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UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

Form 10-Q

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

For the quarterly period ended June 30, 2016

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.)**

275 Wyman Street, Suite 250
Waltham, Massachusetts 02451
(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 ☐

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 ☒ 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	☒ (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 ☒

As of August 5, 2016, there were 24,356,697 shares of the registrant's Common Stock, $0.01 par value per share, outstanding.

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," "estimate," "expect," "intend," "may," "plan," "potentially," "will," "would," or the negative of these terms or other similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. These forward-looking statements include, but are not limited to, statements about:

- the U.S. regulatory review process of our New Drug Application, or NDA, for octreotide capsules in acromegaly, the results of our End of Review meeting with the U.S. Food and Drug Administration, or the FDA, and other plans and strategies following our receipt of a Complete Response Letter, or CRL, to our NDA from the FDA on April 15, 2016, the End of Review Meeting and our receipt of the minutes from such meeting;
- any regulatory approvals that may be issued or denied by the FDA, European Medicines Agency or other regulatory agencies for octreotide capsules in acromegaly or other indications;
- the therapeutic benefits, effectiveness and safety of octreotide capsules;
- our estimates of the size and characteristics of the markets that may be addressed by octreotide capsules;
- the commercial success and market acceptance of octreotide capsules or any future product candidates that are approved for marketing in the United States or other countries;
- 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 octreotide capsules have been developed to treat;
- our ability to leverage our Transient Permeability Enhancer, or 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 octreotide capsules, other product candidates we may develop and successfully commercialize or our TPE technology obsolete;
- our ability to manufacture sufficient amounts of octreotide capsules for clinical trials and commercialization activities;
- our ability to secure collaborators to license, manufacture, market and sell octreotide capsules or any products for which we receive regulatory approval in the future;
- our ability to protect our intellectual property and operate our business without infringing upon the intellectual property rights of others;
- our product development and operational plans generally, including the restructuring plan announced in June 2016; and
- our estimates regarding our capital requirements, our ability to further reduce expenses and extend our cash runway and our need for additional financing.

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 and our prior filings with the SEC. 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. Given these uncertainties, you should not place undue reliance on these forward-looking statements. Except as required by law, we assume no obligation to update or revise these forward-looking statements for any reason, even if new information becomes available in the future.

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 subsidiaries. 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. We do not intend to use or display other companies’ trademarks and trade names to imply a relationship with, or endorsement or sponsorship of us by, any other companies.

Chiasma, Inc.

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PART I — FINANCIAL INFORMATION

Item 1. Financial Statements

Chiasma, Inc.
Condensed Consolidated Balance Sheets

	June 30, 2016	December 31, 2015
	Unaudited	
	(in thousands except share data)	
Assets		
Current Assets		
Cash and cash equivalents	$ 30,483	$ 41,039
Marketable securities	85,147	107,715
Prepaid expenses and other current assets	2,491	2,331
Total current assets	118,121	151,085
Property and equipment, net	2,601	676
Other assets	1,507	1,347
Total assets	$ 122,229	$ 153,108
Liabilities and Stockholders' Equity		
Current liabilities		
Accounts payable	$ 5,081	$ 157
Accrued expenses	9,831	4,657
Other current liabilities	1,812	1,700
Total current liabilities	16,724	6,514
Long-term liabilities	3,711	3,778
Total liabilities	20,435	10,292
Commitments and Contingencies (Note 11)		
Stockholders' equity:		
Common stock, $0.01 par value; authorized 125,000,000 shares at June 30, 2016 and December 31, 2015; issued and outstanding 24,356,697 shares at June 30, 2016, and 24,012,597 shares at December 31, 2015	244	240
Preferred stock, $0.01 par value; authorized 5,000,000 shares; none outstanding	—	—
Additional paid-in capital	262,671	259,969
Accumulated other comprehensive income	138	23
Accumulated deficit	(161,259)	(117,416)
Total stockholders' equity	101,794	142,816
Total liabilities and stockholders' equity	$ 122,229	$ 153,108

See accompanying notes to condensed consolidated financial statements.

Chiasma, Inc.
Condensed Consolidated Statements of Operations
(Unaudited)

	Three Months Ended June 30,		Six Months Ended June 30,	
	2016	2015	2016	2015
	(in thousands except share and per share data)			
Operating expenses:				
Marketing, general and administrative	$ 5,392	$ 3,437	$ 15,386	$ 5,368
Research and development	14,779	4,158	22,005	6,377
Restructuring charges	6,537	—	6,537	—
Total operating expenses	26,708	7,595	43,928	11,745
Loss from operations	(26,708)	(7,595)	(43,928)	(11,745)
Other expenses (income), net	(121)	109	(250)	198
Loss before provision for income taxes	(26,587)	(7,704)	(43,678)	(11,943)
Provision for income taxes	76	69	165	74
Net loss	(26,663)	(7,773)	(43,843)	(12,017)
Accretion of redeemable convertible preferred stock	—	(189)	—	(287)
Net loss attributable to common stockholders	$ (26,663)	$ (7,962)	$ (43,843)	$ (12,304)
Earnings per share attributable to common stockholders				
Basic	$ (1.10)	$ (50.36)	$ (1.81)	$ (106.79)
Diluted	$ (1.10)	$ (50.36)	$ (1.81)	$ (106.79)
Weighted-average shares outstanding:				
Basic	24,321,069	158,104	24,279,580	115,213
Diluted	24,321,069	158,104	24,279,580	115,213

See accompanying notes to condensed consolidated financial statements.

Chiasma, Inc.
Condensed Consolidated Statements of Comprehensive Income (Loss)
(Unaudited)

	Three Months Ended June 30,		Six Months Ended June 30,	
	2016	2015	2016	2015
	(in thousands)			
Net loss	$ (26,663)	$ (7,773)	$ (43,843)	$ (12,017)
Other comprehensive income:				
Unrealized gains on available for sale securities, net	—	—	115	—
Total other comprehensive income	—	—	115	—
Comprehensive loss	$ (26,663)	$ (7,773)	$ (43,728)	$ (12,017)

See accompanying notes to condensed consolidated financial statements.

Chiasma, Inc.
Condensed Consolidated Statement of Stockholders' Equity
(Unaudited)

	Common Stock		Additional Paid-in Capital	Accumulated other comprehensive income	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount				
	(in thousands except share data)					
Balance, December 31, 2015	24,012,597	$ 240	$259,969	$ 23	$ (117,416)	$ 142,816
Stock-based compensation	—	—	2,057	—	—	2,057
Exercise of stock options	289,348	3	591	—	—	594
Exercise of warrants into common stock	54,752	1	4	—	—	5
Additional paid in capital on account of vested portion of restricted stock	—	—	50	—	—	50
Other comprehensive income	—	—	—	115	—	115
Net loss	—	—	—	—	(43,843)	(43,843)
Balance, June 30, 2016	24,356,697	$ 244	$262,671	$ 138	$ (161,259)	$ 101,794

See accompanying notes to condensed consolidated financial statements.

Chiasma, Inc.
Condensed Consolidated Statements of Cash Flows
(Unaudited)

	Six Months Ended June 30,	
	2016	2015
	($ in thousands)	
Cash Flows From Operating Activities:		
Net loss	$ (43,843)	$ (12,017)
Adjustments to reconcile net loss to net cash provided by (used in) operating activities:		
Depreciation	153	99
Stock-based compensation	2,057	872
Amortization of premium on marketable securities, net	16	—
Provision for deferred income taxes	110	1
Non-cash interest expense	124	170
Non-cash restructuring charges	379	—
Gain on sale of property and equipment	—	(4)
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	(333)	(117)
Accounts payable and accrued expenses	10,100	(995)
Other assets	(21)	(10)
Other current and long-term liabilities	1,522	83
Net cash used in operating activities	(29,736)	(11,918)
Cash Flows From Investing Activities:		
Purchase of marketable securities	(78,941)	—
Maturities of marketable securities	101,606	—
Purchases of property and equipment	(2,384)	(105)
Proceeds from sale of property and equipment	—	12
Net cash provided by (used in) investing activities	20,281	(93)
Cash Flows From Financing Activities:		
Payment under license termination agreement	(1,700)	—
Proceeds from issuance of Series E redeemable convertible preferred stock and warrants for common stock, net	—	35,690
Deferred offering costs	—	(987)
Exercise of warrants	5	3
Exercise of stock options	594	412
Net cash provided by (used in) financing activities	(1,101)	35,118
Net increase (decrease) in cash and cash equivalents	(10,556)	23,107
Cash and cash equivalents, beginning of period	41,039	40,160
Cash and cash equivalents, end of period	$ 30,483	$ 63,267
Supplemental Non-Cash Financing Activities:		
Deferred offering costs	$ —	$ 903
Supplemental data of cash flow information:		
Cash paid for income taxes	$ 76	$ 28

See accompanying notes to condensed consolidated financial statements.

