

shares of common stock.

During May 2015, the Company entered into a sublease agreement for commercial office space with an eleven month term. The monthly lease costs are $19,093 and the Company is required to provide a security deposit in the amount of $38,135.

In June 2015, the board of directors approved the grant of options to purchase an aggregate of 628,539 shares of common stock to certain officers, employees and consultants.

On June 30, 2015, the board of directors approved a 1-for-9.132 reverse stock split. As a result, all common stock, warrants and options for common stock, exercise price and net income (loss) per share amounts were adjusted retroactively for all periods presented in these financial statements. Additionally, the conversion price for each share of the Company s redeemable convertible preferred stock was adjusted to reflect this reverse stock split.

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REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

The Board of Directors and Stockholders of Chiasma, Inc.

We have audited the accompanying consolidated balance sheets of Chiasma, Inc. and its subsidiary (collectively, the Company) as of December 31, 2014 and 2013, and the related consolidated statements of operations, redeemable convertible preferred stock and stockholders deficit and cash flows for the years then ended. These consolidated financial statements are the responsibility of the Company s management. Our responsibility is to express an opinion on these consolidated financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. We were not engaged to perform an audit of the Company s internal control over financial reporting. Our audits included consideration of internal control over financial reporting as a basis for designing audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the Company s internal control over financial reporting. Accordingly, we express no such opinion. An audit also includes examining, on a test basis, evidence supporting the amounts and disclosures in the consolidated financial statements, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the consolidated financial statements referred to above present fairly, in all material respects, the consolidated financial position of the Company at December 31, 2014 and 2013, and the results of its consolidated operations and its cash flows for the years then ended in conformity with U.S. generally accepted accounting principles.

/s/ Kost Forer Gabbay & Kasierer

KOST FORER GABBAY & KASIERER

A Member of Ernst & Young Global

Tel-Aviv, Israel

April 16, 2015

Except Note 3, Note 8, Note 9, Note 10,

Note 11, Note 14 and Note 17 to which

the date is July 6, 2015

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CHIASMA, INC.

CONSOLIDATED BALANCE SHEETS

	December 31, 2013	December 31, 2014	Pro Forma Stockholders Equity December 31, 2014 (unaudited)
ASSETS			
Current assets:			
Cash	$ 12,849,579	$ 40,160,435	
Prepaid expenses and other current assets	438,403	311,299	
Total current assets	13,287,982	40,471,734	
Property and equipment, net	1,056,199	615,242	
Other assets	314,119	311,730	
Total assets	$ 14,658,300	$ 41,398,706	
LIABILITIES, REDEEMABLE CONVERTIBLE PREFERRED STOCK, AND STOCKHOLDERS (DEFICIT) EQUITY			
Current liabilities:			
Accounts payable	$ 2,339,578	$ 317,994	
Accrued expenses and other current liabilities	9,242,189	4,000,294	
Deferred revenue and customer advances	2,883,295		
Total current liabilities	14,465,062	4,318,288	
Long-term liabilities	96,704	4,612,450	
Total liabilities	14,561,766	8,930,738	
Commitments and contingencies (Note 13)			
Redeemable convertible preferred stock, $0.01 par value:			
Series B1 preferred, 1,134,997 shares authorized, issued and outstanding at December 31, 2013 and 2014; no shares issued and outstanding pro forma (unaudited); aggregate liquidation preference and redemption value of $7,218,438 at December 31, 2014	9,143,823	9,143,823	$
Series C preferred, 40,719,409 shares authorized; 40,430,250 shares issued and outstanding at December 31, 2013 and	40,430,250	40,430,250	

2014; no shares issued and outstanding pro forma (unaudited); aggregate liquidation preference and redemption value of $40,430,250 at December 31, 2014			
Series D preferred, 38,504,439 shares authorized, issued and outstanding at December 31, 2013 and 2014; no shares issued and outstanding pro forma (unaudited); aggregate liquidation preference and redemption value of $22,054,186 at December 31, 2014	21,157,627	22,054,186	
Series E preferred, 45,000,000 shares authorized; 33,774,763 shares issued and outstanding at December 31, 2014; no shares issued and outstanding pro forma (unaudited); aggregate liquidation preference and redemption value of $33,774,763 at December 31, 2014		32,857,713	
Total redeemable convertible preferred stock	70,731,700	104,485,972	
Stockholders (deficit) equity:			
Common stock, $0.01 par value, 112,000,000 and 175,000,000 shares authorized at December 31, 2013 and 2014, respectively; 43,558 and 44,326 shares issued and outstanding at December 31, 2013 and 2014, respectively; 12,510,857 shares issued and outstanding pro forma (unaudited)	435	443	125,108
Additional paid-in capital	8,861,944	9,489,627	113,850,934
Accumulated deficit	(79,497,545)	(81,508,074)	(81,508,074)
Total stockholders (deficit) equity	(70,635,166)	(72,018,004)	$ 32,467,968
Total liabilities, redeemable convertible preferred stock, and stockholders (deficit) equity	$ 14,658,300	$ 41,398,706	

See accompanying notes to consolidated financial statements.

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CHIASMA, INC.

CONSOLIDATED STATEMENTS OF OPERATIONS

	Year Ended December 31,	
	2013	2014
Revenue from license agreement (Note 6)	$ 73,134,205	$ 13,165,795
Operating expenses:		
Research and development	26,455,121	11,527,385
General and administrative	8,065,332	3,468,866
Total operating expenses	34,520,453	14,996,251
Income (loss) from operations	38,613,752	(1,830,456)
Other expenses, net	1,208,282	4,452
Income (loss) before provision for income taxes	37,405,470	(1,834,908)
Provision for income taxes	1,224,428	175,621
Net income (loss)	36,181,042	(2,010,529)
Accretion of deemed liquidation related to Series D redeemable convertible preferred stock	(38,504,439)	
Accretion of redeemable convertible preferred stock	(3,034,132)	(904,025)
Net loss attributable to common stockholders	$ (5,357,529)	$ (2,914,554)
Net loss per share attributable to common stockholders, basic and diluted	$ (125.29)	$ (66.21)
Weighted average common shares outstanding, basic and diluted	42,760	44,017
Pro forma net loss per share attributable to common stockholders, basic and diluted (unaudited)		$ (0.22)
Pro forma weighted average common shares outstanding, basic and diluted (unaudited)		8,964,035

See accompanying notes to consolidated financial statements.

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CHIASMA, INC.

CONSOLIDATED STATEMENTS OF REDEEMABLE CONVERTIBLE PREFERRED STOCK

	Redeemable Convertible Preferred Stock									
s B1	Preferred	Series C Preferred		Series C	Preferred	Series D Preferred		Series D	Preferr	
s	Amount	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amo	
	$	40,239,409	$ 39,829,238		$	24,265,554	$ 22,835,482		$	
		190,841	190,841							
						14,238,885	12,148,439			
			410,171				1,612,982		1,01	
							38,504,439			
							(54,954,694)			
997	9,143,823	(40,430,250)	(40,430,250)	40,430,250	40,430,250	(38,504,439)	(20,146,648)	38,504,439	20,14	

997	9,143,823		40,430,250	40,430,250		38,504,439	21,15
							89
997	$ 9,143,823	$	40,430,250	$ 40,430,250	$	38,504,439	$ 22,05

See accompanying notes to consolidated financial statements.

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CHIASMA, INC.

