CHIASMA, INC
Form 10-Q
August 31, 2015
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UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

Form 10-Q

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

For the quarterly period ended June 30, 2015

OR

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

For the transition period from _____ to _____

Commission file number: 001-37500

Chiasma, Inc.

(Exact name of registrant as specified in its charter)

Delaware	**76-0722250**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**

60 Wells Avenue, Suite 102

Newton, Massachusetts 02459

(Address of principal executive office) (Zip Code)

Registrant s telephone number, including area code:

(617) 928-5300

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ¨ No x

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§ 232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes x No ¨

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

Large accelerated filer ¨	Accelerated filer ¨
Non-accelerated filer x (Do not check if a smaller reporting company)	Smaller reporting company ¨

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes ¨ No x

As of August 25, 2015, there were 23,930,199 shares of the registrant s Common Stock, $0.01 par value per share, outstanding.

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CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Quarterly Report on Form 10-Q 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, e expect, intend, may, plan, potentially, will, may, would, or the negative of these terms or other similar e intended to identify 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 Quarterly Report on Form 10-Q, regarding, among other things:

- the regulatory review process of our NDA for oral octreotide 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 planned 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; and

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

These risks are not exhaustive. Other sections of this Quarterly Report on Form 10-Q may include additional factors that could adversely impact our business and financial performance. Moreover, we operate in a very competitive and 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 Quarterly Report on Form 10-Q, 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 Quarterly Report on Form 10-Q completely and with the understanding that our actual future results may be materially different from what we expect. The forward-looking statements in this Quarterly Report on Form 10-Q represent our views as of the date of this Quarterly Report. 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 Quarterly Report on Form 10-Q.

Unless the context requires otherwise, references in this Quarterly Report on Form 10-Q to we, us , our and Chiasma refer to Chiasma, Inc. and our subsidiary. We own various U.S. federal trademark registrations and applications, and unregistered trademarks and service marks, including Chiasma, TPE , Mycapssa and our corporate logo. Other trademarks or service marks that may appear in this Quarterly Report on Form 10-Q are the property of their respective holders. For convenience, we do not use the ® and symbols in each instance in which one of our trademarks appears throughout this Quarterly Report on Form 10-Q, but this should not be construed as any indication that we will not assert, to the fullest extent under applicable law, our rights thereto.

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PART I FINANCIAL INFORMATION

Item 1. Financial Statements

Chiasma, Inc.

Condensed Consolidated Balance Sheets

	December 31, 2014 (audited)	June 30, 2015 (unaudited)
Assets		
Current assets:		
Cash	$ 40,160,435	$ 63,266,889
Prepaid expenses and other current assets	311,299	466,031
Total current assets	40,471,734	63,732,920
Property and equipment, net	615,242	570,644
Deferred offering costs		1,890,066
Other assets	311,730	327,248
Total assets	$ 41,398,706	$ 66,520,878
Liabilities and Stockholders Deficit		
Current liabilities:		
Accounts payable	$ 317,994	$ 1,165,602
Current maturities of long-term liabilities		1,700,000
Accrued expenses and other current liabilities	4,000,294	3,062,272
Total current liabilities	4,318,288	5,927,874
Long-term liabilities	4,612,450	3,534,577
Total liabilities	8,930,738	9,462,451
Redeemable convertible preferred stock, $0.01 par value:		
Series B1 preferred, 1,134,997 shares authorized, issued and outstanding at December 31, 2014 and June 30, 2015; aggregate liquidation preference and redemption value of $7,218,438 at June 30, 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 June 30, 2015; aggregate liquidation preference and redemption value of $40,430,250 at June 30, 2015	40,430,250	40,430,250
Series D preferred, 38,504,439 shares authorized, issued and outstanding at December 31, 2014 and June 30, 2015; aggregate liquidation preference and	22,054,186	22,054,186

redemption value of $22,054,186 at June 30, 2015		
Series E preferred, 45,000,000 and 80,774,458 shares authorized December 31, 2014 and June 30, 2015; respectively; 33,774,763 and 69,722,786 shares issued and outstanding at December 31, 2014 and June 30, 2015; respectively; aggregate liquidation preference and redemption value of $69,722,786 at June 30, 2015	32,857,713	67,357,255
Total redeemable convertible preferred stock	104,485,972	138,985,514
Stockholders deficit:		
Common stock, $0.01 par value, 175,000,000 and 250,000,000 shares authorized at December 31, 2014 and June 30, 2015; respectively; 44,326 and 206,631 shares issued and outstanding at December 31, 2014 and June 30, 2015; respectively;	443	2,066
Additional paid-in capital	9,489,627	11,595,958
Accumulated deficit	(81,508,074)	(93,525,111)
Total stockholders deficit	(72,018,004)	(81,927,087)
Total liabilities, redeemable convertible preferred stock and stockholders deficit	$ 41,398,706	$ 66,520,878

The accompanying notes are an integral part of these consolidated financial statements.

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Chiasma, Inc.

Condensed Consolidated Statements of Operations and Comprehensive Loss

(Unaudited)

	Three Months Ended June 30,		Six Months Ended June 30,	
	2014	2015	2014	2015
Revenue from license agreement	$ 5,987,848	$	$ 10,561,326	$
Operating Expenses:				
Research and development	1,200,533	4,158,749	2,850,078	6,377,535
Marketing, general and administrative	547,377	3,436,543	1,501,695	5,367,753
Total operating expenses	1,747,910	7,595,292	4,351,773	11,745,288
Income (loss) from operations	4,239,938	(7,595,292)	6,209,553	(11,745,288)
Other expense, net	39,795	108,796	64,634	198,278
Income (loss) before provision for income taxes	4,200,143	(7,704,088)	6,144,919	(11,943,566)
Provision for income taxes	194,361	68,741	65,102	73,471
Net income (loss)	4,005,782	(7,772,829)	6,079,817	(12,017,037)
Accretion of redeemable convertible preferred stock	(348,074)	(189,054)	(687,818)	(286,575)
Net income (loss) attributable to common stockholders	$ 3,657,708	$ (7,961,883)	$ 5,391,999	$ (12,303,612)
Net income (loss) per share attributable to common stockholders basic	$ 83.42	$ (50.36)	$ 123.38	$ (106.79)
Weighted-average common shares outstanding - basic	43,848	158,104	43,702	115,213
Net income (loss) per share attributable to common stockholders diluted	$ 0.36	$ (50.36)	$ 0.54	$ (106.79)
Weighted-average common shares outstanding - diluted	11,196,563	158,104	11,175,185	115,213

The accompanying notes are an integral part of these consolidated financial statements.