CHIASMA, INC.
Notes to Unaudited Condensed Consolidated Financial Statements
June 30, 2016

1. Description of Business and Summary of Significant Accounting Policies

Chiasma, Inc. is a biopharmaceutical company incorporated in 2001 under the laws of the State of Delaware. Chiasma, Inc. is headquartered in Massachusetts and has two wholly owned subsidiaries; Chiasma (Israel) Ltd., and Chiasma Securities Corp, collectively referred to as "the Company," "we," "us", "our" or "Chiasma". Our product development facilities are in Israel. We are dedicated to improving the lives of patients suffering from orphan diseases by developing and commercializing novel oral therapies that are currently available only as injections. We have completed a multinational Phase 3 clinical trial of our most advanced Transient Permeability Enhancer ("TPE") platform-based product candidate, octreotide capsules, for the treatment of acromegaly and our New Drug Application ("NDA") was accepted for filing by the United States Food and Drug Administration ("FDA") in August 2015. We expect to continue to conduct the international Phase 3 clinical trial of octreotide capsules in acromegaly that we initiated in March 2016 to support potential regulatory approval in Europe. On the Prescription Drug User Fee Act ("PDUFA") date of April 15, 2016, the FDA issued a Complete Response Letter ("CRL") regarding the NDA, indicating that the review is complete and the NDA is not ready for approval in its present form. In June 2016, we participated in an End of Review meeting with the FDA to discuss the concerns the FDA raised in the CRL and have received the minutes of the meeting.

In its CRL, the FDA advised us that it did not believe our application had provided substantial evidence of efficacy to warrant approval, and advised us that we would need to conduct another clinical trial in order to overcome this deficiency. The FDA expressed concerns regarding certain aspects of our single-arm, open-label Phase 3 clinical trial and strongly recommended that we conduct a randomized, double-blind and controlled trial that enrolls patients from the United States and is of sufficiently long duration to ensure that control of disease activity is stable at the time point selected for the primary efficacy assessment. In addition, the FDA advised that, during a recent site inspection, certain deficiencies were conveyed to the representative of one of our suppliers that would need to be resolved before approval.

In the End of Review meeting minutes, the FDA reiterated its strong recommendation for a randomized, double-blind and controlled trial, and introduced the concept of a placebo control as a design element that could address some of the FDA's concerns. While we acknowledge this feedback, we continue to explore various potential paths forward, including a determination as to whether we can produce data sufficient to satisfy the FDA of the efficacy and safety of Mycapssa in adult patients with acromegaly. The FDA stated that it considers pathways alternative to its recommendations to be less ideal and ultimately more risky to our efforts to secure approval of our NDA for octreotide capsules in acromegaly. The FDA strongly recommended that we work with the FDA to reach a common understanding of expectations prior to initiating and executing any alternative plans.

The U.S. regulatory pathway is highly uncertain at this time, and we may never reach a common understanding with the FDA on a path forward to develop Mycapssa in the U.S., or obtain regulatory approval of octreotide capsules in the United States.

In addition to the regulatory uncertainty created by the CRL, we are also subject to risks common to companies in the biopharmaceutical development industry. There can be no assurance that our research and development will be successfully completed, that adequate protection for our 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 our development efforts are successful, it is uncertain when, if ever, we will generate significant product sales. We operate in an environment of rapid technological change and substantial competition from pharmaceutical and biotechnology companies.

Liquidity

We have incurred significant losses from operations since our inception and expect losses to continue for at least the next several years. We are heavily dependent on the regulatory approval and subsequent commercial success of our lead product candidate, octreotide capsules for the treatment of acromegaly in the United States and Europe, both of which may never occur.

We expect to continue to conduct our recently initiated international Phase 3 clinical trial of octreotide capsules in acromegaly to support potential regulatory approval in Europe. In June 2016, we announced a corporate restructuring plan intended to focus our resources on the continued development of Mycapssa for the maintenance treatment of adult acromegaly patients. We are currently revisiting all areas of investment and resources in light of the CRL and our End of Review Meeting with the FDA to potentially enable further reductions of our expenses and extension of our cash runway. We currently expect our existing cash, cash equivalents and marketable securities to fund our operations through at least 2017. As a public company, we will continue to incur costs associated with operating as a public company. Therefore, we expect to continue to incur significant operating losses for the foreseeable future.

Successful transition to attaining profitable operations is dependent upon achieving a level of revenues adequate to support our cost structure. As a result of the CRL and our subsequent interactions with the FDA, our ability to generate product revenues has been delayed indefinitely. We plan to continue to fund our losses from operations and capital funding needs from existing balances of cash, cash equivalents and marketable securities and potentially through the issuance of debt and/or equity or through collaborations or license agreements with other companies. Debt or equity financing may not be available on a timely basis on terms acceptable to us, or at all. If we are not able to secure adequate additional funding, we may be forced to make further reductions in spending, extend payment terms with suppliers, liquidate assets where possible, or suspend or curtail planned programs. Any of these actions could materially harm our business, results of operations and future prospects.

Basis of Presentation

We have 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, certain information and footnote disclosures required by accounting principles generally accepted in the United States ("U.S. GAAP") for annual financial statements have been condensed or omitted. The information included in this quarterly report on Form 10-Q should be read in conjunction with our Annual Report on Form 10-K for the year ended December 31, 2015. The year-end condensed consolidated balance sheet data presented for comparative purposes was derived from our audited financial statements, but does not include all disclosures required by U.S. GAAP. In the opinion of management, we have prepared the accompanying unaudited condensed consolidated financial statements on the same basis as our 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 results of operations for the three and six months ended June 30, 2016, are not necessarily indicative of the operating results for the full year or for any other subsequent interim period.

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 to us of approximately $106.5 million after deducting underwriting discounts and commissions and offering expenses payable by us. In preparation for the IPO, our board of directors and stockholders approved a 1-for-9.132 reverse stock split (the "Reverse Split") of our common stock effective June 30, 2015. In connection with the closing of the IPO on July 21, 2015, all of our outstanding redeemable convertible preferred stock automatically converted into 16,403,011 shares of common stock. All previously reported common stock share amounts in the accompanying financial statements and related notes have been retroactively adjusted to reflect the reverse stock split. The significant increase in shares outstanding in July 2015 is expected to impact the year-over-year comparability of our net loss per share calculations throughout 2016.

Cash Equivalents

Cash and cash equivalents consist of highly liquid instruments purchased with an original maturity of three months or less at the date of purchase.

Marketable Securities

Our investments primarily consist of commercial paper, corporate and government debt securities. These marketable securities are classified as available-for-sale, and as such, are reported at fair value on our condensed consolidated balance sheets. Unrealized holding gains and losses are reported within accumulated other comprehensive income as a separate component of stockholders' equity. The amortized cost of debt securities is adjusted for amortization of premiums and accretion of discounts to maturity. Such amortization, together with interest on securities, are included in other expense (income), net, on our condensed consolidated statements of operations.

If a decline in the fair value of a marketable security below our cost basis is determined to be other than temporary, such marketable security is written down to its estimated fair value as a new cost basis and the amount of the write-down is included in earnings as an impairment charge. The cost of securities sold is based on the specific identification method.

Concentrations of credit risk

Financial instruments that potentially subject us to significant concentration of credit risk consist primarily of cash, cash equivalents, marketable securities and long-term restricted deposits. Periodically, we maintain deposits in financial institutions in excess of government insured limits. Management believes that we are not exposed to significant credit risk as our deposits are held at financial institutions that management believes to be of high credit quality and we have not experienced any significant losses in these deposits. We regularly invest excess operating cash in deposits with major financial institutions and money market funds and in notes issued by the U.S. government, as well as in fixed income investments and U.S. bond funds, both of which can be readily purchased and sold using established markets. We believe that the market risk arising from our holdings of these financial instruments is mitigated based on the fact that many of these securities are either government backed or of high credit rating.

Use of Estimates

The preparation of condensed consolidated financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets, liabilities, revenue, and expenses, and the disclosure of contingent assets and liabilities as of and during the reporting period. We base these estimates and assumptions on historical experience when available, and on various factors that it believes to be reasonable under the specific circumstances. Significant estimates relied upon in preparing the accompanying condensed consolidated financial statements include, but are not limited to, accounting for stock-based compensation, present value of long-term purchase obligation, income taxes, useful lives of long-lived assets, and accounting for certain accruals. We assess the above estimates on an ongoing basis; however, actual results could materially differ from those estimates.

Recently Issued Accounting Pronouncements

In August 2014, the FASB issued new guidance which 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 the standard will be effective for the annual and interim financial statement periods ending after December 15, 2016, with early adoption permitted. We adopted this guidance effective January 2016. The adoption of this standard did not have a material impact on our condensed consolidated financial statements.

In November 2015, the FASB issued new guidance which requires all deferred income taxes be presented on the balance sheet as noncurrent. The new guidance is intended to simplify financial reporting by eliminating the requirement to classify deferred taxes between current and noncurrent. The guidance is effective in 2017 with early adoption is permitted. We adopted this guidance effective June 2016. We applied the guidance prospectively and therefore prior periods have not been retrospectively adjusted. At December 31, 2015, our net current deferred tax asset was $0.1 million. The adoption of this standard did not have a material impact on our condensed consolidated financial statements.

In February 2016, the FASB issued new guidance which establishes a right-of-use model that requires a lessee to record an asset and a lease liability on the balance sheet for all leases with terms longer than 12 months. Leases will be classified as either finance or operating, with classification affecting the pattern of expense recognition in the income statement. The guidance is effective in 2019. A modified retrospective transition approach is required for lessees for capital and operating leases existing at, or entered into after, the beginning of the earliest comparative period presented in the financial statements. We are currently evaluating the impact the standard may have on our consolidated financial statements.

In March 2016, the FASB issued guidance simplifying aspects of the accounting for employee share-based payments, including the accounting for income taxes, forfeitures, statutory withholding requirements, and classification on the statement of cash flows. The standard is effective for interim and annual periods beginning after December 15, 2016, with early adoption permitted. During the three months ended June 30, 2016, we adopted this standard. As a result, we have elected to account for forfeitures as they occur. The adoption of this standard did not have a material impact on our condensed consolidated financial statements.