CONSOLIDATED STATEMENTS OF STOCKHOLDERS DEFICIT

	Common Stock Shares	Common Stock Amount	Additional Paid-in Capital	Accumulated Deficit	Total Stockholders Deficit
Balance, January 1, 2013	32,159	$ 321	$ 9,072,279	$ (77,174,148)	$ (68,101,548)
Stock-based compensation			745,342		745,342
Exercise of stock options	11,399	114	27,775		27,889
Issuance of Series D redeemable convertible preferred stock and warrants for common stock, net of issuance costs of $39,766			2,050,680		2,050,680
Accretion of redeemable convertible preferred stock			(3,034,132)		(3,034,132)
Accretion of deemed liquidation related to Series D redeemable convertible preferred stock				(38,504,439)	(38,504,439)
Net income				36,181,042	36,181,042
Balance, December 31, 2013	43,558	435	8,861,944	(79,497,545)	(70,635,166)
Stock-based compensation			756,495		756,495
Exercise of stock options	768	8	1,679		1,687
Accretion of redeemable convertible preferred stock			(904,025)		(904,025)
Issuance of Series E redeemable convertible preferred stock and warrants for common stock, net of issuance costs of $150,982			773,534		773,534
Net loss				(2,010,529)	(2,010,529)
Balance, December 31, 2014	44,326	$ 443	$ 9,489,627	$ (81,508,074)	$ (72,018,004)

See accompanying notes to consolidated financial statements.

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CHIASMA, INC.

CONSOLIDATED STATEMENTS OF CASH FLOWS

	Year Ended December 31,	
	2013	2014
CASH FLOWS FROM OPERATING ACTIVITIES:		
Net income (loss)	$ 36,181,042	$ (2,010,529)
Adjustments to reconcile net income (loss) to net cash provided by (used in) operating activities:		
Depreciation and amortization	321,582	272,030
Stock-based compensation	745,342	756,495
Non-cash interest expense	157,764	
Change in fair value of Series C redeemable convertible preferred stock warrant liability	60,000	
Loss on sale of property and equipment	221,330	91,361
Changes in operating assets and liabilities:		
Deferred income taxes	(57,171)	27,681
Prepaid expenses and other current assets	173,305	68,778
Accounts payable	1,030,062	(2,021,584)
Accrued expenses and other current liabilities	4,355,255	(5,241,895)
Deferred revenue and customer advances	2,883,295	(2,883,295)
Other assets	23,845	25,602
Long-term liabilities	96,704	4,515,746
Net cash provided by (used in) operating activities	46,192,355	(6,399,610)
CASH FLOWS FROM INVESTING ACTIVITIES:		
Decrease (increase) in value of other assets	(5,601)	7,432
Purchases of property and equipment	(23,372)	
Proceeds from sale of property and equipment	11,459	77,566
Net cash (used in) provided by investing activities	(17,514)	84,998
CASH FLOWS FROM FINANCING ACTIVITIES:		
Repayment of long-term debt	(11,087,586)	
Proceeds from issuance of Series D redeemable convertible preferred stock and warrants for common stock, net	14,199,119	
Redemption of Series D redeemable convertible preferred stock	(54,954,694)	
Proceeds from issuance of Series E redeemable convertible preferred stock and warrants for common stock, net		33,623,781
Exercise of stock options	27,889	1,687
Net cash (used in) provided by financing activities	(51,815,272)	33,625,468
NET (DECREASE) INCREASE IN CASH	(5,640,431)	27,310,856

Cash, beginning of year	18,490,010	12,849,579
Cash, end of year	$ 12,849,579	$ 40,160,435
SUPPLEMENTAL NON-CASH FINANCING ACTIVITIES:		
Conversion of warrants into Series C redeemable convertible preferred stock	$ 190,841	$
SUPPLEMENTAL DISCLOSURES OF CASH FLOW INFORMATION:		
Cash paid for interest	$ 920,648	$
Cash paid for income taxes	$ 1,175,861	$ 113,506

See accompanying notes to consolidated financial statements.

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CHIASMA, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

1. Nature of Business and Basis of Presentation

Nature of business

Chiasma, Inc. is a late-stage biopharmaceutical company incorporated in 2001 under the laws of the State of Delaware. The Company is dedicated to improving the lives of patients suffering from orphan diseases by developing and commercializing novel oral therapies that are available only as injections. The Company has completed a multinational Phase 3 clinical trial of its most advanced Transient Permeability Enhancer platform-based product candidate, oral octreotide, for the treatment of acromegaly. Since its inception, the Company has devoted substantially all of its efforts to business planning, research and development, recruiting management and technical staff, and raising capital, and has financed its operations through the issuance of redeemable convertible preferred stock, long-term debt, and proceeds from a license agreement.

Chiasma, Inc. is headquartered in Massachusetts and has a wholly owned subsidiary, Chiasma (Israel) Ltd. Chiasma, Inc. and Chiasma (Israel) Ltd. are herein collectively referred to as the Company. The Company s product development facilities are in Israel.

The Company is subject to risks common to companies in the biopharmaceutical development industry. There can be no assurance that the Company s research and development will be successfully completed, that adequate protection for the Company s intellectual property will be obtained, that any products developed will obtain required regulatory approval or that any approved products will be commercially viable. Even if the Company s development efforts are successful, it is uncertain when, if ever, the Company will generate significant product sales. The Company operates in an environment of rapid technological change and substantial competition from pharmaceutical and biotechnology companies.

Basis of Presentation

The accompanying consolidated financial statements are prepared in conformity with accounting principles generally accepted in the United States of America (U.S. GAAP) and are stated in U.S. dollars. The consolidated financial statements have been prepared on the basis of continuity of operations, realization of assets and the satisfaction of liabilities in the ordinary course of business.

Successful transition to attaining profitable operations is dependent upon achieving a level of revenues adequate to support the Company s cost structure. The Company plans to continue to fund its losses from operations and capital funding needs through the issuance of debt and/or equity or through collaborations or license agreements with other companies. Debt or equity financing may not be available on a timely basis on terms acceptable to the Company, or at all. If the Company is not able to secure adequate additional funding, the Company may be forced to make reductions in spending, extend payment terms with suppliers, liquidate assets where possible, or suspend or curtail planned programs. Any of these actions could materially harm the Company s business, results of operations and future prospects.

Guarantees and indemnifications

As permitted under Delaware law, the Company indemnifies its officers, directors, and employees for certain events or occurrences that happen by reason of the relationship with, or position held at, the Company. Through December 31, 2014, the Company had not experienced any losses related to these indemnification obligations, and no claims were outstanding. The Company does not expect significant claims related to these indemnification obligations and, consequently, concluded that the fair value of these obligations is negligible, and no related reserves were established.

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Use of estimates

The preparation of financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets, liabilities, revenue, and expenses, and the disclosure of contingent assets and liabilities as of and during the reporting period. The Company bases estimates and assumptions on historical experience when available and on various factors that it believes to be reasonable under the circumstances. Significant estimates relied upon in preparing the accompanying consolidated financial statements related to revenue recognition, the fair value of common stock and other equity instruments, accounting for stock-based compensation, present value of long-term purchase obligation, income taxes, useful lives of long-lived assets, and accounting for certain accruals. The Company assesses the above estimates on an ongoing basis; however, actual results could materially differ from those estimates.

Unaudited pro forma financial information

The unaudited pro forma consolidated balance sheet information at December 31, 2014 has been prepared to reflect the automatic conversion of all shares of redeemable convertible preferred stock outstanding at December 31, 2014 into 12,466,531 shares of common stock as if a proposed initial public offering had occurred on December 31, 2014. For purposes of pro forma basic and diluted net loss per share attributable to common stockholders, all shares of redeemable convertible preferred stock have been treated as if they have been converted to common stock in all periods in which such shares were outstanding. Accordingly, the pro forma basic and diluted loss per share attributable to common stockholders do not include the effects of the accretion of redeemable convertible preferred stock to redemption value.

2. Summary of Significant Accounting Policies

Principles of consolidation

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

Foreign currency translation

The Company uses the U.S. dollar as its functional currency. Monetary assets and liabilities denominated in foreign currency are remeasured at current rates and non-monetary assets denominated in foreign currency are recorded at historical exchange rates. Realized and unrealized exchange gains or losses from transactions and remeasurement adjustments are reflected in other income (expense), net, in the accompanying consolidated statements of operations.

Comprehensive income (loss)

Net income (loss) equals comprehensive income (loss) for all periods presented; therefore, a separate consolidated statement of comprehensive income (loss) is not included in the accompanying consolidated financial statements.