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Chiasma, Inc.

Condensed Consolidated Statement of Redeemable Convertible Preferred Stock and Stockholders Deficit

(Unaudited)

Redeemable Convertible Preferred Stock									Addi
Series C Preferred		Series D Preferred		Series E Preferred		Total	Common Stock		Pai
Shares	Amount	Shares	Amount	Shares	Amount	Amount	Shares	Amount	Ca
40,430,250	$ 40,430,250	38,504,439	$ 22,054,186	33,774,763	$ 32,857,713	$ 104,485,972	44,326	$ 443	$ 9,4
									8
							37,544	375	
							124,761	1,248	
				35,948,023	34,212,967	34,212,967			1,4
					286,575	286,575			(2
40,430,250	$ 40,430,250	38,504,439	$ 22,054,186	69,722,786	$ 67,357,255	$ 138,985,514	206,631	$ 2,066	$ 11,5

The accompanying notes are an integral part of these consolidated financial statements.

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Chiasma, Inc.

Condensed Consolidated Statements of Cash Flows

(Unaudited)

	Six Months Ended June 30,	
	2014	**2015**
CASH FLOWS FROM OPERATING ACTIVITIES		
Net income (loss)	$ 6,079,817	$ (12,017,037)
Adjustments to reconcile net income (loss) to net cash used in operating activities:		
Depreciation and amortization	141,027	98,574
Stock-based compensation	508,905	871,821
Gain on sale of property and equipment	(9,356)	(4,286)
Changes in operating assets and liabilities:		
Deferred income taxes	(106,187)	513
Prepaid expenses and other current assets	54,148	(116,990)
Accounts payable	(2,150,420)	358,453
Accrued expenses and other current liabilities	(4,684,880)	(1,351,745)
Deferred revenue	(278,826)	
Other assets	(1,155)	(9,712)
Long-term liabilities	101,157	252,527
Net cash used in operating activities	(345,770)	(11,917,882)
CASH FLOWS FROM INVESTING ACTIVITIES		
Decrease (increase) in value of other assets	24,608	(44,060)
Proceeds from sale of property and equipment	10,862	11,500
Purchases of property and equipment		(61,190)
Net cash provided by (used in) investing activities	35,470	(93,750)
CASH FLOWS FROM FINANCING ACTIVITIES		
Proceeds from the issuance of Series E convertible preferred stock and warrants for common stock, net		35,690,345
Deferred offering costs		(987,189)
Exercise of stock options	1,687	410,272
Exercise of warrants		3,429
Proceeds on account of exercise of options		1,229
Net cash provided by financing activities	1,687	35,118,086
Net increase (decrease) in cash	(308,613)	23,106,454

Cash at beginning of period	12,849,579	40,160,435
Cash at end of period	$ 12,540,966	$ 63,266,889
SUPPLEMENTAL DISCLOSURE OF CASH FLOW INFORMATION		
Cash paid for income taxes	$ 13,810	$ 27,720
SUPPLEMENTAL DISCLOSURE OF NON-CASH INVESTING AND FINANCING ACTIVITIES		
Deferred offering costs	$	$ 902,877

The accompanying notes are an integral part of these consolidated financial statements.

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CHIASMA, INC.

Notes to Unaudited Condensed Consolidated Financial Statements

1. Nature of the Business and Summary of Significant Accounting Policies

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 and has filed a New Drug Application (NDA) with the United States Food and Drug Administration (FDA). In August, 2015, the Company received notice that the NDA was accepted for filing to permit a substantive review. The FDA also has conditionally accepted the proposed trade name of Mycapssa for oral octreotide. 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 research and 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.

Liquidity

The Company has incurred significant losses from operations since its inception and expects losses to continue for the foreseeable future. The Company s success depends primarily on the successful development and regulatory approval of its product candidates, including its lead product oral octreotide capsules.

The Company expects its research and development expenses to increase in connection with its planned European Phase III clinical trial of oral octreotide for the treatment of patients with acromegaly, its planned Phase II clinical trial of oral octreotide for the treatment of patients with neuroendocrine tumors (NET) and other potential studies of oral octreotide. In addition, if the Company obtains marketing approval for oral octreotide, it may incur significant sales, marketing, in-licensing and outsourced manufacturing expenses, as well as continued research and development expenses. As a result of becoming a public company on July 15, 2015, the Company expects to incur additional costs associated with operating as a public company. Therefore, the Company expects to continue to incur significant and increasing operating losses for the foreseeable future.

The Company may seek additional capital through a combination of private and public equity offerings, debt financings and collaborations and strategic and licensing arrangements. If adequate funds are not available to the

Company on a timely basis, or at all, the Company may be required to terminate or delay clinical trials or other development activities for oral octreotide or for one or more indications for which it is developing octreotide, or delay its establishment of sales and marketing capabilities or other activities that may be necessary to commercialize oral octreotide, if the Company obtains marketing approval.

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 (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, 2014 and 2013 and notes thereto, included in the Company s prospectus filed with the SEC pursuant to Rule 424(b)(4) on July 16, 2015 (the Prospectus).

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.