2. Investments

Our investments consisted of the following as of June 30, 2016 and December 31, 2015 (in thousands):

	June 30, 2016			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
Money market funds	$ 26,736	$ —	$ —	$ 26,736
Corporate notes	85,009	143	(5)	85,147
Total	$111,745	$ 143	$ (5)	$ 111,883

	December 31, 2015			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
Money market funds	$ 23,300	$ —	$ —	$ 23,300
Corporate notes	118,542	53	(30)	118,565
Total	$141,842	$ 53	$ (30)	$ 141,865

As of June 30, 2016, we do not consider those securities that are in an unrealized loss position to be other-than-temporarily impaired, as we have the ability to hold such investments until recovery of the fair value. We utilize the specific identification method in computing realized gains and losses. We had no realized gains and losses on our available-for-sale securities for the three and six months ended June 30, 2016 or 2015.

The fair values of our investments by classification in our condensed consolidated balance sheets as of June 30, 2016 and December 31, 2015 were as follows (in thousands):

	June 30, 2016	December 31, 2015
Cash and cash equivalents	$ 26,736	$ 34,150
Marketable securities	85,147	107,715
Total	$ 111,883	$ 141,865

Cash and cash equivalents in the table above exclude cash of $3.7 million and $6.9 million as of June 30, 2016 and December 31, 2015, respectively. The contractual maturity dates of all of our investments are less than one year.

3. Fair Value Measurements of Financial Instruments

Fair value is defined as the exchange price that would be received for an asset or paid to transfer a liability (an exit price) in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants at the measurement date. The fair value accounting guidance requires that assets and liabilities carried at fair value be classified and disclosed in one of the following three categories:

- *Level 1* — Quoted prices in active markets for identical assets or liabilities that we have the ability to access at the measurement date.
- *Level 2* —Inputs other than quoted prices in active markets that are observable for the asset or liability, either directly or indirectly.
- *Level 3* —Inputs that are unobservable for the asset or liability.

To the extent that valuation is based on models or inputs that are less observable or unobservable in the market, the determination of fair value requires more judgment. Accordingly, the degree of judgment exercised by us in determining fair value is greatest for instruments categorized in Level 3. A financial instrument's level within the fair value hierarchy is based on the lowest level of any input that is significant to the fair value measurement.

The fair value measurements of our financial instruments are summarized in the table below (in thousands):

	Fair Value Measurements at June 30, 2016:			
	Quote Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)	Balance as of June 30, 2016
Cash equivalents:				
Money market funds	$ 26,736	$ —	$ —	$ 26,736
Total cash equivalents	$ 26,736	$ —	$ —	$ 26,736
Marketable securities:				
Corporate notes	$ —	$ 85,147	$ —	$ 85,147
Total marketable securities	—	85,147	—	85,147
Total	$ 26,736	$ 85,147	$ —	$ 111,883

	Fair Value Measurements at December 31, 2015:			
	Quote Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)	Balance as of December 31, 2015
Cash equivalents:				
Money market funds	$ 23,300	$ —	$ —	$ 23,300
Corporate notes	—	10,850	—	10,850
Total cash equivalents	$ 23,300	$ 10,850	$ —	$ 34,150
Marketable securities:				
Corporate notes	$ —	$ 107,715	$ —	$ 107,715
Total marketable securities	—	107,715	—	107,715
Total	$ 23,300	$ 118,565	$ —	$ 141,865

4. Earnings per Share Attributable to Common Stockholders

We compute basic earnings per share attributable to common stockholders by dividing net income (loss) attributable to common stockholders by the weighted average number of common shares outstanding for the period. During periods in which we incurred a net loss, we allocate no net loss to participating securities because they do not have a contractual obligation to share in our net loss. We compute diluted earnings per common share after giving consideration to all potentially dilutive common shares, including stock options, and warrants outstanding during the period except where the effect of such non-participating securities would be antidilutive. All 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, 2016 and 2015.

5. Accrued Expenses

As of June 30, 2016 and December 31, 2015, accrued expenses consisted of the following (in thousands):

	June 30, 2016	December 31, 2015
Accrued marketing, general and adminstrative expenses	$ 850	$ 1,486
Accrued research and development expenses	1,639	1,376
Accrued payroll and employee benefits	1,337	1,795
Accrued restructuring costs	6,005	—
Total accrued expenses	$ 9,831	$ 4,657

6. License Agreement

In December 2012, we signed a license agreement with F. Hoffmann-La Roche Ltd. and Hoffmann-La Roche Inc. (collectively "Roche"), which was effective in January 2013, and granted Roche an exclusive, non-transferable license to our intellectual property related to the octreotide capsules.

In July 2014, Roche terminated the license agreement. Following the termination of the license agreement, we are not entitled to further payments from Roche, Roche has no remaining rights to octreotide capsules and we retain all rights to octreotide capsules and all related intellectual property. Subsequent to the termination, we purchased from Roche active pharmaceutical ingredient ("API") supplies to continue the development and manufacturing of octreotide capsules as well as Roche's proposed trade name ("Mycapssa") for octreotide capsules for an aggregate amount of $5.1 million payable in three equal annual installments of $1.7 million beginning in 2016. We made the first $1.7 million payment in March 2016. 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, we have no other financial and operational obligations to Roche.

7. 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 $35.9 million, with issuance costs of $0.3 million. In connection with the issuance of Series E preferred, we issued to the holders of Series E preferred warrants to purchase 984,116 shares of our common stock, with an exercise price of $9.13 per share, and allocated $1.5 million of the net proceeds to the warrants based on their relative fair value on the issuance date which was accounted for as a discount on Series E preferred and recorded as additional paid-in capital.

In connection with the closing of our initial public offering on July 21, 2015, all of our outstanding redeemable convertible preferred stock automatically converted into 16,403,011 shares of common stock.

8. Warrants

The following common stock warrants have been issued by the Company:

Issued In Connection With	Shares of Common Stock Underlying Warrants	Exercise Price Per Share	Issuance Date	Expiration Date
Series C preferred	54,752	$ 0.09	June 24, 2011	June 24, 2016
Series D redeemable convertible preferred stock, second closing	849,033	$ 0.09	October 22, 2012	October 22, 2022
Series D redeemable convertible preferred stock, third closing	849,033	$ 0.09	March 28, 2013	March 28, 2022
Series E redeemable convertible preferred stock	624,622	$ 9.13	December 15, 2014	December 15, 2024
Series E redeemable convertible preferred stock	984,116	$ 9.13	February 20, 2015	February 20, 2025
Total	3,361,556			

There were 54,752 warrants exercised during the three and six months ended June 30, 2016. There were 3,567,015 outstanding warrants as of June 30, 2016.

9. Stock Incentive Plans

In 2008, our board of directors adopted the 2008 Stock Incentive Plan (the "2008 Plan"), which provided for the grant of incentive stock options, nonqualified stock options, and restricted stock to employees, directors, and nonemployees of the Company up to 3,547,741 shares of common stock. Option awards expire 10 years from the grant date and generally vest over four years, but vesting conditions can vary at the discretion of our Board of Directors.

In July 2015 the Company approved the 2015 Stock Option and Incentive Plan (the "2015 Plan"), which became effective upon our IPO. The 2015 Plan allows the grant of incentive stock options, nonqualified stock options, and restricted stock to employees, directors, and nonemployees of the Company up to 3,566,296 shares of common stock. In connection with the adoption of the 2015 Plan, no further option grants are permitted under the 2008 Plan and any expirations, cancellations, or terminations under the previous plan are available for issuance under the 2015 Plan. On January 1, 2016, the number of shares reserved and available for issuance under the 2015 Stock Plan increased by 960,504 shares of common stock pursuant to a provision in the 2015 Stock Plan that provides that the number of shares reserved and available for issuance will automatically increase each January 1, beginning on January 1, 2016, by 4% of the number of shares of common stock issued and outstanding on the immediately preceding December 31 or such lesser number as determined by the compensation committee of the Board of Directors. As of June 30, 2016, the total number of shares authorized for stock award plans is 7,114,037 of which 2,613,690 remain available for grant. There are 4,210,999 stock options outstanding as of June 30, 2016.

Stock-based compensation for the three and six months ended June 30, 2016 and 2015 consisted of the following (in thousands):

	Three Months Ended June 30,		Six Months Ended June 30,	
	2016	2015	2016	2015
Marketing, general and administrative	$ (106)	$ 308	$ 1,236	$ 393
Research and development	403	343	821	479
Total	$ 297	$ 651	$ 2,057	$ 872

Primarily as result of the workforce reduction discussed in Note 12, approximately 766,000 options were forfeited during the three months ended June 30, 2016.

The fair value of each stock option issued was estimated at the date of grant using the Black-Scholes option model with the following weighted-average assumptions:

	Six Months Ended June 30,	
	2016	2015
Expected volatility	75%	75%
Expected term (years)	6.20	6.25
Risk-free interest rate	1.42%	1.70%
Expected dividend yield	0%	0%

We issued approximately 1,164,000 option grants during the six months ended June 30, 2016. The weighted-average grant date fair value per share of options granted during the six months ended June 30, 2016 was $6.69. We issued approximately 2,258,000 option grants in the six months ended June 30, 2015. The weighted-average grant date fair value per share of options granted during the six months ended June 30, 2015 was $4.15.