Segment information

Operating segments are identified as components of an enterprise about which separate discrete financial information is available for evaluation by the chief operating decision maker, the Company s Chief Executive Officer, in making decisions regarding resource allocation and assessing performance. The Company views its operations and manages its business in one operating segment.

Other assets

Other assets consist of long-term restricted deposits and prepayments. Long-term restricted deposits represent interest-bearing money market accounts held as a security deposit against a bank guarantee issued with respect to the Company s leased laboratory and office space in Israel.

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Concentrations of credit risk

Financial instruments that potentially subject the Company to significant concentration of credit risk consist primarily of cash and long-term restricted deposits. Periodically, the Company maintains deposits in financial institutions in excess of government insured limits. Management believes that the Company is not exposed to significant credit risk as the Company s deposits are held at financial institutions that management believes to be of high credit quality and the Company has not experienced any losses in these deposits.

Property and equipment

Property and equipment are stated at cost, net of accumulated depreciation and amortization. Expenditures for maintenance and repairs are charged to operations as incurred, whereas major betterments are capitalized as additions to property and equipment. Depreciation and amortization are recorded using the straight-line method over the estimated useful lives of the assets, as follows:

Asset Category	Estimated Useful Lives
Computer equipment and software	3 years
Office furniture and equipment	7 17 years (mainly 7)
Laboratory equipment	7 17 years (mainly 10)
Leasehold improvements	The lesser of lease term or estimated useful lives

Impairment of long-lived assets

The Company reviews long-lived assets for impairment whenever events or changes in circumstances indicate that the carrying amount of the asset may not be recoverable. When such events occur, the Company compares the carrying amounts of the assets to their undiscounted expected future cash flows the assets are expected to generate and to be recognized. The amount of impairment loss to be recognized is the excess of the carrying value over the fair value of the related asset. For the years ended December 31, 2013 and 2014, no impairments have been recorded.

Financial instruments

The Company s financial instruments consist of accounts payable, accrued expenses, common stock warrants, and redeemable convertible preferred stock warrants. The carrying amounts of accounts payable and accrued expenses approximate their fair value due to the short-term nature of those financial instruments. Redeemable convertible preferred stock warrants are recorded at fair value.

Fair value measurements

The Company follows the guidance in Financial Accounting Standards Board (FASB) Accounting Standards Codification 820, *Fair Value Measurements and Disclosures*, which defines fair value and establishes a fair value hierarchy that prioritizes the inputs to valuation techniques used to measure fair value. The hierarchy gives the highest priority to unadjusted quoted prices in active markets for identical assets or liabilities (Level 1 measurements) and the lowest priority to unobservable inputs (Level 3 measurements). The three levels of the fair value hierarchy are described below:

Level 1 Inputs are quoted prices (unadjusted) in active markets for identical assets or liabilities that the reporting entity has the ability to access at the measurement date.

Level 2 Valuations based on quoted prices in markets that are not active or for which all significant inputs are observable, either directly or indirectly.

Level 3 Prices or valuations that require inputs that are both significant to the fair value measurement and unobservable.

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To the extent that valuation is based on models or inputs that are less observable or unobservable in the market, the determination of fair value requires more judgment. Accordingly, the degree of judgment exercised by the Company in determining fair value is greatest for instruments categorized in Level 3. A financial instrument s level within the fair value hierarchy is based on the lowest level of any input that is significant to the fair value measurement.

Fair value is a market-based measure considered from the perspective of a market participant rather than an entity-specific measure. Therefore, even when market assumptions are not readily available, the Company s own assumptions are set to reflect those that market participants would use in pricing the asset or liability at the measurement date. The Company uses prices and inputs that are current as of the measurement date, including during periods of market dislocation. Due to market conditions, the observability of prices and inputs may change for many instruments. These conditions may cause an instrument to be reclassified from one level to another.

Employment termination costs

The Company accrues employment termination liabilities when (a) management, having the authority to approve the action, commits to a plan of termination; (b) the plan identifies the number of employees to be terminated, their job classifications or functions, their locations, and the expected completion date; (c) the plan establishes the terms of the arrangement, including the benefits that employees will receive upon termination, in sufficient detail to enable employees to determine the type and amount of benefits they will receive upon involuntary termination; (d) it is unlikely that significant changes to the plan will be made or withdrawn; and (e) the plan has been communicated to the affected employees. When employees are required to render services beyond the minimum retention period through the involuntary termination date in order to receive the termination benefits, a liability is measured initially at the communication date based on the fair value of the liability, and is recognized ratably over the future service period through expected termination date. The Company reverses the liability when events or circumstances occur that discharge or remove its responsibility to settle the termination liability.

Revenue recognition

Revenue is recognized when the four basic criteria of revenue recognition are met: (1) persuasive evidence that an arrangement exists, (2) delivery has occurred or services have been rendered, (3) the fee is fixed or determinable, and (4) collectability is reasonably assured. When one or more of the revenue recognition criteria are not met, the Company defers the recognition of revenue and records deferred revenue until such time that all criteria are met. For the years ending December 31, 2013 and 2014, the Company s revenue was derived from our now terminated license agreement (see Note 6). The terms of the agreement include a non-refundable upfront fee; contingent development, commercial, and clinical milestone payments; reimbursement of certain research and development costs; and royalty payments on sales.

Revenue arrangements with multiple elements are divided into separate units of accounting if certain criteria are met, including whether the delivered element has stand-alone value to the customer. When deliverables are separable, consideration received is allocated to the separate units of accounting based on the relative selling price of each deliverable and the appropriate revenue recognition principles are applied to each unit.

The Company recognizes revenue using the proportional performance method when services are rendered. Under the proportional performance method, revenue is recognized based on costs incurred to date as a percentage of total estimated cost to complete.

At the inception of the license agreement, the Company evaluates whether each milestone is substantive on the basis of the contingent nature of the milestone. This evaluation includes an assessment of whether: (a) the consideration is

commensurate with either the Company s performance to achieve the milestone or the enhancement of the value of the delivered items as a result of a specific outcome from the Company s

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performance to achieve the milestone; (b) the consideration relates solely to past performance; and (c) the consideration is reasonable relative to all of the deliverables and payment terms within the arrangement. In making this assessment, the Company evaluates factors such as the clinical, regulatory, commercial and other risks that must be overcome to achieve the respective milestone, the level of effort and investment required, and whether the milestone consideration is reasonable relative to all deliverables and payment terms in the arrangement. The Company recognizes revenues related to substantive milestones in full in the period in which the substantive milestone is achieved.

The Company recognizes royalty revenue, if any, based upon actual and estimated net sales by the licensee of licensed products in licensed territories and in the period the sales occur.

Long-term purchase obligation

Long-term purchase obligation, included within long-term liabilities, represents aggregate amounts payable for the purchases of certain active pharmaceutical ingredient (API) supplies and a trade name for the drug pursuant to an agreement entered into following the termination of the license agreement (see Note 6). The amount is payable in three equal annual amounts and is recorded at its present value. The difference between the aggregate purchase price and the present value of the installment payments represents the interest component of the financing arrangement and is accreted over the payment term and classified as interest expense. Costs associated with the purchase of API were charged to research and development, and costs associated with the trade name were charged to general and administrative in the accompanying consolidated statements of operations.

Research and development

Research and development costs are expensed as incurred. Research and development costs include payroll and personnel expense, consulting costs, external contract research and development expenses, raw materials, drug product manufacturing costs, and allocated overhead including depreciation and amortization, rent, and utilities. Research and development costs that are paid in advance of performance are capitalized as a prepaid expense and amortized over the service period as the services are provided.

Clinical trial costs

Clinical trial costs are a component of research and development expenses. The Company accrues and expenses clinical trial activities performed by third parties on an evaluation of the progress to completion of specific tasks using data such as patient enrollment, clinical site activation, and other information provided to the Company by its vendors.

Patent costs

Patent costs are expensed as incurred as their realization is uncertain. These costs are classified as general and administrative in the accompanying consolidated statements of operations.