On July 21, 2015, the Company completed the sale of 7,319,750 shares of its common stock in its initial public offering (the IPO), at a price to the public of $16.00 per share, resulting in net proceeds to the Company of approximately $106.4 million after deducting underwriting discounts and commissions and estimated offering expenses payable by the Company. In preparation for the IPO, the Company s board of directors and

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stockholders approved a 1-for-9.132 reverse stock split (the Reverse Split) of the Company s common stock effective June 30, 2015. All share and per share amounts in the unaudited financial statements contained herein and notes thereto have been retroactively adjusted, where necessary, to give effect to the Reverse Split. In connection with the closing of the IPO on July 21, 2015, all of the Company s outstanding redeemable convertible preferred stock automatically converted into 16,403,011 shares of common stock. The significant increase in shares outstanding in July 2015 is expected to impact the year-over-year comparability of the Company s net loss per share calculations over the next year.

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, 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, Financial Accounting Standards Board (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 July 2015, the FASB affirmed its proposal to defer the effective date of the guidance in ASU 2014-09 for all entities by one year. As a result, if the proposal is formally adopted by the issuance of a new ASU, the new revenue standard (currently discussed in ASU 2014-09) would be effective for the Company for annual reporting periods beginning after December 15, 2017. The FASB also affirmed its proposal to permit all entities to early adopt the guidance in the new revenue standard, but not before annual periods beginning after December 15, 2016.

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 Income (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 stockholders by the weighted-average common shares outstanding for the period. Because the

Company has reported net loss attributable to common stockholders for the three and six months ended June 30, 2015, basic and diluted net loss per share attributable to common stockholders are the same for these 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 anti-dilutive impact due to net losses reported during the three and six months ended June 30, 2015.

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The following table sets forth the computation of basic and diluted earnings per share:

	Three Months Ended June 30,		Six Months Ended June 30,	
	2014	2015	2014	2015
Numerator:				
Net income (loss) attributable to common stockholders, basic	$ 3,657,708	$ (7,961,883)	$ 5,391,999	$ (12,303,612)
Accretion of redeemable convertible preferred stock	348,074		687,818	
Net income (loss) attributable to common stockholders, diluted	$ 4,005,782	$ (7,961,883)	$ 6,079,817	$ (12,303,612)
Denominator:				
Weighted average common shares outstanding, basic	43,848	158,104	43,702	115,213
Effects of dilutive securities:				
Warrants to purchase common stock	1,722,067		1,722,067	
Options to employees	662,623		641,391	
Preferred shares	8,768,025		8,768,025	
Weighted average common shares outstanding, diluted	11,196,563	158,104	11,175,185	115,213
Net income (loss) per share attributable to common stockholders, basic	$ 83.42	$ (50.36)	$ 123.38	$ (106.79)
Net income (loss) per share attributable to common stockholders, diluted	$ 0.36	$ (50.36)	$ 0.54	$ (106.79)

For the three and six months ended June 30, 2014, 467,888 and 489,120 options, respectively, have been excluded from the calculation of the diluted income per share since their effect was anti-dilutive.

3. Accrued Expenses and Other Current Liabilities

Accrued expenses and other current liabilities consist of the following:

	December 31, 2014	June 30, 2015
Accrued professional fees and others	$ 373,727	$ 939,316
Accrued research and development expenses	3,028,389	1,292,809
Accrued payroll and employee benefits	598,178	830,147
	$ 4,000,294	$ 3,062,272

Total accrued expenses and other current liabilities	

4. License Agreement

In December 2012, the Company executed 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 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 six months ended June 30, 2014, the Company recognized $10,561,326 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 and six month periods ended June 30, 2015.

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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) 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 to the 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.

6. Warrants

A summary of warrant activity is as follows:

	Three Months Ended June 30,		Six Months Ended June 30,	
	2014	2015	2014	2015
Warrants outstanding, beginning of period	1,752,818	3,624,012	1,752,818	2,677,440
Exercised				(37,544)
Issuances				984,116
Warrants outstanding, end of period	1,752,818	3,624,012	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	75%
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 $2.62.

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, at an exercise price of $5.57 per share. 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 $3.72.

During April and May 2015, directors and former employees exercised options to purchase an aggregate of 124,761 shares of common stock. 116,258 of the shares were issued as restricted stock as they were exercised prior to full vesting. The proceeds from the issuance of the restricted stock are presented as long term liability, since the Company has the right to acquire back the unvested portion of the restricted stock following termination of the services of their holder. The long term liability is released to additional paid in capital per the original vesting schedule of the options. As of June 30, 2015 the outstanding balance of the liability was $ 369,600.

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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 at an exercise price of $8.13 per share. 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 $5.47.

Stock-based compensation expense is classified in the consolidated statements of operations as follows:

	Three Months Ended June 30,		Six Months Ended June 30,	
	2014	2015	2014	2015
Stock-based compensation expense:				
Research and development	$ 224,830	$ 342,951	$ 270,720	$ 479,157
Marketing, general and administrative	155,378	307,911	238,185	392,664
	$ 380,208	$ 650,862	$ 508,905	$ 871,821

For stock option awards, the fair value of the options is estimated at the grant date using the Black-Scholes option-pricing model, taking into account the terms and conditions upon which options are granted. The fair value of the options is amortized on a straight-line basis over the requisite service period of the awards. The weighted average grant date fair value per share relating to outstanding stock options granted during the three and six months ended June 30, 2015 was $4.24 and $4.15 respectively.

The fair value of each option granted to employees and directors was calculated on the date of grant or the date of modification of a grant using the following weighted average assumptions:

	Three Months Ended June 30,		Six Months Ended June 30,	
	2014	2015	2014	2015
Expected stock price volatility	85%	75%	85%	75%
Risk-free interest rate	1.32%	1.70%	1.32%	1.70%
Expected term (years)	4.02	6.25	4.02	6.25
Expected dividend yield	0%	0%	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 the 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 stock price volatility: As the Company had been operating as a private company, there is not sufficient historical volatility for the expected term of the options. Therefore, the Company used 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.