10. Income Taxes

Our effective rate differs from the U.S. federal statutory income tax rate of 34% primarily due to a full valuation allowance against our U.S. deferred tax asset in each period presented and lower statutory rates from our Israeli subsidiary.

We have reviewed the tax positions taken, or to be taken, in our tax returns for all tax years currently open to examination by a taxing authority. As of June 30, 2016, the gross amount of unrecognized tax benefits including interest and penalties was $0.6 million.

We remain subject to examination until the statute of limitations expires for each respective tax jurisdiction. The statute of limitations will be open with respect to these tax positions until 2020. A reconciliation of beginning and ending amount of our unrecognized tax benefits is as follows (in thousands):

	2016
Uncertain tax position at the beginning of year	$443
Additions for uncertain tax positions of prior year	—
Additions for uncertain tax positions of current year	150
Reductions for settlements with taxing authorities	—
Reductions for lapses of the applicable statutes of limitations	—
Uncertain tax position at the end of the period	$593

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. As of June 30, 2016, a summary of the tax years that remain subject to examination in our taxing jurisdictions is as follows:

United States	2012 and forward
Israel	2011 and forward

However, carryforward attributes that were generated prior to 2012 in the United States may still be adjusted upon examination by federal, state or local tax authorities if they either have been or will be used in a future period.

11. Commitments and Contingencies

As of March 31, 2016, we were contractually committed to purchasing approximately $16.9 million of commercial manufacturing supplies and services over the subsequent 15 months, of which approximately $7.4 million of supplies and services ordered were non-cancellable and delivered during the second quarter of 2016. Following our receipt of the CRL, we indefinitely suspended our commercial production commitments in May 2016, which resulted in aggregate contractual financial penalties of approximately $4.7 million that were recorded in our condensed consolidated statement of operations as restructuring charges (see Note 12). The suspension notices released us from any remaining undelivered supply and service commitments described above. We paid $4.4 million for API purchases in June 2016 and $7.3 million related to API and contractual financial penalties in July 2016 which fulfilled our contractual commercial API purchase commitments.

We conduct operations in leased facilities, which are accounted for as operating leases. Certain leases include renewal options. In addition, we lease automobiles and equipment under operating leases. There were no assets held under capital leases at June 30, 2016 or December 31, 2015. In conjunction with the facility leases, we provided bank guarantees in the aggregate amount of $1.3 million as security deposits at June 30, 2016, which were classified as other assets in the accompanying condensed consolidated balance sheets. At June 30, 2016, the minimum rental commitments under all non-cancelable operating leases with initial or remaining terms of more than one year was approximately $12.1 million through 2025.

Legal Proceedings

On June 9, 2016, Chiasma, Inc. and certain of our officers were named as defendants in a purported federal securities class action lawsuit filed in the United States District Court for the District of Massachusetts, styled *Gerneth v. Chiasma, Inc., et al*. This lawsuit challenges our public statements regarding our Phase 3 clinical trial methodology for Mycapssa (octreotide) capsules and our ability to obtain FDA approval for the marketing and sale of Mycapssa, in violation of Sections 10(b) and 20(a) of the Securities Exchange Act of 1934, as amended, and Rule 10b-5 promulgated thereunder, and Sections 11 and 15 of the Securities Act of 1933, as amended. The plaintiff seeks to represent a class consisting of all purchasers of our common stock from July 15, 2015 to April 17, 2016. We believe this lawsuit is meritless and intend to vigorously defend against it. At this time, no assessment can be made as to the likely outcome of this lawsuit or whether the outcome will be material to us.

From time to time, we may be subject to various legal proceedings and claims that arise in the ordinary course of our business activities. We are not aware of any claim or litigation, the outcome of which, if determined adversely to us, would have a material effect on our financial position or results of operations.

12. Restructuring Charges

In June 2016, we announced a corporate restructuring plan that included immediate reduction of approximately 33% of our workforce, including substantially all of our commercial personnel. As a result, we recorded restructuring charges for one-time employee severance benefits and related costs, one-time non-cash restructuring charges related to previously capitalized commercial software and manufacturing suspension fees totaling approximately $6.5 million during the three months ended June 30, 2016. The components of our restructuring charges are as follows (in thousands):

	Three and Six Months Ended June 30, 2016
Severance benefits and related costs	$ 1,465
Non-cash restructuring charges	379
Manufacturing suspension fees	4,693
Total	$ 6,537

Activity related to accrued restructuring costs is as follows (in thousands):

	Six Months Ended June 30, 2016
Balance at beginning of year	$ —
Plus:	
Current year restructuring costs	6,537
Less:	
Payment of employee severance costs	126
Payment of manufacturing suspension fees	27
Non-cash restructuring charges	379
Balance at end of period	$ 6,005

In July 2016, we paid approximately $4.4 million of the manufacturing suspension fees.

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

The following discussion and analysis of our financial condition and results of operations should be read in conjunction with our unaudited condensed 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 Annual Report on Form 10-K for the year ended December 31, 2015.

Overview

We are a 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 reduce or 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, octreotide capsules, for the treatment of acromegaly. We expect to continue to conduct the international Phase 3 clinical trial of octreotide capsules in acromegaly that we initiated in March 2016 to support potential regulatory approval in Europe. We believe octreotide capsules, if approved by regulatory authorities, may be the first somatostatin analog available for oral administration. Our octreotide capsules have been granted orphan designation in the United States and the European Union for the treatment of acromegaly. Our New Drug Application, or NDA, for octreotide capsules was accepted for filing by the United States Food and Drug Administration, or the FDA or the Agency, in August 2015. On the Prescription Drug User Fee Act, or PDUFA, date of April 15, 2016, the FDA issued a Complete Response Letter, or CRL, regarding the NDA, indicating that the review is complete and the NDA is not ready for approval in its present form. In June 2016, we participated in an End of Review meeting with the FDA to discuss the concerns the FDA raised in the CRL and have received the minutes of the meeting.

In its CRL, the FDA advised us that the Agency did not believe our application had provided substantial evidence of efficacy to warrant approval, and advised us that we would need to conduct another clinical trial in order to overcome this deficiency. The FDA expressed concerns regarding certain aspects of our single-arm, open-label Phase 3 clinical trial and strongly recommended that we conduct a randomized, double-blind and controlled trial that enrolls patients from the United States and is of sufficiently long duration to ensure that control of disease activity is stable at the time point selected for the primary efficacy assessment. In addition, the FDA advised that, during a recent site inspection, certain deficiencies were conveyed to the representative of one of our suppliers that would need to be resolved before approval. The FDA did not note any safety concerns related to Mycapssa in the CRL, but subsequently indicated in the End of Review meeting minutes that the size, duration, dropout rate and absence of a control group in our previous Phase 3 trial were factors limiting an overall safety assessment.

In the End of Review meeting minutes, the FDA reiterated its strong recommendation for a randomized, double-blind and controlled trial, and introduced the concept of a placebo control as a design element that could address some of the FDA's concerns. While we acknowledge this feedback, we continue to evaluate various potential paths forward, including a determination as to whether we can produce data sufficient to satisfy the FDA of the efficacy and safety of Mycapssa in adult patients with acromegaly. The Agency stated that it considers pathways alternative to its recommendations to be less ideal and ultimately more risky to our efforts to secure approval of our NDA for octreotide capsules in acromegaly. The FDA strongly recommended that we work with the Agency to reach a common understanding of expectations prior to initiating and executing any alternative plans. We believe additional discussions with the FDA will enable our executive team and Board to chart the most prudent path forward for Chiasma and our shareholders.

We cannot provide any assurance that the trial strongly recommended and preferred by the FDA, if conducted by us, or any other alternative development pathway, whether acceptable or unacceptable to FDA, will result in the approval of our NDA for octreotide capsules. If our efforts to address the FDA's concerns are unsuccessful, we may be unable to obtain U.S. regulatory approval for the marketing and sale of octreotide capsules at all. Conducting one or more additional clinical trials would significantly delay our ability to secure regulatory approval and introduce new risks and uncertainties depending on the trial design and timing of any trials conducted. Conducting a randomized, double-blind and controlled trial in this indication, as strongly recommended by the Agency, would be particularly challenging. For example, it may be difficult to identify patients with acromegaly willing to enroll in a trial with this design, the trial could take years to complete, and the FDA's review of the data would also likely consume significant time. The company cannot estimate how long this process could take but it could be several years. We may not have sufficient capital resources to fully fund any new trials that the FDA requires as a condition to approval, in particular the controlled trial strongly recommended by the FDA.

We retain worldwide rights to develop and commercialize octreotide capsules with no royalty obligations to third parties. We intend to commercialize octreotide capsules ourselves in the United States, if approved, and we plan to explore collaboration opportunities for commercializing octreotide capsules in Europe and the rest of the world. Our goal is to become a leading patient-focused

biopharmaceutical company by developing and commercializing octreotide capsules for acromegaly and other orphan indications, and leveraging our TPE platform to develop and commercialize novel oral products for other debilitating diseases currently treated by injectable therapies.