Redeemable convertible preferred stock

The Company classifies redeemable convertible preferred stock as temporary equity in the accompanying consolidated balance sheets due to redemption rights granted to the holders that are outside of the Company s control. The Company recorded redeemable convertible stock initially at the original issuance price net of issuance costs and discounts, if any, according to relative fair value method. When the initial recorded amount is less than the redemption value, the Company accretes the recorded amount up to the redemption value over the redemption period using the

effective interest method, plus dividends expected to be paid upon redemption, if any. The Company accretes the deemed liquidation upon the occurrence of any such event. On the effective date of a Qualified IPO, as defined in the Company s certificate of incorporation, the redeemable convertible preferred stock will automatically convert into common stock.

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Warrants

The Company issued common stock warrants to investors and redeemable convertible preferred stock warrants to its lender. Common stock warrants were initially recorded based on their relative fair value in relationship to the total fair value of the hybrid debt or equity instruments. Redeemable convertible preferred stock warrants were initially recorded at fair value.

Series C redeemable convertible preferred stock (Series C preferred) warrants issued in connection with a loan agreement (see Note 7) were classified as liabilities and were initially recorded at fair value and remeasured at each period end while these instruments were outstanding. Changes in fair value were recognized in other expenses, net in the consolidated statements of operations. The warrant liabilities were valued using a Black-Scholes option-pricing model (Black-Scholes).

Common stock warrants issued in connection with the issuance of redeemable convertible preferred stock (see Note 8) were classified as a component of stockholders equity because they are free standing financial instruments that are legally detachable and separately exercisable from the redeemable convertible preferred stock, are contingently exercisable, do not embody an obligation for the Company to repurchase its own shares, and permit the holders to receive a fixed number of common shares upon exercise. In addition, the common stock warrants require physical settlement and do not provide any guarantee of value or return. Common stock warrants were initially recorded at their relative fair value and were not subsequently remeasured. Common stock warrants were valued using Black-Scholes.

Stock-based compensation

The Company accounts for all stock-based compensation granted to employees and nonemployees using a fair value method. Stock-based compensation is measured at the grant date fair value of employee stock option grants and is recognized over the requisite service period of the awards, usually the vesting period, on a straight-line basis, net of estimated forfeitures. Stock-based compensation awards to nonemployees are subject to revaluation over their vesting terms. For performance based awards where the vesting of the options may be accelerated upon the achievement of certain milestone performance, vesting and the related stock-based compensation is recognized as an expense when the achievement of the milestone is probable over the requisite service period.

For modification of stock compensation awards, the Company records the incremental fair value of the modified award as stock-based compensation on the date of modification for vested awards or over the remaining vesting period for unvested awards. The incremental compensation is the excess of the fair value of the modified award on the date of modification over the fair value of the original award immediately before the modification.

The Company records estimated forfeitures at the time of grant. To the extent that actual forfeitures differ from the Company s estimates, the differences are recorded as a cumulative adjustment in the period the estimates were adjusted. Stock-based compensation expense recognized in the consolidated financial statements is based on awards that are ultimately expected to vest.

Income taxes

The consolidated financial statements reflect provisions for federal, state, local and foreign income taxes. Deferred tax assets and liabilities represent future tax consequences of temporary differences between the financial statement carrying amounts and the tax basis of assets and liabilities and for loss carryforwards using enacted tax rates expected to be in effect in the years in which the differences reverse. A valuation allowance is recorded when it is more likely

than not that some or all of the deferred tax assets will not be realized.

The Company determines whether it is more likely than not that a tax position will be sustained upon examination. If it is not more likely than not that a position will be sustained, none of the benefit attributable to

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the position is recognized. The tax benefit to be recognized for any tax position that meets the more-likely-than-not recognition threshold is calculated as the largest amount that is more than 50% likely of being realized upon resolution of the contingency. The Company accounts for interest and penalties related to uncertain tax positions as part of its other expenses.

Contingent liabilities

The Company accounts for its contingent liabilities in accordance with ASC No. 450, *Contingencies* . A provision is recorded when it is both probable that a liability has been incurred and the amount of the loss can be reasonably estimated. With respect to legal matters, provisions are reviewed and adjusted to reflect the impact of negotiations, estimated settlements, legal rulings, advice of legal counsel and other information and events pertaining to a particular matter. As of December 31, 2013 and 2014, the Company is not a party to any ligation that could have a material adverse effect on the Company s business, financial position, results of operations or cash flows.

Net loss per share attributable to common stockholders and unaudited pro forma net loss per share attributable to common stockholders

The Company computes basic net loss per share attributable to common stockholders by dividing net loss attributable to common stockholders by the weighted average number of common shares outstanding for the period. Net loss attributable to common stockholders and participating redeemable convertible preferred stock is allocated to each share on an as-converted basis as if all of the net loss for the period had been distributed. During periods in which the Company incurred a net loss, the Company allocates no net loss to participating securities because they do not have a contractual obligation to share in the net loss of the Company. The Company computes diluted net loss per common share after giving consideration to all potentially dilutive common shares, including stock options, and warrants outstanding during the period except where the effect of such non-participating securities would be antidilutive.

Recently issued accounting pronouncements

In May 2014, FASB issued Accounting Standards Update (ASU) No. 2014-09, *Revenue from Contracts with Customers* (ASU 2014-09), which amends the guidance for revenue recognition to replace numerous industry-specific requirements. ASU 2014-09 implements a five-step process for customer contract revenue recognition that focuses on transfer of control, as opposed to transfer of risk and rewards. ASU 2014-09 also requires enhanced disclosures regarding the nature, amount, timing, and uncertainty of revenues and cash flows from contracts with customers. Other major provisions include ensuring the time value of money is considered in the transaction price, and allowing estimates of variable consideration to be recognized before contingencies are resolved in certain circumstances. The amendments in ASU 2014-09 are effective for reporting periods beginning after December 15, 2016, and early adoption is not permitted. Entities can transition to the standard either retrospectively or as a cumulative-effect adjustment as of the date of adoption. The Company is currently in the process of evaluating the effect the adoption of ASU 2014-09 may have on its consolidated financial statements.

In August 2014, the FASB issued ASU No. 2014-15, *Disclosure of Uncertainties about an Entity s Ability to Continue as a Going Concern* (ASU 2014-15). ASU 2014-15 requires management to assess an entity s ability to continue as a going concern and to provide related disclosures in certain circumstances. The requirements of ASU 2014-15 will be effective for the annual financial statement period beginning after December 15, 2016, with early adoption permitted. The Company is currently in the process of evaluating the impact of adopting ASU 2015-15.

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3. Net Loss Per Share Attributable to Common Stockholders

Basic net loss per share attributable to common stockholders is computed by dividing the net loss attributable to common stockholder by the weighted-average common shares outstanding for the period. Because the Company has reported net loss attributable to common stockholders for the years ended December 31, 2013 and 2014, basic and diluted net loss per share attributable to common stockholders are the same as basic net loss per share attributable to common stockholders for those periods.

All redeemable convertible preferred stock, common stock warrants, and stock options have been excluded from the computation of diluted weighted-average shares outstanding because such securities would have an antidilutive impact due to net losses reported during 2013 and 2014.

The unaudited pro forma basic and diluted net loss per share attributable to common stockholders for the year ended December 31, 2014 has been computed using the weighted-average common shares outstanding after giving pro forma effect to the automatic conversion of all shares of redeemable convertible preferred stock into shares of common stock as if such conversions had occurred at the beginning of 2014 or the date of original issuance, if later.