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 term (in years): Expected term represents the period that the Company s share option grants are expected to be outstanding. As the Company had been operating as a private company, there is not sufficient historical share data to calculate the expected term of the options. Therefore, the Company elected to utilize the simplified method to value share option grants issued to employees. 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.

Expected dividend yield: The Company does not anticipate paying any dividends in the foreseeable future.

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For options granted to non-employees, the expected life of the option used is ten years, which is the contractual term of each such option. All other assumptions used to calculate the grant date fair value are generally consistent with the assumptions used for options granted to employees.

The table below summarizes activity related to stock options:

	Number of Stock Options	Weighted-Average Exercise Price	Weighted-Average Remaining Life (in years)	Aggregate Intrinsic Value
Outstanding as of December 31, 2014	1,501,062	$ 2.04	7.02	$ 2,466,647
Granted	2,258,417	6.16		
Exercised	(124,761)	3.29		
Forfeited	(2,508)	3.96		
Outstanding as of June 30, 2015	3,632,210	$ 4.56	8.46	$ 41,568,280
Exercisable as of June 30, 2015	874,499	$ 1.57	4.84	$ 12,620,206
Vested or expected to vest as of June 30, 2015	3,632,210	$ 4.56	8.46	$ 41,568,280

At June 30, 2015, there was $10,760,169 of unrecognized compensation cost related to stock options, which is expected to be recognized over a weighted-average period of 3.68 years.

8. Income Taxes

Provision for income taxes was $68,741 and $194,361 for the three months ended June 30, 2015 and 2014, respectively. Provision for income taxes was $73,471 and $65,102 for the six months ended June 30, 2015 and 2014, respectively. The Company s effective rate 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 in each period presented.

As of June 30, 2015 and 2014, the Company had provided a liability for $318,646 and $193,569 respectively, for uncertain tax positions related to various income tax matters which was classified as other long-term liabilities. As of June 30, 2015 and 2014, the Company accrued interest related to uncertain tax positions of $10,139 and $4,292, 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 June 30, 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. Commitments

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 was required to provide a security deposit in the amount of $38,135.

10. Subsequent Event

On July 21, 2015, the Company completed the sale of 7,319,750 shares of its common stock in its IPO, at a price to the public of $16.00 per share, resulting in net proceeds to the Company of approximately $106.4 million after deducting underwriting discounts and commissions and estimated offering expenses payable by the Company. The following events occurred subsequent to June 30, 2015:

On July 21, 2015 all of the Company s outstanding redeemable convertible preferred stock automatically converted into 16,403,011 shares of common stock and;

On July 21, 2015 the Company s amended and restated certificate of incorporation became effective, authorizing 125,000,000 shares of common stock and 5,000,000 shares of undesignated preferred stock.

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The table below shows, on a pro forma basis, the impact of the Company s IPO on certain condensed consolidated balance sheet items as if the transaction occurred on June 30, 2015:

	June 30, 2015	Pro forma June 30, 2015
Cash	$ 63,266,889	$ 170,671,958
Deferred offering costs	1,890,066	
Redeemable convertible preferred stock	138,985,514	
Common stock	2,066	239,294
Additional paid-in capital	11,595,958	256,762,124
Total Stockholders (deficit) equity	$ (81,927,087)	$ 163,476,307

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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 Quarterly Report on Form 10-Q and the audited financial information and the notes thereto included in our final prospectus for our initial public offering filed pursuant to Rule 424(b) under the Securities Act of 1933, as amended (the Securities Act), with the Securities and Exchange Commission (the SEC) on July 16, 2015 (the Prospectus).

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. 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. On August 14, 2015, we received notice from the FDA that our NDA was accepted for filing to permit a substantive review. The FDA has granted a standard review for the NDA and has set a target review date under the Prescription Drug User Fee Act, or PDUFA, of April 15, 2016. The FDA also has conditionally accepted the proposed trade name of Mycapssa for oral octreotide. 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, if approved. 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 chronic 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 June 30, 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 June 30, 2015, our cash was $63.3 million, of which $0.9 million was held by Chiasma (Israel) Ltd., our wholly owned Israeli subsidiary.

Since inception, we have incurred significant operating losses. Our net loss was $12.0 million for the six months ended June 30, 2015, as compared to net income of $6.1 million for the six months ended June 30, 2014. As of June 30, 2015, we had an accumulated deficit of $93.5 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. 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.

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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 redemption, the holders of these shares received a cash payment of $55.0 million plus the issuance of newly authorized shares of preferred stock.

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 ingredient, or API, supplies 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 the six months ended June 30, 2014 we recognized revenue of $10.6 million. For the three months ended June 30, 2014, we recognized revenue of $6.0 million. We did not recognize any revenue during the three and six month periods ended June 30, 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.

Recent Developments

On July 21, 2015, we completed the sale of 7,319,750 shares of our common stock in our initial public offering at a price to the public of $16.00 per share, resulting in net proceeds of approximately $106.4 million after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

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 until at least mid-2016. 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 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 research and development employees and related expenses. As we expand the clinical development of oral octreotide and initiate development of additional product candidates, we expect the amount of research and development spending to continue to grow. We have incurred a total of $100.3 million in research and development expenses from inception through June 30, 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 development generally have higher development costs than those in earlier stages of development,

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primarily due to the increased size and duration of late-stage clinical trials and scale of manufacturing. We plan to increase our research and development expenses for the foreseeable future as we seek to obtain regulatory approval for oral octreotide both inside and outside the United States and to expand the indications for oral octreotide, and to further advance our nonclinical and earlier stage research and 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 long-term purchase obligations.

Provision for Income Taxes

Our effective tax rate was (0.6%) and 1.1% for the six months ended June 30, 2015 and June 30, 2014 respectively. During the six months ended June 30, 2015 and 2014, we reported provision for income taxes of approximately $73,000 and $65,000, respectively.