We were incorporated in 2001 and commenced active operations in the same year. Our operations to date have been limited to organizing and staffing our company, business planning, raising capital, developing our TPE technology, identifying potential drug candidates, undertaking nonclinical studies and, beginning in 2010, conducting clinical trials and preparing for regulatory submissions. To date, we have financed our operations primarily through private placements, funding received from a licensing agreement, a loan agreement and our initial public offering. 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, 2016, we have raised an aggregate of $366.2 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, $106.5 million from issuing shares of common stock in our initial public offering, or IPO, $161.4 million was from the issuance of private securities and $12.0 million was from borrowings under a loan agreement. In 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, 2016, our consolidated cash, cash equivalents and marketable securities were $115.6 million, of which $1.2 million was held by Chiasma (Israel) Ltd., our wholly owned Israeli subsidiary.

We have incurred significant operating losses since our inception. Our net loss was $43.8 million for the six months ended June 30, 2016 and $35.9 million for the year ended December 31, 2015. As of June 30, 2016, we had an accumulated deficit of $161.3 million. We expect to incur significant operating losses over the next several years. These losses, combined with prior losses will continue to have an adverse effect on our cash resources, stockholders' equity and working capital. We expect to continue to conduct the international Phase 3 clinical trial of octreotide capsules in acromegaly that we initiated in March 2016 to support potential regulatory approval in Europe.

In June 2016, we announced a corporate restructuring plan intended to focus our resources on the continued development of Mycapssa for the maintenance treatment of adult acromegaly patients. We continue to revisit all areas of investment and resources in light of the CRL and our End of Review Meeting with the FDA to potentially enable further reductions of our expenses and extension of our cash runway. Because of the numerous risks and uncertainties facing our company and associated with developing and commercializing pharmaceutical products generally, we are unable to predict the extent of any future losses or when we will become profitable, if at all.

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity offerings, debt financings, 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 collaboration 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.

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 octreotide capsules. 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.

In July 2014, Roche terminated the license agreement. Pursuant to the termination of the license agreement, we are not entitled to further payments from Roche, Roche has no remaining rights to octreotide capsules and we retain all rights to octreotide capsules and all related intellectual property. Subsequent to the termination, we purchased from Roche active pharmaceutical ingredient, or API, supplies to continue the development and manufacturing of octreotide capsules, together with Roche's proposed trade name, "Mycapssa" for octreotide capsules, for an aggregate amount of $5.1 million, payable in three annual installments of $1.7 million beginning in 2016. We made the first $1.7 million payment in March 2016. Other than these payments, we have no further financial or operational obligations to Roche.

Financial Overview

Revenue

We do not have a product approved and, as a result, have yet to generate revenue from product sales. In light of the CRL received from the FDA and our subsequent End of Review meeting, we do not expect to begin generating product revenue for some time, if at all. If we fail to identify and agree on a path forward for our NDA with the FDA, complete the development of octreotide capsules or

any future product candidates in a timely manner or at all, or obtain regulatory approval for octreotide capsules or any future product candidates, our ability to generate product sales, and our consolidated results of operations and financial position, would be adversely affected.

Research and Development

Research and development expenses consist of expenses incurred in performing research and development activities, including compensation and benefits for full-time research and development employees, an allocation of facilities expenses, overhead expenses, nonclinical pharmacology and toxicology studies, manufacturing process-development and scale-up activities, clinical trial and related clinical manufacturing expenses, fees paid to contract research organizations, or CROs, investigative sites, and other external expenses. In the early phases of development, our research and development costs include expanding our technology platform as well as early development of specific product candidates. The majority of our research and development expenses has been spent on the development of octreotide capsules, including the manufacturing validation, regulatory and clinical activities, and 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, primarily due to the increased size and duration of late-stage clinical trials. We expect to continue to conduct the international Phase 3 clinical trial of octreotide capsules in acromegaly that we initiated in March 2016 to support potential regulatory approval in Europe. The successful development of octreotide capsules 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 octreotide capsules or the period, if any, in which material net cash inflows from any product candidates may commence. Clinical development timelines, the probability of success and development costs can differ materially from expectations. For example, in both the CRL and the End of Review meeting, the FDA strongly recommended that we conduct a randomized, double-blinded, controlled clinical trial of octreotide capsules that enrolls patients from the United States and is of sufficiently long duration to ensure that control of disease activity is stable at the time point selected for the primary efficacy assessment. If we were to conduct such a trial or other trials that the FDA deems acceptable for resubmission of our NDA, or if we experience significant delays in our ongoing Phase 3 clinical trial to support the submission of our Marketing Authorization Application, or MAA, to the European Medicines Agency, or EMA, we could be required to expend significant additional financial resources and time on the completion of clinical development.

As of March 31, 2016, we were contractually committed to purchasing approximately $16.9 million of commercial manufacturing supplies and services over the subsequent 15 months, of which approximately $7.4 million of supplies and services ordered were non-cancellable and delivered during the second quarter of 2016. Following our receipt of the CRL, we indefinitely suspended our commercial production commitments, which resulted in aggregate contractual financial penalties of approximately $4.7 million that were recorded in our condensed consolidated statement of operations as restructuring charges for the quarter ended June 30, 2016, as further described below. The suspension notices released us from any remaining undelivered supply and service commitments described above.

We continue to revisit all areas of investment and resources to potentially enable a further reduction of our expenses and extension of our cash runway.

Marketing, General and Administrative

Marketing expenses consist of professional fees related to preparation for the potential commercialization of octreotide capsules, if approved, as well as salaries and related benefits for commercial employees. In anticipation of marketing approval of our NDA, and prior to the receipt of the CRL in April 2016, we accelerated our preparation for commercialization of octreotide capsules, and we anticipated that these expenses would materially increase throughout 2016. Following our receipt of the CRL and the End of Review meeting, we announced a corporate restructuring plan intended to focus our resources on the continued development of Mycapssa for the maintenance treatment of adult acromegaly patients. This plan included a reduction of approximately 33% of our workforce, including substantially all of our commercial personnel.

General and administrative expenses consist primarily of salaries and related benefits, including stock-based compensation, related to our executive, finance, legal, 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.

Restructuring Charges

Restructuring charges consist of employee severance benefits and related costs, asset write-off resulting from restructuring plans, suspension fees associated with commercial manufacturing agreements, and other expenses associated with restructuring our operations.

Other Expenses, Net

Other expenses consist mainly of interest incurred on our long-term obligations, net of interest income earned on our investments.

Provision for Income Taxes

We are subject to federal and state income taxes for earnings generated in the United States, and foreign taxes on earnings of our wholly-owned Israeli subsidiary. Our consolidated tax expense is affected by the mix of our taxable income (loss) in the United States and foreign subsidiary permanent items, discrete items, and unrecognized tax benefits.

Critical Accounting Policies and Use of Estimates

We have adopted various accounting policies to prepare our consolidated financial statements in accordance with accounting principles generally accepted in the United States, or U.S. GAAP. Our most significant accounting policies are described in Note 1 to our consolidated financial statements included in our Annual Report on Form 10-K for the fiscal year ended December 31, 2015. There have been no material changes in our critical accounting policies during the three and six months ended June 30, 2016, except for our significant accounting policies related to accounting for employee share-based payments, which is discussed in Note 1 to the condensed consolidated financial statements included in this Quarterly Report on Form 10-Q. The preparation of our consolidated financial statements in conformity with U.S. GAAP requires us to make estimates and assumptions that affect the amounts reported in our consolidated financial statements and accompanying notes. Our estimates and assumptions, including those related to the accounting for stock-based compensation, present value of long-term purchase obligation, income taxes, useful lives of long-lived assets, and accounting for certain accruals. We assess the above estimates on an ongoing basis; however, actual results could materially differ from those estimates.

Results of Operations for the Three and Six Months Ended June 30, 2016 and 2015

Research and Development

The following is a comparison of research and development expenses for the three and six months ended June 30, 2016 and 2015 (in thousands, except percentages):

	Three Months Ended June 30,				Six Months Ended June 30,			
	2016	2015	$ Change	Percent change	2016	2015	$ Change	Percent change
Research and development	$14,779	$4,158	$10,621	255%	$22,005	$6,377	$15,628	245%

For the three months ended June 30, 2016, our total research and development expenses increased by $10.6 million to $14.8 million. For the six months ended June 30, 2016, our total research and development expenses increased by $15.6 million to $22.0 million. The increases were primarily due to approximately $7.4 million of API purchases during the three months ended June 30, 2016, our ongoing Phase 3 clinical trial of octreotide capsules for the treatment of acromegaly to support the submission of a MAA to the EMA, activities associated with the manufacturing process validation, and an increase in salaries and related expenses due to the hiring of research and development employees.

Marketing, General and Administrative

The following is a comparison of marketing, general and administrative expenses for the three and six months ended June 30, 2016 and 2015 (in thousands, except percentages):

	Three Months Ended June 30,				Six Months Ended June 30,			
	2016	2015	$ Change	Percent change	2016	2015	$ Change	Percent change
Marketing	$1,403	$1,530	$ (127)	(8%)	$ 6,995	$2,330	$ 4,665	200%
General and administrative	3,989	1,907	2,082	109%	8,391	3,038	5,353	176%
Total marketing, general and administrative expenses	$5,392	$3,437	$ 1,955	57%	$15,386	$5,368	$10,018	187%

For the three months ended June 30, 2016, our marketing expenses decreased by $0.1 million to $1.4 million. For the six months ended June 30, 2016, our marketing expenses increased by $4.7 million to $7.0 million. For the three months ended June 30 2016, the decrease was primarily driven by reductions in stock based compensation resulting from the reduction in force of substantially all of our commercial personnel and a reduction in pre-commercial activity expenditures following the CRL. For the six months ended June 30, 2016, the increase was primarily due to pre-commercial activities related to octreotide capsules and greater compensation-related expenses associated with our expanded U.S. marketing and sales leadership team in anticipation of our expected FDA approval of octreotide capsules in April 2016 for commercialization in the U.S, which did not occur.