Unaudited pro forma basic and diluted net loss per share attributable to common stockholders are computed as follows:

	Year Ended December 31, 2014 (unaudited)
Numerator Net loss attributable to common stockholders, basic and diluted	$ (2,010,529)
Denominator:	
Weighted-average common shares outstanding, basic and diluted	44,017
Adjustment for assumed effect of conversion of redeemable convertible preferred stock	8,920,018
Pro forma weighted average common shares outstanding, basic and diluted	8,964,035
Pro forma net loss per share, basic and diluted	$ (0.22)

4. Property and Equipment

Property and equipment consists of the following:

	December 31,	
	2013	2014
Computer equipment and software	$ 174,666	$ 131,969

Office furniture and equipment	150,842	114,958
Laboratory equipment	1,511,633	1,396,129
Leasehold improvements	552,381	333,740
Property and equipment, at cost	2,429,522	1,976,796
Less accumulated depreciation and amortization	1,333,323	1,361,554
Property and equipment, net	$ 1,056,199	$ 615,242

Depreciation and amortization expense for the years ended December 31, 2013 and 2014 was $321,582 and $272,030, respectively.

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5. Accrued Expenses and Other Current Liabilities

Accrued expenses and other current liabilities consist of the following:

	December 31,	
	2013	2014
Accrued professional fees	$ 95,866	$ 373,727
Accrued research and development expenses	6,998,971	3,028,389
Accrued payroll and employee benefits	2,046,809	598,178
Accrued income taxes	100,543	
Total accrued expenses and other current liabilities	$ 9,242,189	$ 4,000,294

In March 2013, following the signing of the Roche license agreement, discussed in detail in Note 6 below, and in anticipation of transferring the Company s intellectual property related to oral octreotide to Roche, management and the board of directors approved a special severance arrangement for certain employees of Chiasma (Israel) Ltd. who were identified for termination. These employees were entitled to a one-time payment upon their involuntary termination by the Company. No payment would be made for voluntary terminations or in the event the Company canceled the employee termination plan. Because the affected employees were required to continue providing services through the termination date in order to receive payment, the Company recorded the fair value of the termination payments over the period from the date the plans were approved and communicated to the affected employees through the expected termination date. The employee termination process was expected to be completed within one year.

The Company estimated the aggregate one-time termination benefit to be $1,847,172, which approximated the fair value of the liability on the day the termination plan was approved and communicated to affected employees. During 2013 and 2014, the Company paid a total of $640,219 and $480,483, respectively, of special severance arrangements to departing employees. As of December 31, 2013, $1,206,953 was recorded as termination liability. In July 2014 following Roche s decision to terminate the license agreement, the Company canceled the employee termination plan. Accordingly, with the exception of one employee, liabilities previously recorded under the involuntary termination plan were reversed. As of December 31, 2014, a balance of $11,800 remained as a component of accrued expenses on the consolidated balance sheets and represented one employee who remained earmarked for involuntary termination.

A summary of the termination liability for the years ended December 31, 2013 and 2014 is as follows:

	Year Ended December 31,	
	2013	2014
Employee termination accrual, beginning of year	$	$ 1,206,953
Charges	1,847,172	648,847
Arrangements	(640,219)	(480,483)
Reversals		(1,361,518)
Employee termination accrual, end of year	$ 1,206,953	$ 11,800

During the year ended December 31, 2013, the Company recorded $1,490,136 of termination costs as research and development expenses and $357,036 as general and administrative expenses, respectively. During the year ended December 31, 2014, the Company recorded $576,534 of net reversals of the termination liability as research and development expenses and $138,137 as general and administrative expenses, respectively.

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6. License Agreement

In December 2012, the Company signed a license agreement with F. Hoffmann-La Roche Ltd. and Hoffmann-La Roche Inc. (collectively Roche), which was effective in January 2013, and granted Roche an exclusive, non-transferable license to the Company s intellectual property related to the oral octreotide. Under the terms of the agreement, Roche obtained worldwide rights to research, develop, make, import, export, sell, market or distribute the commercial product. The Company retained certain research and development activities under a joint development plan. The Company retained all rights to the intellectual property contained in the agreement. The agreement provided for an upfront payment of $65,000,000, future consideration of up to $530,000,000 in development and commercial milestones, and the right to receive tiered, double-digit royalties on net sales of oral octreotide.

The Company s total service obligations of $85,000,000 were recognized over the expected service period using the proportional performance method of revenue recognition. During the year ended December 31, 2013, the Company received a total of $75,000,000 from Roche related to the license agreement, which included the upfront payment of $65,000,000 and the first milestone payment of $10,000,000. An additional $10,000,000 was received during January 2014 related to the second milestone payment. The Company evaluated the transaction and concluded that the license right did not have stand-alone value. As a result, the arrangement primarily represented a research and development arrangement provided by the Company and all elements of the arrangement were considered one unit of accounting. In 2013, the Company recognized $73,134,205 as revenue for services provided during the year using the proportional performance method based on costs included in research and development expenses. Deferred revenue and customer advances at December 31, 2013 totaled $2,883,295 which included $1,017,500 received from Roche for expected reimbursable costs that had not yet been incurred by the Company.

In April 2014, the Company and Roche entered into a joint development plan. Under the plan, the Company was to receive an aggregate amount of $2,678,000 covering certain costs incurred by the Company to be payable in three installments. During 2014, the Company received the first installment of $1,300,000.

In July 2014, Roche terminated the license agreement. Upon termination, Roche returned all rights and documentation granted under the agreement to the Company. The Company was relieved of further obligations under the agreement and recognized the remaining revenue of $13,165,795 as revenues. Subsequent to the termination, the Company purchased from Roche active pharmaceutical ingredient (API) supplies to continue the development and manufacturing of oral octreotide as well as Roche s proposed trade name for oral octreotide for an aggregate amount of $5,100,000 payable in three equal annual installments of $1,700,000 in January 2016, January 2017 and January 2018. The difference between the aggregate purchase price and the present value of the installment payments represents the interest component of the financing arrangement and is being recorded as interest expense over the payment term. Other than these payments, the Company has no other financial and operational obligations to Roche. Following the termination of the license agreement, the Company is not entitled to further payments from Roche, Roche has no remaining rights to oral octreotide and the Company retains all rights to oral octreotide and all related intellectual property.

7. Long-term Debt

The Company had a secured loan agreement with General Electric Capital Corporation to borrow up to $12,000,000. Amounts borrowed under the loan bore interest at 10.85% per annum and matured in 42 months. In February 2013, the Company prepaid the outstanding principal, accrued interest, and prepayment fees totaling $11,065,843. Following the repayment, the secured loan agreement was terminated and the Company was released of all security obligations and pledges. There were no outstanding borrowings or other credit facilities available to the Company at December 31, 2013 and 2014.

In connection with the loan, the Company issued to the lender warrants to purchase 480,000 shares of Series C preferred at an exercise price of $1.00 per share. The warrants were accounted for as a liability and carried at fair

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value with changes in fair value recorded in the consolidated statements of operations. In March 2013, the lender exercised the warrants on a cashless basis into 190,841 shares of Series C preferred calculated using the fair value of Series C preferred on the exercise date. The fair value of the warrants at the time of exercise was recorded as Series C preferred. The change in fair value of the warrants during 2013 through the time of exercise of $60,000 was recorded in the consolidated statements of operations as other expenses.

8. Warrants

In addition to the warrants described in Note 7, the following common stock warrants have been issued by the Company:

Issued In Connection With	Shares of Common Stock Underlying Warrants	Exercise Price Per Share	Issuance Date	Expiration Date
Series C preferred	54,752	$ 0.09	June 24, 2011	June 24, 2016
Series D redeemable convertible preferred stock, second closing	849,033	$ 0.09	October 22, 2012	October 22, 2022
Series D redeemable convertible preferred stock, third closing	849,033	$ 0.09	March 28, 2013	March 28, 2022
Series E redeemable convertible preferred stock	924,622	$ 9.13	December 15, 2014	December 15, 2024
Total	2,677,440			

A summary of warrant activity during 2013 and 2014 is as follows:

	Common Stock Warrants	Series C Preferred Warrants
Warrants outstanding, January 1, 2013	903,785	480,000
Issuances	849,033	
Exercises		(480,000)
Warrants outstanding, December 31, 2013	1,752,818	
Issuances	924,622	
Warrants outstanding, December 31, 2014	2,677,440	

The reconciliation of the fair value of Series C preferred warrants using Level 3 inputs is as follows:

Balance, January 1, 2013	$ 130,841
Increase in fair value recorded in financial expenses, net	60,000
Balance on March 27, 2013 immediately before exercising for Series C preferred	$ 190,841

The Series C preferred warrants were valued using Black-Scholes.