Our deferred tax assets at June 30, 2015 and December 31, 2014 were $39,000 and $40,000, respectively. Deferred tax assets were reported net of valuation allowances of $15.5 million and $11.3 million at June 30, 2015 and December 31, 2014, respectively, 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 June 30, 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 June 30, 2015 and December 31, 2014, we had provided a liability of $0.3 million and $0.2 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 unaudited condensed consolidated financial statements included elsewhere in this Quarterly Report on Form 10-Q, we believe that the following accounting policies are critical to the process of making significant judgments and estimates in the preparation of our unaudited condensed consolidated financial statements and understanding and evaluating our reported financial results.

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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 record deferred revenue until such time that all criteria are met. For the three and six months ending June 30, 2014 our revenue was derived solely 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 and six months ended June 30, 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.

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. 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.

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 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.

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.

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

	Three Months Ended June 30,		Six Months Ended June 30,	
	2014	2015	2014	2015
Expected stock price volatility	85%	75%	85%	75%
Risk-free interest rate	1.32%	1.70%	1.32%	1.70%
Expected term (years)	4.02	6.25	4.02	6.25
Expected dividend yield	0%	0%	0%	0%

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

	Three Months Ended June 30,		Six Months Ended June 30,	
	2014	2015	2014	2015
Research and development	$ 225	$ 343	$ 271	$ 479
Marketing, general and administrative	155	308	238	393
Total	$ 380	$ 651	$ 509	$ 872

Income Taxes

The consolidated financial statements presented elsewhere in this Quarterly Report on Form 10-Q 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 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 June 30, 2015 and December 31, 2014, we have provided a liability of $0.3 million and $0.2 million, respectively. We account for interest and penalties related to uncertain tax positions as part of our other expenses.

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Results of Operations for the Three Months Ended June 30, 2014 and 2015

Revenue

The following is a comparison of revenue for the three months ended June 30, 2014 and 2015 (in thousands, except percentages):

	Three Months Ended June 30,			
	2014	2015	Decrease	
Revenue from license agreement	$ 5,988	$	$ 5,988	100%

Revenue during the three months ended June 30, 2014 was generated solely from our license agreement with Roche and was recognized on a proportional performance basis. During the three months ended June 30, 2014, we recognized $6.0 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 June 30, 2015.

Research and Development

The following is a comparison of research and development expenses for the three months ended June 30, 2014 and 2015 (in thousands, except percentages):

	Three Months Ended June 30,			
	2014	2015	Increase	
Research and development	$ 1,201	$ 4,159	$ 2,958	246%

During the three months ended June 30, 2015, our total research and development expenses increased by $3.0 million, or 246%, compared to the three months ended June 30, 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, as well as initiation activities with respect to our planned additional phase 3 clinical trial.

The following table is a comparison of the components of our research and development expenses during the three-months ended June 30, 2014 and 2015 (in thousands, except percentages):

	Three Months Ended June 30,		
	2014	2015	Increase
External research and development expenses:			

Oral octreotide	$ 363	$ 2,604	$ 2,241	618%
Internal research and development expenses	838	1,555	717	86%
Total research and development expenses	$ 1,201	$ 4,159	$ 2,958	246%

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Marketing, General and Administrative

The following is a comparison of marketing, general and administrative expenses for the three months ended June 30, 2014 and 2015 (in thousands, except percentages):

	Three Months Ended June 30,			
	2014	2015	Increase	
Marketing	$	$ 1,530	$ 1,530	100%
General and administrative	547	1,907	1,360	248%
Total marketing, general and administrative expenses	$ 547	$ 3,437	$ 2,890	528%

For the three months ended June 30, 2015, our marketing expenses increased by $1.5 million, or 100%, compared to the same period in 2014, related to the initiation of pre-commercial activities related to oral octreotide.

For the three months ended June 30, 2015, our general and administrative expenses increased by $1.4 million, or 248%, compared to the same period in 2014, related to increased strategic financial consulting costs, compensation related expenses associated with the hiring of senior executives and other administrative employees, as well as increased intellectual property protection related legal fees.

Other Expense, net

Other expenses totaled $0.1 million for the three months ended June 30, 2015, compared to $40,000 for the same period in 2014. The increase was the result of the imputed interest associated with the long-term obligation related to the acquisition of API and trade name Mycapssa from Roche.

Provision for Income Taxes

Our total tax provision was $69,000 for the three months ended June 30, 2015, representing an effective tax rate of (0.9%), as compared to a tax provision of $0.2 million for the three months ended June 30, 2014, representing an effective tax rate of 4.63%.

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.

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Results of Operations for the Six Months Ended June 30, 2014 and 2015

Revenue

The following is a comparison of revenue for the six months ended June 30, 2014 and 2015 (in thousands, except percentages):

	Six Months Ended June 30,			
	2014	2015	Decrease	
Revenue from license agreement	$ 10,561	$	$ 10,561	100%

Revenue during the six months ended June 30, 2014 was generated solely from our license agreement with Roche and was recognized on a proportional performance basis. During the six months ended June 30, 2014, we recognized $10.6 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 six months ended June 30, 2015.

Research and Development

The following is a comparison of research and development expenses for the six months ended June 30, 2014 and 2015 (in thousands, except percentages):

	Six Months Ended June 30,			
	2014	2015	Increase	
Research and development	$ 2,850	$ 6,378	$ 3,528	124%

During the six months ended June 30, 2015, our total research and development expenses increased by $3.5 million, or 124%, compared to the six months ended June 30, 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, as well as initiation activities with respect to our planned additional phase 3 clinical trial.