For the three months ended June 30, 2016, our general and administrative expenses increased by $2.1 million to $4.0 million. For the six months ended June 30, 2016, our general and administrative expenses increased by $5.4 million to $8.4 million. The increases were primarily due to greater compensation-related expenses associated with our expanded U.S. office as well as increased professional and consulting fees associated with being a public company.

Restructuring Charges

In June 2016, we announced a corporate restructuring plan, including an immediate reduction of approximately 33% of our workforce, including substantially all of our commercial personnel. As a result, we recorded restructuring charges totaling $6.5 million during the three months ended June 30, 2016, including one-time employee severance benefits and related costs of $1.5 million, one-time non-cash restructuring charges related to previously capitalized commercial software of $0.4 million and one-time manufacturing suspension fees of $4.7 million. In July 2016, we paid approximately $4.4 million of the manufacturing suspension fees.

Other (Income) Expense, net

Other income totaled $0.3 million for the six months ended June 30, 2016, compared to $0.2 million of other expenses for the same period in 2015. The improvement was driven by interest income generated from the investment of our IPO proceeds and a decrease in 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 $0.2 million for the six months ended June 30, 2016, representing an effective tax rate of (0.4%), as compared to a tax provision of $0.1 million for the six months ended June 30, 2015, representing an effective tax rate of (0.6%).

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, 2016, we have raised an aggregate of $366.2 million to fund our operations, of which $86.3 million was through our license agreement with Roche, approximately $106.5 million from selling shares of common stock in our IPO, $161.4 million from the issuance of private securities, and $12.0 million 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, 2016, our cash and cash equivalents were $30.5 million, of which $1.2 million was held by our Israeli subsidiary. In addition, as of June 30, 2016, we have $85.1 million invested in short term marketable securities.

Plan of Operations and Future Funding Requirements

We expect that our primary uses of capital will be associated with seeking regulatory approval of octreotide capsules in the United States and Europe, including additional development after we evaluate various pathways to determine whether we can produce additional data sufficient to satisfy the FDA of the efficacy and safety of Mycapssa in adult patients with acromegaly, manufacturing of octreotide capsules for market consumption and clinical trial uses, clinical trial costs (including the international Phase 3 clinical trial that we initiated in March 2016 to support European regulatory approval of octreotide capsules and a possible additional clinical trial or trials to support United States regulatory approval of octreotide capsules), legal and regulatory expenses related to seeking regulatory approval of octreotide capsules in the United States and Europe, 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.

In June 2016, following the CRL and our End of Review meeting, we announced a corporate restructuring plan intended to focus our resources on the continued development of Mycapssa for the potential maintenance treatment of adult acromegaly patients. This plan

included a reduction of approximately 33% of our workforce, including substantially all of our commercial personnel. We continue to revisit all areas of investment and resources to potentially enable further reductions in our expenses and extend our cash runway. We currently expect our existing cash, cash equivalents and marketable securities to fund our operations through at least 2017. Because of the uncertainty created by the CRL, we cannot estimate the actual amounts necessary to successfully complete the development and commercialization of octreotide capsules 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, but not limited to:

- the costs, timing and outcome of regulatory review of octreotide capsules and any future product candidates;
- the progress and results of our clinical trials of octreotide capsules;
- the costs and timing of future commercialization activities, including product manufacturing, marketing, sales and distribution, for octreotide capsules and any other future product candidates for which we receive marketing approval;
- proceeds, if any, received from commercial sales of octreotide capsules and any future product candidates for which we receive marketing approval;
- 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 or explore or consummate other strategic transactions.

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. We are currently eligible to file a shelf registration statement and believe that shelf registration statements can contribute, when used, to greater financial flexibility. To that end, we plan to consider filing a shelf registration statement on Form S-3 with the Securities and Exchange Commission in the future. 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, 2016 and 2015 (in thousands):

	Six Months Ended June 30,	
	2016	2015
Cash flows provided by (used in):		
Operating activities	$ (29,736)	$ (11,918)
Investing activities	20,281	(93)
Financing activities	(1,101)	35,118

Operating Activities

Net cash used in operating activities was $29.7 million for the six months ended June 30, 2016, and primarily consisted of $43.8 million in net loss, adjusted for non-cash items of $2.8 million (primarily stock-based compensation of $2.1 million and non-cash restructuring charges of $0.4 million) and was offset by working capital increases of $11.3 million (primarily driven by the increase in accounts payable and accrued expenses driven by API purchases and restructuring charges). Net cash used in operating activities was $11.9 million for the six months ended June 30, 2015, and primarily consisted of $12.0 million in net loss, adjusted for non-cash items of $1.1 million (primarily stock-based compensation) and working capital decreases of $1.0 million (primarily driven by the decrease in accounts payable and accrued expenses). The increase in our cash used was driven by our Phase 3 trial in Europe, purchases of API, pre-commercial marketing expenditures, activities associated with the manufacturing process validation, compensation-related expenses associated with our expanded U.S. office as well as increased professional service fees.

Investing Activities

Net cash provided by investing activities was $20.3 million for the six months ended June 30, 2016, primarily related to the maturity of marketable securities and was partially offset by $2.4 million of purchases of property and equipment, compared to $0.1 million in cash used in investing activities for the six months ended June 30, 2015, primarily related to the purchase of property and equipment.

Financing Activities

Net cash used in financing activities was $1.1 million during the six months ended June 30, 2016, primarily related to the first $1.7 million installment payment related to the termination of the Roche license agreement and was partially offset by proceeds from stock option exercises, compared to cash provided by financing activities of $35.1 million for the six months ended June 30, 2015, resulting primarily from the sale and issuance of the second tranche of our Series E redeemable convertible preferred stock and common stock warrants.

Contractual Obligations

As of March 31, 2016, we were contractually committed to purchasing approximately $16.9 million of commercial manufacturing supplies and services over the subsequent 15 months, of which approximately $7.4 million of supplies and services ordered were non-cancellable and delivered during the second quarter of 2016. Following our receipt of the CRL, we indefinitely suspended our commercial production commitments in May 2016, which resulted in aggregate contractual financial penalties of approximately $4.7 million which were recorded in our condensed consolidated statement of operations as restructuring charges for the quarter ended June 30, 2016. The suspension notices released us from any remaining undelivered supply and service commitments described above. We paid $4.4 million of the API purchases in June 2016 and the $7.3 million related to API and contractual financial penalties in July 2016 which fulfilled our contractual commercial API purchase commitments.

We conduct our operations in leased facilities, which are accounted for as operating leases. Certain leases include renewal options. In addition, we lease automobiles and equipment under operating leases. There were no assets held under capital leases at June 30, 2016 or December 31, 2015. In conjunction with the facility leases, we provided bank guarantees in the aggregate amount of $1.3 million as security deposits at June 30, 2016, which were classified as other assets in the accompanying condensed consolidated balance sheets. At June 30, 2016, the minimum rental commitments under all non-cancelable operating leases with initial or remaining terms of more than one year was approximately $12.1 million through 2025.

Off-Balance Sheet Arrangements

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

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.

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, 2016, we had $30.5 million in cash and cash equivalents, consisting of cash in checking accounts at U.S. and Israeli banking institutions as well as money market funds. In addition, as of June 30, 2016, we had $85.1 million of marketable securities consisting of short-term corporate notes. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates. An immediate 100 basis point change in interest rates would cause a decrease in the value of our short-term investments of $0.3 million. As of June 30, 2016, we did not have any outstanding borrowings, and as a result 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 seek 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 have been approximately 23%, 27% and 12%, respectively. As of June 30, 2016, we held $1.2 million in Israeli banks and petty cash funds to support our Israeli operations, approximately half 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, 2016, 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, 2016, 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.

PART II — OTHER INFORMATION

Item 1. Legal Proceedings

On June 9, 2016, Chiasma, Inc. and certain of our officers were named as defendants in a purported federal securities class action lawsuit filed in the United States District Court for the District of Massachusetts, styled *Gerneth v. Chiasma, Inc., et al*. This lawsuit challenges our public statements regarding our Phase 3 clinical trial methodology for Mycapssa (octreotide) capsules and our ability to obtain FDA approval for the marketing and sale of Mycapssa, in violation of Sections 10(b) and 20(a) of the Securities Exchange Act of 1934, as amended, and Rule 10b-5 promulgated thereunder, and Sections 11 and 15 of the Securities Act of 1933, as amended. The plaintiff seeks to represent a class consisting of all purchasers of our common stock from July 15, 2015 to April 17, 2016. We believe this lawsuit is meritless and intend to vigorously defend against it. At this time, no assessment can be made as to the likely outcome of this lawsuit or whether the outcome will be material to us.

Item 1A. Risk Factors

Investing in our common stock involves a high degree of risk. The risk factors described below pertain to us as of the date hereof and following (i) our receipt in April 2016 of a Complete Response Letter, or CRL, from the U.S. Food and Drug Administration, or FDA, regarding our New Drug Application, or NDA, for Mycapssa (octreotide) capsules for the maintenance treatment of U.S. adult patients with acromegaly and (ii) our participation in an End of Review meeting with the FDA in June 2016 regarding the CRL and our subsequent receipt of the related meeting minutes, in each case, as described elsewhere in this Quarterly

Report on Form 10-Q. These risk factors should be carefully considered although the risks described below are not the only risks facing us. Additional risks and uncertainties not currently known to us or that we currently deem to be immaterial also may materially adversely affect our business, financial condition or operating results and could cause the market price of our common stock to fluctuate or decline. The risk factors set forth below with an asterisk (*) next to the title are new risk factors or risk factors containing changes from the risk factors previously disclosed in Item 1A of our Annual Report on Form 10-K for the fiscal year ended December 31, 2015, as filed with the SEC.