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9. Redeemable Convertible Preferred Stock

During the years ended December 2012 and 2013, the Company issued an aggregate of 38,504,439 shares of Series D redeemable convertible preferred stock (the Series D preferred) and warrants to purchase up to an aggregate of 1,698,066 shares of Common Stock at an exercise price of $ 0.09 per share (the Warrants), for aggregate gross proceeds of $38,504,439, of which $ 34,834,570 was allocated to the Series D preferred and $3,562,336 was allocated to the Warrants, net of issuance cost in the amount of $107,533. Since the Series D preferred was issued in conjunction with freestanding detachable warrants, the proceeds from the issuance were allocated to each freestanding instrument based on their relative fair value.

The Company accreted the discount amount due to the Warrants allocation and issuance cost, using the interest method, until August 2014 which was the earliest redemption date of the instrument according to the Company s certificate of incorporation then in effect.

In March 2013, the Company redeemed its Series B1 redeemable convertible preferred stock (Series B1 preferred), Series C preferred, and Series D preferred (collectively, the Original Preferred Stock) using proceeds received from the license agreement with Roche (see Note 6), which redemption was effected in accordance with the deemed liquidation provisions of the Company s certificate of incorporation then in effect. Pursuant to such deemed liquidation provisions, upon such an event the Series D preferred was entitled to a redemption amount equal to its original issuance price plus $38,504,439. Accordingly, the Company immediately recognized the change in the redemption value in the amount of $38,504,439 against accumulated deficit. The consideration for the redemption consisted of a cash payment of $54,954,694 and the issuance of 1,134,997 shares of Series B1 redeemable convertible preferred stock (Series B1 preferred), 40,430,250 shares of Series C redeemable convertible preferred stock (Series C preferred), and 38,504,439 shares of Series D redeemable convertible preferred stock (Series D preferred , and collectively with the Series B1 preferred and Series C preferred, the Prime Preferred Stock). The Prime Preferred Stock bears similar terms, rights and preferences as the Original Preferred Stock, other than changes to reflect redemption payment of Series D preferred described above. In addition, the holders of the Original Preferred Stock received rights to receive future contingent payments under the Roche license agreement. Upon termination of the license agreement, these rights were also terminated.

The initial carrying value of the Prime Preferred Stock equaled the carrying value of the Original Preferred Stock on the redemption date. The Company accreted the carrying value of the Series D preferred to its redemption value until August 2014, which was the earliest redemption date of the Series D preferred according to the Company s certificate of incorporation.

In December 2014, the Company issued 33,774,763 shares of Series E redeemable convertible preferred stock (Series E preferred) at $1.00 per share, resulting in gross proceeds of $33,774,763, with issuance costs of $150,982. In connection with the issuance of Series E preferred, the Company issued to the holders warrants to purchase 924,622 shares of the Company s common stock and allocated $773,534 of the net proceeds to the warrants based on their relative fair value on the issuance date which was accounted for as a discount on Series E preferred and recorded as additional paid-in capital.

The rights, preferences, and privileges of Series E preferred and Prime Preferred Stock are as follows:

Voting

The holders of Series E preferred, Series D preferred and Series C preferred have full voting rights and powers similar to the rights and powers of the common stockholders on an as-converted basis. The holders of Series B1 preferred are

not entitled any voting rights.

Dividends

Holders of all series of redeemable convertible preferred stock are entitled to receive dividends at 8% per annum of their respective original issuance price, payable when and if declared by the Company s board of directors.

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Optional conversion

Each share of Series E preferred, Series C preferred and Series B1 preferred are convertible at the option of the holders thereof into common stock on a 1-for-9.132 (after reverse stock split) basis. Shares of Series D preferred are not convertible at the option of the holder.

Mandatory conversion

Upon either: (i) the closing of the sale of shares of the Company s common stock to the public at a price of at least $1.50 per share in an underwritten public offering pursuant to an effective registration statement under the Security Act of 1933, as amended, resulting in at least $40,000,000 of gross proceeds to the Company (a Qualified IPO), or (ii) the date and time, or the occurrence of an event, specified by vote or written consent of the holders of more than 50% of the then outstanding shares of Series E preferred and Series C preferred voting together as a single class on an as-converted basis, all outstanding shares of redeemable convertible preferred stock will automatically be converted into fully paid and non-assessable shares of common stock on a 1-for-9.132 (after reverse stock split) basis.

Liquidation preference

In the event of any liquidation, dissolution, or winding up of the Company (liquidation event) or a deemed liquidation event, as defined in the Company s certificate of incorporation, the holders of Series E preferred are entitled to receive a liquidation amount of $1.00 per share, plus any dividends declared but unpaid, prior to any distribution of assets of the Company to the holders of Prime Preferred Stock. In the event the assets of the Company available for distribution are insufficient to pay the full amount to which the holders of Series E preferred are entitled, the holders of Series E preferred will share ratably any assets available for distribution in proportion to the relative shares held by each.

After full payment of Series E preferred preferential amounts and in preference to the distribution of available assets to the holders of Series C preferred and Series B1 preferred, holders of Series D preferred are entitled to receive the greater of (1) $0.57 per share, plus any dividends declared but unpaid, or (2) an amount equal to the excess of the liquidation amount payable to common stockholders over $0.43 per share.

After full payment of the Series E preferred preferential amounts and Series D preferred preferential amounts and prior to any distribution of assets of the Company to the holders of Series B1 preferred and common stock, holders of Series C preferred are entitled to receive a liquidation amount of $1.00 per share, plus any dividends declared but unpaid.

The holders of Series B1 preferred are entitled to receive from available assets, after payment to the Series E preferred, Series D preferred, and Series C preferred and prior to any distribution of assets of the Company to the common stockholders, an amount of $6.36 per share, plus any dividends declared but unpaid.

After the payment of all preferential amounts required to be paid to the holders of Series E preferred, Series D preferred, Series C preferred, and Series B preferred, any remaining assets of the Company available for distribution shall be distributed among the common stockholders, Series C preferred, and Series E preferred pro-rata on an as converted to common stock basis until the amount payable to the common stockholders equals $0.43 per share. Thereafter, any remaining assets of the Company available for distribution are to be distributed among the common stockholders, Series C preferred, Series D preferred, and Series E preferred pro-rata on an as-converted to common stock basis.

Redemption rights

Unless prohibited by Delaware law governing distributions to stockholders, redeemable convertible preferred shares are redeemable on or after December 15, 2017 upon request by more than 60% of the holders of the

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Series E preferred, Series D preferred and Series C preferred voting together as a single class. Within 60 days of a notice of redemption, shares of Series C preferred, as determined by the board of directors, will be redeemed at a price equal to the greater of (1) $1.00 per share plus any dividends declared but unpaid, or (2) the fair value of a share of Series C preferred as determined by the board of directors. Shares of Series D preferred are redeemable at a price equal to the greater of (1) $0.57 plus any dividends declared but unpaid, or (2) the fair value of a share of Series D preferred as determined by the board of directors. Shares of Series E preferred will be redeemed at a price equal to the greater of (1) $1.00 per share, plus any dividends declared but unpaid, or (2) the fair value of a share of Series E preferred, as determined by the board of directors. Shares of Series B1 preferred will be redeemed at a price equal to $6.36, plus any dividends declared but unpaid.

The Company has the right to redeem shares of Series B1 preferred at any time upon the delivery of a written redemption notice, in whole or in part, at a price of $6.36 per share.