The following table is a comparison of the components of our research and development expenses during the six months ended June 30, 2014 and 2015 (in thousands, except percentages):

	Six Months Ended June 30,			
	2014	2015	Increase	
External research and development expenses:				
Oral octreotide	$ 727	$ 4,069	$ 3,342	460%
Internal research and development expenses	2,123	2,309	186	9%

Total research and development expenses	$ 2,850	$ 6,378	$ 3,528	124%

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Marketing, General and Administrative

The following is a comparison of marketing, general and administrative expenses for the six months ended June 30, 2014 and 2015 (in thousands, except percentages):

	Six Months Ended June 30,			
	2014	2015	Increase	
Marketing	$	$ 2,330	$ 2,330	100%
General and administrative	1,502	3,038	1,536	102%
Total marketing, general and administrative expenses	$ 1,502	$ 5,368	$ 3,866	257%

For the six months ended June 30, 2015, our marketing expenses increased by $2.3 million, or 100%, compared to the same period in 2014, related to the initiation of pre-commercial activities related to oral octreotide.

For the six months ended June 30, 2015, our general and administrative expenses increased by $1.5 million, or 102%, compared to the same period in 2014, related to increased strategic financial consulting cost, compensation related expenses associated with senior executives and other administrative employees, as well as increased intellectual property protection related legal fees.

Other Expense, net

Other expenses totaled $0.2 million for the six months ended June 30, 2015 compared to $65,000 for the same period in 2014. The increase was the result of the imputed interest associated with the long-term obligation related to the acquisition of API and trade name Mycapssa from Roche.

Provision for Income Taxes

Our total tax provision was $73,000 for the six months ended June 30, 2015, representing an effective tax rate of (0.6%), as compared to a tax provision of $65,000 for the six months ended June 30, 2014, representing an effective tax rate of 1.1%.

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.

Liquidity and Capital Resources

Since our inception and through June 30, 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 June 30, 2015, our cash was $ 63.3 million, of which $0.9 million was held by our Israeli subsidiary.

Indebtedness

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.

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 our initial public offering and our cash as of June 30, 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 non-clinical

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studies and clinical trials is costly, and the timing of progress in these studies 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.

Cash Flows

The following is a summary of cash flows for the six months ended June 30, 2014 and 2015 (in thousands):

	Six Months Ended June 30,	
	2014	2015
Net cash used in operating activities	$ (346)	$ (11,918)
Net cash provided by (used in) investing activities	35	(94)
Net cash provided by financing activities	2	35,118

Net Cash Used in Operating Activities

Net cash used in operating activities was $11.9 million for the six months ended June 30, 2015, compared to $0.3 million for the six months ended June 30, 2014.

During the six months ended June 30, 2015, we used internal cash resources to finance our operating activities. During the six months ended June 30, 2014, our cash used was net of the milestone payments invoiced to Roche. Our spending increased in the six months ended June 30, 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, increased financial consulting cost, compensation related expenses associated with senior executives and other administrative employees as well as increased intellectual property protection related legal fees.

Net Cash Provided by (Used in) Investing Activities

Net cash used in investing activities was $94,000 for the six months ended June 30, 2015, compared to cash provided by investing activities of $35,000 for the six months ended June 30, 2014. The increase in cash used in investing activities in the six months ended June 30, 2015 as compared to the six months ended June 30, 2014 was primarily the result of acquisition of equipment and increase in facility leasing deposits.

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Net Cash Provided by Financing Activities

Net cash provided by financing activities during the six months ended June 30, 2015 of $35.1 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, compared to cash provided by financing activities of $2,000 for the six months ended June 30, 2014 resulting from the exercise of stock options.

Off-Balance Sheet Arrangements

As of June 30, 2015 and December 31, 2014 we did not have any off-balance sheet arrangements.

NOL Carryforwards

At June 30, 2015, we had federal NOL carryforwards of $34.2 million. The federal NOL carryforwards expire at various dates through 2035. At June 30, 2015, there are no NOL carryforwards in our Israeli subsidiary.

Under Section 382 of the Internal Revenue Code of 1986, as amended (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. We are currently in process of evaluating whether the recent Series E Preferred equity financing and IPO gave rise to an event of cumulative change in our ownership of more than 50%.

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.

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Item 3. 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 June 30, 2015, we had $63.3 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 June 30, 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 19.8%, 1.2% and 8.2%, respectively. As of June 30, 2015, we held $0.9 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.

Item 4. Controls and Procedures

Management s Evaluation of our Disclosure Controls and Procedures

We maintain disclosure controls and procedures (as defined in Rules 13a-15(e) or 15d-15(e) under the Securities Exchange Act of 1934, as amended, or the Exchange Act) that are designed to ensure that information required to be disclosed in the reports that we file or submit under the Exchange Act is (1) recorded, processed, summarized, and reported within the time periods specified in the SEC s rules and forms and (2) accumulated and communicated to our management, including our principal executive officer and principal financial officer, as appropriate, to allow timely decisions regarding required disclosure.

Based on this evaluation, our management, with the participation of our principal executive officer and principal financial officer, evaluated the effectiveness of our disclosure controls and procedures as of the end of the period covered by this report. In designing and evaluating our disclosure controls and procedures, our management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives, and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Our principal executive officer and principal financial officer have concluded based upon the evaluation described above that, as of June 30, 2015, our disclosure controls and procedures were effective at the reasonable assurance level.

We continue to review and document our disclosure controls and procedures, including our internal controls and procedures for financial reporting, and may from time to time make changes aimed at enhancing their effectiveness and to ensure that our systems evolve with our business.

Changes in Internal Control Over Financial Reporting

During the three months ended June 30, 2015, there have been no changes in our internal control over financial reporting, as such term is defined in Rules 13a-15(f) and 15(d)-15(f) promulgated under the Securities Exchange Act of 1934, that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

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PART II OTHER INFORMATION

Item 1. Legal Proceedings

As of the date of this filing, we were not party to any legal matters or claims. In the future, we may become party to legal matters and claims arising in the ordinary course of business, the resolution of which we do not anticipate would have a material adverse impact on our financial position, results of operations or cash flows.