Risks Related to the Development and Potential Regulatory Approval and Commercialization of Mycapssa (Octreotide) Capsules and any Future Product Candidates

In light of our receipt of a CRL from the FDA regarding our NDA for Mycapssa (octreotide) capsules for the maintenance treatment of U.S. adult patients with acromegaly and our subsequent participation in an End of Review Meeting with the FDA, the U.S. regulatory pathway for octreotide capsules is uncertain and we may never obtain regulatory approval in the United States.

On June 15, 2015, we submitted an NDA to the FDA for the marketing and sale of octreotide capsules, an oral drug proposed for the maintenance therapy of adult patients with acromegaly. The NDA was accepted for filing by the FDA in August 2015. On the Prescription Drug User Fee Act, or PDUFA, date of April 15, 2016, the FDA issued a CRL regarding the NDA, indicating that their review is complete and the NDA is not ready for approval in its present form. In its CRL, the FDA advised us that it did not believe our application provided substantial evidence of efficacy to warrant approval, and advised us that we would need to conduct another clinical trial in order to overcome this deficiency. The FDA expressed concerns regarding certain aspects of our single-arm, open-label Phase 3 clinical trial and strongly recommended that we conduct a randomized, double-blind and controlled trial that enrolls patients from the United States and is of sufficiently long duration to ensure that control of disease activity is stable at the time point selected for the primary efficacy assessment. In addition, the FDA advised that, during a recent site inspection, certain deficiencies were conveyed to the representative of one of our suppliers that would need to be resolved before approval. In addition, while the FDA did not note any safety concerns related to Mycapssa in the CRL, it subsequently indicated in the End of Review meeting minutes that the size, duration, dropout rate and absence of a control group in our Phase 3 clinical trial were factors limiting an overall safety assessment.

In the CRL, the FDA encouraged us to request an End of Review meeting to discuss the path forward for our NDA. In June 2016, we participated in an End of Review meeting with the FDA to discuss the concerns the FDA raised in the CRL and are in receipt of the minutes of that meeting. In the End of Review meeting minutes, the FDA reiterated its strong recommendation for a randomized, double-blind and controlled trial, and introduced the concept of a placebo control as a design element that could address some of the FDA's concerns. While we acknowledge this feedback, we continue to evaluate various potential paths forward, including a determination as to whether we can produce data sufficient to satisfy the FDA of the efficacy and safety of Mycapssa in adult patients with acromegaly. The FDA stated that it considers pathways alternative to its recommendations to be less ideal and ultimately more risky to our efforts to secure approval of our NDA for octreotide capsules in acromegaly. The FDA strongly recommended that we work with the FDA to reach a common understanding of expectations prior to initiating and executing any alternative plans. We cannot provide any assurance that the trial strongly recommended by the FDA, if conducted by us, or any other alternative development pathway, whether acceptable or unacceptable to FDA, will result in the approval of our NDA for octreotide capsules.

As previously disclosed, varying interpretations of the data obtained from nonclinical and clinical testing or manufacturing of our product candidates could delay, limit or prevent regulatory approval of octreotide capsules 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 octreotide capsules after reviewing the data from the seven-month core treatment period of our Phase 3 clinical trial of octreotide capsules 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 octreotide capsules, 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 2014). 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, the FDA also 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 would carry more weight in the efficacy evaluation than the extension data. The FDA also informed us that, in its view, a single-arm study was 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 submitted in our NDA from our single-arm study, and whether these findings would be robust enough to warrant approval, would be review issues as the agency evaluated our NDA.

If our efforts to address the concerns raised by the FDA are unsuccessful, we may be unable to obtain U.S. regulatory approval for the marketing and sale of octreotide capsules at all or without submitting new or additional clinical data to the FDA, which may require that we conduct one or more additional clinical trials. The FDA strongly recommended that we conduct a randomized, double-blind and controlled trial that enrolls patients from the United States and is of sufficiently long duration to ensure that control of disease activity is stable at the time point selected for the primary efficacy assessment. In addition, in the minutes from our End of Review

meeting, the FDA introduced the concept of a placebo control as a design element that could address some of the FDA's concerns. Conducting one or more additional clinical trials would significantly delay our ability to secure regulatory approval and introduce new risks and uncertainties depending on the trial design and timing of any trials conducted. Conducting a randomized, double-blind and controlled trial, perhaps with a placebo control, in this indication, as strongly recommended by the Agency, would be particularly challenging. For example, it may be difficult to identify patients with acromegaly willing to enroll in a trial with this design, the trial could take years to complete, and the FDA's review of the data would also likely consume significant time. The company cannot estimate how long this process could take but it could be several years. We may not have sufficient capital resources to fully fund any new trials that the FDA requires as a condition to approval, in particular a randomized, double-blind and controlled trial of sufficiently long duration.

The U.S. regulatory pathway is highly uncertain at this time, and we may never reach a common understanding with the FDA on a path forward to develop Mycapssa in the U.S., or obtain regulatory approval of octreotide capsules in the United States. If that were to occur, it would have a material adverse effect on our operations and financial condition.

We are heavily dependent on the regulatory approval and subsequent commercial success of octreotide capsules for the treatment of acromegaly in the United States and Europe, 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 octreotide capsules for the treatment of acromegaly in the United States, Europe and other countries. Our ability to generate revenues will depend on our ability to obtain regulatory approval and successfully commercialize octreotide capsules. Our receipt of a CRL from the FDA to our NDA for octreotide capsules will likely result in a significant delay in our ability to commercialize octreotide capsules in the United States, if we are ever able to obtain U.S. regulatory approval at all.

Even if we receive regulatory approval, the timing of the commercial launch of octreotide capsules in the United States is dependent upon a number of factors, including, but not limited to, hiring and retaining sales and marketing personnel (especially since we terminated substantially all of our commercial personnel in June 2016), pricing and reimbursement timelines, the production of sufficient quantities of commercial drug product (especially since we indefinitely suspended all of our commercial manufacturing commitments during the second quarter of 2016) and implementation of a distribution infrastructure. In addition, the FDA may introduce significant restrictions to the label for octreotide capsules in an effort to address the concerns it has raised in the CRL and the End of Review meeting. Any such restrictions or concerns about efficacy within the medical community could significantly impact market adoption and commercial performance of octreotide capsules. However, and in light of the CRL, we cannot anticipate when we will be able to commercialize octreotide capsules in the United States, if at all.

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 octreotide capsules in the United States, Europe and elsewhere. This represents a significant investment in the clinical and regulatory success of octreotide capsules, which is uncertain. The success of octreotide capsules, if approved, will depend on several factors, including:

- execution of an effective sales and marketing strategy for the commercialization of octreotide capsules;
- acceptance by patients, the medical community and third-party payors;
- the incidence and prevalence of acromegaly in those markets in which octreotide capsules is approved;
- the prevalence and severity of side effects, if any, experienced with octreotide capsules;
- 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 octreotide capsules;
- successful implementation of our manufacturing processes and production of sufficient quantities of commercial drug product;
- maintaining compliance with regulatory requirements, including current good manufacturing practices, or cGMPs and overcoming the deficiency with our supplier referenced in the CRL or take other measures satisfactory to the FDA; 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 octreotide capsules, our development costs may increase and our ability to generate revenue or profits, or to raise additional capital could be impaired, all of which could result in our market value and stock price declining significantly.

If we are not able to obtain required regulatory approvals for octreotide capsules, we will not be able to commercialize this 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 octreotide capsules for the maintenance therapy of acromegaly, which was accepted for filing to permit a substantive review. The FDA issued a CRL regarding our NDA on our PDUFA date of April 15, 2016, indicating that the NDA was not able to be approved during this review cycle and strongly recommending that we conduct a randomized, double-blinded, controlled trial. In the End of Review meeting, the FDA reiterated its strong recommendation for a randomized, double-blind and controlled trial.

In October 2015, the European Medicines Agency, or EMA, accepted the design, enrollment criteria and required duration of our Phase 3 trial to evaluate the non-inferiority of octreotide capsules to injectable somatostatin analogs in adult patients with acromegaly. This clinical trial, to which the first patient was enrolled in the United States in March 2016, is an open-label, randomized, active-controlled study that is currently anticipated to include approximately 150 patients in the European Union, the United States and certain other countries. This clinical trial is currently designed to show comparative effectiveness as required by the EMA, to support MAA submission and approval, has not been reviewed by the FDA for purposes of addressing the efficacy concerns identified by the FDA in the CRL, is not designed to meet the criteria set forth by the FDA in the CRL and End of Review meeting minutes, and may not be acceptable to the FDA for the purpose of gaining U.S. approval. The FDA may never approve our NDA, our ongoing Phase 3 clinical trial may not be successful, or acceptable to the FDA or EMA to support regulatory approval in the United States or Europe, respectively, the CRL could adversely impact the EMA's review of our regulatory submission, and therefore we may never receive approval to market octreotide capsules 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, and these regulations differ from country to country and change over time. We are not permitted to market octreotide capsules 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 June 2015 submission of our NDA for octreotide capsules in acromegaly to the FDA, we have not yet submitted comparable applications to other regulatory authorities. If our development efforts for octreotide capsules, including regulatory approval, are not successful for its planned indications or are delayed, or if adequate demand for octreotide capsules is not generated, our business will be harmed.