10. Common Stock

On June 30, 2015, the board of directors approved a 1-for-9.132 reverse stock split. As a result, all common stock, warrants and options for common stock, exercise price and net income (loss) per share amounts were adjusted retroactively for all periods presented in these financial statements. Additionally, the conversion price of each share of the Company s redeemable convertible preferred stock was adjusted to reflect this reverse stock split.

Common stockholders are entitled to one vote for each share of common stock held at all meetings of stockholders. Common stockholders are entitled to receive dividends declared out of funds legally available, subject to the payment in full of all preferential dividends to which the holders of the redeemable convertible preferred stock are entitled. In the event of any voluntary or involuntary liquidation, dissolution or winding up of the Company, after the payment of all preferential amounts to the holders of redeemable convertible preferred stock are entitled, the common stockholders share ratably in the remaining assets of the Company available for distribution.

The Company has reserved the following shares of common stock for future issuance:

	December 31, 2014
Conversion of Series B1 preferred	124,282
Conversion of Series C preferred	4,427,314
Conversion of Series D preferred	4,216,428
Conversion of Series E preferred	3,698,507
Exercises of common stock warrants	2,677,440
Exercises of stock options	1,501,062
Conversion of shares of Series C preferred available for future issuance	31,664
Conversion of shares of Series E preferred available for future issuance	1,229,219
Shares available for future stock incentive plan awards	194,335
Total	18,100,251

11. Stock Incentive Plan

In 2008, the Company s board of directors adopted the 2008 Stock Incentive Plan (the 2008 Plan), which provided for the grant of incentive stock options, nonqualified stock options, and restricted stock to employees, directors, and nonemployees of the Company. Stock option awards generally vest based on the grantee s continued service with the Company during a specified period following grant as determined by the board of directors and expire 10 years from the grant date. Option awards granted generally vest over four years, but vesting conditions can vary at the discretion of the Company s board of directors. A total of 1,722,512 shares of common stock were authorized for issuance in accordance with the provisions of the 2008 Plan, of which 27,115 were exercised, and 194,335 shares available for future awards at December 31, 2014.

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Stock options

The fair value of each stock option issued to employees was estimated at the date of grant using Black-Scholes with the following weighted-average assumptions:

	Year Ended December 31,	
	2013	2014
Expected volatility	85%	80%
Expected term (years)	6.25	6.25
Risk-free interest rate	1.08%	1.79%
Expected dividend yield	0%	0%

Exercise price: In determining the exercise prices for stock options granted, the board of directors considered the fair value of common stock as of each grant date. The fair value of common stock underlying the stock options was determined by the board of directors at each award grant date based upon a variety of factors, including the results obtained from independent third-party valuations, the Company s financial position and historical financial performance, the status of technological developments within the Company s products, the composition and ability of the current clinical and management team, an evaluation or benchmark of the Company s competition, the current business climate in the marketplace, the illiquid nature of common stock, arm s length sales of the Company s capital stock, the effect of the rights and preferences of the redeemable convertible preferred stockholders, and the prospects of a liquidity event, among others.

Expected volatility: As the Company is privately owned, there is not sufficient historical volatility for the expected term of the stock options. Therefore, the Company uses an average historical share price volatility based on an analysis of reported data for a peer group of comparable publicly traded companies which were selected based upon industry similarities.

Expected term (years): Expected term represents the period that the Company s option grants are expected to be outstanding. There is not sufficient historical share exercise data to calculate the expected term of the stock options. Therefore, the Company elected to utilize the simplified method to value option grants. Under this approach, the weighted-average expected life is presumed to be the average of the vesting term and the contractual term of the option.

Risk-free interest rate: The Company determined the risk-free interest rate by using a weighted-average equivalent to the expected term based on the U.S. Treasury yield curve in effect as of the date of grant.

Expected dividend yield: The Company does not anticipate paying any dividends in the foreseeable future.

Forfeitures: Forfeitures are estimated at the time of grant and revised, if necessary, in subsequent periods if actual forfeitures differ from estimates.

The fair value of each nonemployee stock option is estimated at the date of grant using Black-Scholes with assumptions generally consistent with those used for employee stock options, with the exception of expected term, which is the contractual life.

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A summary of stock option activity under the 2008 Plan for employees and non-employees is presented below:

	Number of Stock Options	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term (Years)	Aggregate Intrinsic Value
Outstanding, January 1, 2014	1,130,509	$ 2.18		
Granted	689,642	$ 3.19		
Exercised	(768)	$ 2.20		
Forfeited/Expired	(318,321)	$ 2.11		
Outstanding, December 31, 2014	1,501,062	$ 2.04	7.02	$ 2,466,647
Exercisable, December 31, 2014	706,659	$ 1.31	4.40	$ 1,700,242
Vested and expected to vest, December 31, 2014	1,501,062	$ 2.04	7.02	$ 2,466,647

The weighted-average grant date per-share fair value of stock options granted during 2013 and 2014 were $3.20 and $2.63, respectively. The aggregate intrinsic value of stock options exercised during the years ended December 2013 and 2014 was $28,365 and $1,231, respectively. At December 31, 2014, there was $2,046,659 of unrecognized compensation cost related to stock options, which is expected to be recognized over a weighted-average period of 3.37 years.

Stock-based compensation expense is classified in the consolidated statements of operations as follows:

	Year Ended December 31,	
	2013	2014
Research and development	$ 297,550	$ 424,218
General and administrative	447,792	332,277
Total	$ 745,342	$ 756,495

During 2013, the Company s board of directors modified the terms of the then outstanding stock options by (a) extending exercisability of the options to the second anniversary upon termination of employment or services, and (b) accelerating the vesting of stock options upon Roche filing for regulatory approval under the license agreement. In addition, during 2014, the board of directors modified the exercise price of certain stock options granted to employees and executives. The incremental compensation expenses, resulting from comparing the fair value of stock options immediately before and immediately after the modifications, for the years ended December 31, 2013 and 2014 totaled $156,180 and $369,700, respectively. In 2013, $39,614 of the incremental compensation expenses was classified as research and development expense and $116,566 was classified as general and administrative expense. In 2014, $298,995 of the incremental compensation expenses was classified as research and development expense and $70,805

was classified as general and administrative expense in the accompanying consolidated financial statements.

12. Income Taxes

Income (loss) before provision for income taxes consists of the following:

	Year Ended December 31,	
	2013	2014
Domestic	$ 37,009,511	$ (1,492,573)
Foreign	395,959	(342,335)
Total	$ 37,405,470	$ (1,834,908)

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The components of income tax provision (benefit) consist of the following:

	Year Ended December 31,	
	2013	2014
Current provision for income taxes:		
U.S. federal	$ 1,023,829	$ 1,234
Foreign	257,770	146,706
Total current provision for income taxes	1,281,599	147,940
Deferred tax (benefit) provision foreign	(57,171)	27,681
Total provision for income taxes	$ 1,224,428	$ 175,621

A reconciliation setting forth the differences between the effective tax rates of the Company and the U.S. federal statutory tax rate is as follows:

	Year Ended December 31,	
	2013	2014
U.S. federal tax provision at statutory rate	34.00%	34.00%
Foreign rate differences	(0.17)	1.09
Non-deductible foreign stock compensation	0.26	(10.88)
Effect of other permanent differences	0.40	(4.30)
Changes in state apportionment, net of federal impact	0.06	9.94
Uncertain tax positions	0.25	(8.00)
Change in valuation allowance	(32.97)	(34.06)
Other adjustments	1.47	2.64
Effective tax rate	3.30%	(9.57)%

During 2013, the Company generated taxable income in the United States which was reduced fully by net operating loss (NOL) carryforwards for federal tax purposes. However, due to NOL carryforward limitations under the alternative minimum tax regime, the Company incurred $1,023,829 of alternative minimum tax liability.

At December 31, 2013 and 2014, refundable income taxes totaling $96,171 and $95,065, respectively, were classified as prepaid expenses and other current assets in the consolidated balance sheets. Accrued income taxes totaling $100,543 was classified in accrued expenses and other current liabilities at December 31, 2013. There were no accrued income taxes at December 31, 2014.