Item 1A. Risk Factors

Investing in our common stock involves a high degree of risk. You should carefully consider the risks described below, as well as the other information in this Quarterly Report on Form 10-Q and in our other public filings before making an investment decision. Our business, prospects, financial condition, or operating results could be harmed by any of these risks, as well as other risks not currently known to us or that we currently consider immaterial. If any such risks or uncertainties actually occur, our business, financial condition or operating results could differ materially from the plans, projections and other forward-looking statements included in the section titled Management s Discussion and Analysis of Financial Condition and Results of Operations and elsewhere in this report and in our other public filings. The trading price of our common stock could decline due to any of these risks, and as a result, you may lose all or part of your investment.

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

There can be no assurance that our NDA submitted to the FDA for oral octreotide will be approved and there can be no assurance that the FDA will complete its review of our NDA by the PDUFA date.

On June 15, 2015, we submitted to the U.S. Food and Drug Administration, or the FDA, a new drug application, or an NDA, for the marketing and sale of octreotide capsules, an oral drug proposed for the maintenance therapy of adult patients with acromegaly. On August 14, 2015, we received notice from the FDA that our NDA was accepted for filing to permit a substantive review. The FDA has granted a standard review for the NDA and has set a target review date under the Prescription Drug User Fee Act, or PDUFA, of April 15, 2016. The FDA also has conditionally accepted the proposed trade name of Mycapssa for oral octreotide Acceptance of the NDA filing does not represent final evaluation of the adequacy of the data submitted in the NDA and is not a guarantee of approval. The FDA may ultimately deny approval of the application and require additional testing or data. There also can be no assurance that the FDA will complete its review by the PDUFA target date. If any of the foregoing occur it could have a material adverse effect on our operations and financial condition.

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;

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- successful implementation of our manufacturing processes that are included in our 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.

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 FDA, for oral octreotide for the maintenance therapy of acromegaly, which has been accepted for filing to permit a substantive review. The FDA has set a target PDUFA date of April 15, 2016. 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, 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 and may impose pricing restrictions. 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 obtain regulatory approval in the United States or elsewhere;

the FDA or comparable foreign regulatory authorities may identify deficiencies with the manufacturing processes or facilities of third-party manufacturers with which we contract for clinical and commercial supplies or may later suspend or withdraw approval of our products;

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

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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 (in addition to the seven-month core data provided by Roche in May). 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 other studies, before oral octreotide can be approved.

We have only limited experience in filing the applications necessary to gain regulatory approvals and have relied before and expect to continue 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 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.

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.

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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 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;

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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 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

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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;
- 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,

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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.

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 pharmaceutical 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.

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;

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

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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.

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 our initial public offering, or IPO, 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.

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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;
- 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, 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.

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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 August 28, 2015, we had 28 full-time 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 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.

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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;
- 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

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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.

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.

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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

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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;

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

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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

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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

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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.

We do not have commercial manufacturing agreements in place with any contract manufacturer. We are currently in negotiations, however we may not be able to reach an agreement containing terms that are acceptable to us, or at all.

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.

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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.

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, 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.

We have funded our operations to date through proceeds from sales of redeemable convertible preferred stock and, to a lesser extent, the issuance of convertible notes. On July 21, 2015, we completed the sale of 7,319,750 shares of our common stock in our IPO, at a price to the public of $16.00 per share, resulting in net proceeds of approximately $106.4 million after deducting underwriting discounts and commissions and estimated offering expenses payable by us. From our inception through June 30, 2015, we had received net proceeds of $161.4 million from such transactions, excluding amounts raised in the IPO. As of June 30, 2015, our cash was $63.3 million, excluding amounts raised in the IPO. Since inception, we have incurred significant operating losses. Our net loss was $12.0 million for the six months ended June 30, 2015 and $2.0 million for the year ended December 31, 2014. As of June 30, 2015, we had an accumulated deficit of $93.5 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 public company, we will incur additional costs associated with operating as a public company. As a result, we expect to continue to incur significant and increasing operating losses for the foreseeable future. Because of the numerous risks and uncertainties associated with developing 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.

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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.

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 our IPO and our cash as of June 30, 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.

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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. 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 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, Anand Varadan, our Chief Commercial 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.

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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. In connection with our IPO, we 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 of oral octreotide and any future product candidates we may develop could be delayed.

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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 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.

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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.

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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.

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.

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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.

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.

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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, 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.

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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.

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.

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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

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

At June 30, 2015, we had federal net operating loss, or NOL, carryforwards of $34.2 million. The federal NOL carryforwards expire at various dates through 2035. At June 30, 2015 there were no NOL carryforwards in our Israeli subsidiary.

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. We are currently in process of evaluating whether the recent equity financing and IPO gave rise to an event of cumulative change in our ownership of more than 50%.

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, purchased an aggregate of 1,681,250 shares of our common stock in our IPO at the IPO price. Accordingly, our executive officers, directors and principal stockholders collectively control 67.5% of our outstanding common stock. 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.

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, 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;
- 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.

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In addition, we are 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.

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.

On July 21, 2015, we completed the sale of 7,319,750 shares of our common stock in our IPO, at a price to the public of $16.00 per share. There has been a public market for our common stock for only a short period of time. Although our common stock is listed on The NASDAQ Global Select Market, an active public market for our common stock may not emerge or be sustained.

In addition, the market price for our common stock may fluctuate significantly in response to a number of 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;

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.

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 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 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 of our IPO, 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 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.

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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.

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.

We are subject to the reporting requirements of the Securities Exchange Act of 1934 (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 our IPO, we had 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 connection with our IPO lapse, the trading price of our common stock could decline significantly. As of July 31, 2015, we have 23,930,199 outstanding shares of common stock, assuming no exercise of outstanding options or warrants. Of these shares, 7,319,750 shares of common stock are freely tradable, without restriction, in the public market.

After the lock-up agreements pertaining to our IPO 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, the 2,602,283 shares reserved for future issuance under our stock option plans and the 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 closing of our IPO, holders of approximately 16,543,995 shares of our common stock will have the right to require us to register these shares under 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.

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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. Currently, four securities analysts have initiated coverage on our company. In the event that 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.

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

Unregistered Sales of Equity Securities

Upon closing of our IPO, all of the outstanding shares of our convertible preferred stock were converted into 16,403,011 shares of common stock. The shares of common stock issued pursuant to such conversion were issued in reliance on the exemption from registration provided by Section 3(a)(9) of the Securities Act, which exemption is available for transactions involving securities exchanged by the issuer with its existing security holders exclusively where no commission or other remuneration is paid or given directly or indirectly for soliciting such exchange.

Between April 1, 2015 and June 30, 2015, we granted stock options to purchase an aggregate of 2,135,773 shares of our common stock, with exercise prices ranging from $5.57 to $8.13 per share, to our employees, directors and consultants pursuant to our 2008 Stock Incentive Plan.

We deemed the grants of stock options described above as exempt pursuant to Section 4(a)(2) of the Securities Act or to be exempt from registration under the Securities Act in reliance on Rule 701 of the Securities Act as offers and sales of securities under compensatory benefit plans and contracts relating to compensation in compliance with Rule 701. Each of the recipients of securities in any transaction exempt from registration had ether received or had adequate access, through employment, business or other relationships, to information about us.

No underwriters were used in the foregoing transactions.

Use of Proceeds from Initial Public Offering of Common Stock

On July 21, 2015, we closed the sale of 7,319,750 shares of common stock to the public (inclusive of 954,750 shares of common stock sold by us pursuant to the full exercise of an overallotment option granted to the underwriters) at a price of $16.00 per share, before underwriting discounts. The offer and sale of the shares in our initial public offering was registered under the Securities Act pursuant to registration statements on Form S-1 (File No. 333-204949), which was filed with the SEC on June 15, 2015 and amended subsequently and declared effective by the SEC on July 17, 2015. Following the sale of the shares in connection with the closing of our initial public offering, the offering terminated. The offering did not terminate before all the securities registered in the registration statements were sold. Barclays Capital Inc. and Cowen and Company, LLC acted as joint book-running managers of the offering, and William Blair and Company, LLC and Oppenheimer & Co. Inc. acted as co-managers of the offering.

We raised approximately $106.4 million in net proceeds after deducting underwriting discounts and commissions and estimated offering expenses payable by us. None of these expenses consisted of direct or indirect payments made by us to directors, officers or persons owning 10% or more of our common stock or to their associates, or to our affiliates.

There has been no material change in the planned use of proceeds from our initial public offering as described in our final prospectus filed with the SEC on July 16, 2015 pursuant to Rule 424(b)(4). We invested the funds received in cash equivalents and other short-term investments in accordance with our investment policy.

Item 6. Exhibits

The exhibits filed as part of this Quarterly Report on Form 10-Q are set forth on the Exhibit Index, which is incorporated herein by reference.

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SIGNATURES

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

CHIASMA, INC.

August 31, 2015

By: /s/ Mark Leuchtenberger
Mark Leuchtenberger
President, Chief Executive Officer and Director

(Principal Executive Officer)

August 31, 2015

By: /s/ Mark J. Fitzpatrick
Mark J. Fitzpatrick
Chief Financial Officer

(Principal Financial and Accounting Officer)

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EXHIBIT INDEX

Exhibit No.	Description	Incorporated by Reference to: Form or Schedule	Exhibit No.	Filing Date with SEC	SEC File Number
3.1	Amended and Restated Certificate of Incorporation of Chiasma, Inc.	8-K	3.1	July 21, 2015	001-37500
3.2	Amended and Restated By-Laws of Chiasma, Inc.	8-K	3.2	July 21, 2015	001-37500
4.1	Specimen of Common Stock Certificate of Chiasma, Inc.	S-1/A	4.1	July 6, 2015	333-204949
10.1	2015 Stock Option and Incentive Plan and forms of agreement thereunder.	S-1/A	10.3	July 6, 2015	333-204949
10.2	2015 Employee Stock Purchase Plan.	S-1/A	10.4	July 6, 2015	333-204949
10.3	Senior Executive Cash Incentive Bonus Plan	S-1/A	10.5	June 15, 2015	333-204949
10.4	Amended and Restated Employment Agreement dated as of May 29, 2015 by and between the Company and Mark Leuchtenberger.	S-1/A	10.6	June 15, 2015	333-204949
10.5	Employment Agreement dated as of May 8, 2015 by and between the Company and Mark J. Fitzpatrick.	S-1/A	10.8	June 15, 2015	333-204949
10.6	Form of Indemnification Agreement, to be entered into between the Company and its directors and officers.	S-1/A	10.10	July 6, 2015	333-204949
10.7	Sublease effective as of May 12, 2015 by and between Cyber-Ark Software, Inc. and the Company.	S-1/A	10.12	June 15, 2015	333-204949
10.8	Non-Employee Director Compensation Policy	S-1/A	10.13	July 6, 2015	333-204949
31.1*	Certification of Principal Executive Officer pursuant to Exchange Act rules 13a-14 or 15d-14.				
31.2*	Certification of Principal Financial Officer pursuant to Exchange Act rules 13a-14 or 15d-14.				
32.1+	Certification of Principal Executive Officer and Principal Financial Officer pursuant to Exchange Act rules 13a-14(b) or 15d-14(b) and 18 U.S.C. Section 1350.				
101.INS*	XBRL Instance Document.				
101.SCH*	XBRL Taxonomy Extension Schema Document.				
101.CAL*	XBRL Taxonomy Extension Calculation Document.				

101.DEF*	XBRL Taxonomy Extension Definition Linkbase Document.
101.LAB*	XBRL Taxonomy Extension Labels Linkbase Document.
101.PRE*	XBRL Taxonomy Extension Presentation Link Document.

* Filed herewith.

+ The certification furnished in Exhibit 32.1 hereto is deemed to be furnished with this Quarterly Report on Form 10-Q and will not be deemed to be filed for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, except to the extent that the Registrant specifically incorporates it by reference.