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Deferred income taxes reflect the net tax effects of temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income and for tax carryforwards. Significant components of the Company s deferred tax assets and liabilities are as follows:

	Year Ended December 31, 2013	2014
Deferred tax assets:		
Federal net operating loss carryforwards	$ 4,215,575	$ 7,789,503
Tax credit carryforwards	1,023,829	1,023,829
Intangible and other related assets	290,768	277,636
Accrued expenses	881,251	1,865,619
Deferred revenue	4,034,370	
Stock compensation	269,415	329,547
Other	55,871	79,534
Total deferred tax assets	10,771,079	11,365,668
Valuation allowance	(10,703,770)	(11,326,041)
Net deferred tax assets	$ 67,309	$ 39,627

When realization of a deferred tax asset is more likely than not to occur, the benefit related to the deductible temporary differences attributable to operations is recognized as a reduction of income tax expense. Valuation allowances are provided against deferred tax assets when, based on all available evidence, it is considered more likely than not that some portion or all of the recorded deferred tax assets will not be realized in future periods. The Company cannot be certain that future U.S. taxable income will be sufficient to realize its deferred tax assets. Accordingly, a full valuation allowance has been provided against its U.S. net deferred tax assets. The valuation allowance increased $622,271 in 2014 primarily as a result of an increase in NOL carryforwards. The Company continues to monitor the need for a valuation allowance based on the profitability of its future operations.

At December 31, 2014, the Company had federal NOL carryforwards totaling approximately $22,829,000 that expire at various dates through 2034. At December 31, 2014, the Company had Israeli NOL carryforwards totaling approximately $551,000 that have an indefinite carryforward period. At December 31, 2014, the Company had approximately $1,000,000 of federal alternative minimum tax credit carryforwards that do not expire.

Under Section 382 of the Internal Revenue Code of 1986, as amended, substantial changes in the Company s ownership may limit the amount of NOL carryforwards that can be utilized annually in the future to offset its U.S. federal taxable income. Specifically, this limitation may arise in the event of a cumulative change in ownership of the Company of more than 50% within any three-year period. Management has determined that the Company experienced an ownership change for purposes of Section 382 in August 2005 and May 2008. These ownership changes resulted in annual limitations to the amount of NOL carryforwards that can be utilized to offset future taxable income, if any, at the federal level. The annual limit is approximately $95,000 for 2014, and each year thereafter. These annual limitations resulted in the loss of the Company s ability to utilize approximately $8,900,000 in federal NOL carryforwards, which resulted in a write-off of approximately $3,000,000 of federal deferred tax assets prior to 2013.

The Company s Israeli subsidiary has been recognized as a research and development company by the Head of the Israeli Administration of Industrial Research and Development and is entitled to tax benefits by virtue of the

beneficiary enterprise status granted to part of its business activities under the Israeli Law for the Encouragement of Capital Investments 1959 (the Law). The tax benefits include reduced tax rates on the research and development portion of its income during the first ten years of the benefit period (commenced in 2008). The continued application of the tax benefits is subject to certain conditions as defined by Israeli law.

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The subsidiary has undistributed earnings of approximately $1,461,000 as of December 31, 2014, which is considered to be permanently reinvested in the operations of the subsidiary. At such time in the future as the Company may elect to distribute such earnings to the parent company, it could result in federal and Israeli tax liability.

The Company files income tax returns in the United States and in various U.S. states and Israel. The associated tax filings remain subject to examination by applicable tax authorities for a certain length of time following the tax year to which those filings relate. In the United States and Israel, the 2011 and subsequent tax years remain subject to examination by the applicable taxing authorities as of December 31, 2014. However, carryforward attributes that were generated prior to 2011 in the United States may still be adjusted upon examination by federal, state or local tax authorities if they either have been or will be used in a future period.

As of December 31, 2013 and 2014, the Company had provided a liability for $94,291 and $240,997, respectively, for uncertain tax positions related to various income tax matters which was classified as other long-term liabilities. For the years ended December 31, 2013 and 2104, the Company had provided for accrued interest related to uncertain tax positions of $2,413 and $2,707, respectively. These uncertain tax positions would impact the Company s effective tax rate, if recognized. The Company does not expect that the amounts of uncertain tax positions will change significantly within the next 12 months.

A reconciliation of uncertain tax positions is as follows:

	Year Ended December 31,	
	2013	2014
Balance at beginning of year	$	$ 96,704
Additions	96,704	149,412
Balance at end of year	$ 96,704	$ 246,116

The Company recognizes interest and penalties accrued related to uncertain tax positions as an other expense. To date, the Company has recognized $5,120 in interest and penalties related to uncertain tax positions.

13. Commitments and Contingencies

The Company has a long-term purchase obligation with respect to API and trade name, with payments and terms described in Note 6.

The Company leases laboratory and office space in Israel. Total rent expense for all operating leases in 2013 and 2014 was $340,258 and $305,158, respectively. As of December 31, 2014, future minimum lease payments of $155,444 are due in 2015. In conjunction with the lease, the Company provided a bank guarantee in the amount of $195,047 as a security deposit at December 31, 2014.

14. Related Party Transactions

In August 2014, the Company signed a consulting agreement with one of the Company s investors and a representative of this investor to serve as senior medical advisor. Costs incurred for services rendered by the senior medical advisor during 2014 totaling $128,200 were classified as research and development expenses with $75,000 in accrued expenses at December 31, 2014.

In October 2014, the Company granted its senior medical advisor options to purchase 122,605 shares of common stock at an exercise price of $2.74 per share.

In December 2014, the Company entered into a consulting agreement with a representative of another investor to provide financial and strategic consulting services to the Company. Fees incurred during 2014 totaling $62,500 were classified as general and administrative expenses. There were no unpaid balances as of December 31, 2014.

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15. Employee Benefit Plan

Pursuant to the Israeli Severance Pay Law 1963, Israeli employees are entitled to severance pay equal to one month s salary for each year of employment, or a portion thereof. The employees of Chiasma (Israel) Ltd. are included under Section 14 of the Severance Pay Law, under which these employees are entitled to monthly deposits, which relieve the Company from future obligations under this law. As a result, no assets or liabilities are recorded in the accompanying consolidated balance sheets. During the years ended December 31, 2013 and 2014, the Company recorded expenses of $234,640 and $199,744, respectively.

16. Other expenses, net

Other expenses, net is as follows:

	Year Ended December 31,	
	2013	2014
(Loss) gain on foreign currency transactions, net	$ (72,481)	$ 38,964
Interest income	4,535	2,518
Interest expense	(1,065,664)	(26,649)
Change in fair value of Series C redeemable convertible preferred stock warrant liability	(60,000)	
Other expenses	(14,672)	(19,285)
Total	$ (1,208,282)	$ (4,452)

17. Subsequent Events

The Company has evaluated subsequent events which may require adjustment to or disclosure in the consolidated financial statements through April 16, 2015, the date on which the December 31, 2014 consolidated financial statements were originally issued.

In February 2015, the Company increased the number of shares authorized under Series E preferred to a total of 80,774,458 and subsequently issued 35,948,023 shares of Series E preferred at $1.00 per share for gross proceeds of $35,948,023, with issuance costs of $250,677. In connection with the issuance of Series E preferred, the Company issued holders of Series E preferred warrants to purchase 984,116 shares of the Company s common stock, which is accounted for as a discount on the issuance of Series E preferred.

In February and April 2015, the board of directors approved the grant of options to purchase an aggregate of 1,629,878 shares of common stock to certain officers, directors, employees and a consultant.

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6,365,000 Shares

Common Stock

Prospectus

July 15, 2015

Barclays

Cowen and Company

William Blair

Oppenheimer & Co.

Through and including August 9, 2015 (the 25th day after the date of this prospectus), all dealers effecting transactions in these securities, whether or not participating in this offering, may be required to deliver a prospectus. This delivery requirement is in addition to the obligation of dealers to deliver a prospectus when acting as underwriters and with respect to their unsold allotments or subscriptions.