The success of octreotide capsules 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 octreotide capsules' 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 octreotide capsules 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 octreotide capsules;
- the data collected from our 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, one of which was identified by the FDA in its CRL, 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. 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, as the FDA strongly recommended in the CRL.

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. Octreotide capsules 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 octreotide capsules 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 octreotide capsules 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 or entity 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 nonclinical and clinical programs to seek regulatory approval for octreotide capsules for registration filing in the United States using the FDA's 505(b)(2) regulatory pathway and using the hybrid application pathway, which is analogous to the 505(b)(2) regulatory pathway, in Europe. As such, our NDA in the United States relied, and we intend that 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 designed our development programs to take advantage of Section 505(b)(2) and the hybrid application pathway to support potential regulatory approval of octreotide capsules 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 or initiated, such as the randomized, double-blind and controlled clinical trial strongly recommended by the FDA in the CRL and End of Review meeting. The relevant regulatory authorities also may determine that we have not provided sufficient data to justify reliance on prior investigations involving the approved immediate-release injectable octreotide product.

In addition, notwithstanding the approval of many products by the FDA pursuant to Section 505(b)(2), in the past some pharmaceutical companies and others have objected to the FDA's interpretation of Section 505(b)(2). For example, parties have filed citizen petitions objecting to the FDA approving a Section 505(b)(2) NDA on scientific, 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. 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 octreotide capsules 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 initiated a second Phase 3 clinical trial of octreotide capsules in acromegaly to support approval by the EMA, and may eventually initiate clinical trials of octreotide capsules in indications other than acromegaly, such as neuroendocrine tumors, or NETs, assuming financing is available to us and prior regulatory approvals of octreotide capsules in acromegaly are obtained.

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 that we believe were generated in our completed clinical trials for octreotide capsules 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 comparable results. For example, the EMA required that we use multiple time points in the Phase 3 clinical trial that we initiated in March 2016 rather than a single time point for the primary endpoint determination used for our initial Phase 3 clinical trial. The EMA agreed that we use the same cut off of IGF-1 < 1.3 times the upper limit of normal as the threshold for response. The fact that we have not used such an endpoint previously for regulatory submissions introduces an additional level of uncertainty in the outcome of this Phase 3 European clinical trial, or for other studies using this methodology for assessing the success of our product candidate. We cannot provide assurance that the FDA or EMA will view the results as we do or that any future trials of octreotide capsules, including our current Phase 3 clinical trial in acromegaly to support regulatory approval in Europe, any additional clinical trials we may conduct to support regulatory approval in the United States, 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 octreotide capsules for the treatment of acromegaly, any future clinical trial results of octreotide capsules may not be successful in any particular indication. A number of factors could contribute to a lack of favorable safety and efficacy results for octreotide capsules for acromegaly or 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 octreotide capsules for the treatment of acromegaly or other indications, and any other product candidates we may develop, may be adversely impacted.

Further, our NDA relied upon the FDA's 505(b)(2) regulatory pathway for octreotide capsules 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 octreotide capsules 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 octreotide capsules 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 ongoing or future trials of octreotide capsules 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, negatively impact our commercial prospects and cause our market value and stock price to fall.

Delays in the completion of the Phase 3 clinical trial we initiated in March 2016 to support marketing approval of octreotide capsules in acromegaly in Europe, any future clinical trials we may conduct to support regulatory approval of octreotide capsules in the United States, the clinical trials of octreotide capsules for other indications, if conducted, or any future clinical trials we may 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 octreotide capsules. For example, in October 2015, the EMA required us to revise our protocol for our recently initiated Phase 3 clinical trial to extend the control period from six months to nine months. The final protocol accepted by EMA therefore resulted in additional time to complete our second Phase 3 clinical trial of octreotide capsules. While we initiated this international Phase 3 clinical trial of octreotide capsules in acromegaly in March 2016 to show parallel comparative safety and effectiveness as required by the EMA, we do not know whether future trials will begin or whether the EMA Phase 3 trial will be completed on schedule, if at all, or will be successful. The commencement and completion of the EMA Phase 3 trial or other clinical trials that may be conducted 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;
- 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 octreotide acetate or octreotide capsules or any other product candidate we may develop being found deficient in its processes, as the FDA noted in its CRL to our NDA, or 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 octreotide capsules 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 licenses or permits necessary to perform our clinical trials, not performing our clinical trials on our anticipated schedule or employing methods that are inconsistent 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 octreotide capsules 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, such as the delay in approval of octreotide capsules due to the CRL to our NDA, or if we need to perform more or larger clinical studies than planned. If we experience delays in the 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 octreotide capsules 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 octreotide capsules 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 octreotide capsules 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 octreotide capsules 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 octreotide capsules or any future product candidates we may develop beyond those that we may propose to conduct, or if we are unable to successfully complete our clinical trials or other studies, we may be delayed in obtaining regulatory approval of octreotide capsules and any future product candidates we may develop, we may not be able to obtain regulatory approval at all or we may obtain approval of indications that are not as broad as intended. Our product development costs will also increase if we experience delays in testing or approvals, and we may not have sufficient funding to complete the testing and approval process for octreotide capsules 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 octreotide capsules and any other product candidates that we may pursue, which could delay or prevent clinical trials of octreotide capsules and any future product candidates we may develop and potentially harm our business.

Identifying and qualifying patients to participate in clinical trials of octreotide capsules 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 octreotide capsules and any future product candidates we may develop as well as completion of required follow-up periods. If patients are unable or 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 octreotide capsules and any future product candidates we may develop may be delayed. These delays could result in increased costs, delays in advancing octreotide capsules 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 may evaluate octreotide capsules 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. For example, while we are enrolling patients in the United States, Europe and other countries, we are not permitted to enroll patients from our prior clinical trials in our ongoing Phase 3 clinical trial to support MAA submission and approval in the E.U. Further, the issuance of the CRL by FDA may negatively impact physician or patient attitudes towards octreotide capsules which could significantly delay enrollment in this study. In addition, conducting a randomized, double-blind and controlled trial in the United States, as strongly recommended by the FDA in the CRL, would be particularly challenging as we believe it would be difficult to identify patients with acromegaly willing to enroll in a trial with this design, and we believe such a trial could take several years to complete and submit to FDA for review.

Patient enrollment is affected by factors including the:

- 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;
- possibility of receiving placebo rather than active drug in certain controlled trials;
- 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
- ability to monitor patients adequately during and after treatment.

If we have difficulty enrolling a sufficient number of patients to conduct our clinical trials, 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 octreotide capsules and any future product candidates we may develop in lieu of prescribing existing treatments that have established safety and efficacy profiles. 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 the:

- difficulty in establishing or managing relationships with CROs and physicians;
- different requirements and standards for conducting clinical trials;
- inability to locate qualified local consultants, physicians and partners; and
- 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 octreotide capsules for acromegaly, we may still face future development and regulatory challenges that could inhibit or preclude our ability to commercialize octreotide capsules for any indication.

Even if we obtain regulatory approval of octreotide capsules for the treatment of acromegaly, NET and other indications we may pursue, or any other product candidates we may develop, they will be subject to ongoing requirements by the FDA and comparable foreign regulatory authorities governing manufacturing, quality control, further development, labeling, packaging, storage, distribution, safety surveillance, import, export, advertising, promotion, recordkeeping and reporting of safety and other post-market information. If approved, the safety profile of octreotide capsules 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 octreotide capsules 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 octreotide capsules, if it achieves marketing approval, may include restrictions on use, which could limit the marketability of octreotide capsules and impair our ability to have octreotide capsules gain market acceptance. If we do not receive approval of octreotide capsules for the treatment of acromegaly, we may not be able to develop or commercialize octreotide capsules in NET or other indications.

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, among other things:

- 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 octreotide capsules, if approved, 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 octreotide capsules, if approved, 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 octreotide capsules and any other product candidates we may develop are likely to be efficacy, safety and tolerability profile, reliability, convenience of administration, price and reimbursement and effectiveness of our promotional activities. For example, physicians may choose not to prescribe octreotide capsules, if approved, because a lower percentage of patients met the criteria for response in our Phase 3 clinical trial after treatment with octreotide capsules compared to their baseline response rates on injectable therapy. Competition could also force us to lower prices or could result in reduced sales.

The current injectable pharmaceutical treatment options for patients suffering from acromegaly are marketed by large pharmaceutical companies with substantial resources and well-established presences 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. 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 most 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 competitive with or superior to other products on the market;
- obtain required regulatory approvals;
- adequately communicate the benefits of octreotide capsules, if approved;
- attract and retain qualified personnel;
- obtain and maintain patent and/or other proprietary protection for octreotide capsules and any future product candidates we may develop; and
- in certain geographies, obtain collaboration arrangements to develop and commercialize octreotide capsules 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 octreotide capsules or any future product candidates we may develop obsolete or non-competitive before we can recover the expenses of developing and commercializing octreotide capsules 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 octreotide capsules 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 octreotide capsules 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 are an estimated 69,000 individuals with acromegaly worldwide. 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. In thirteen studies of acromegaly prevalence since 1980, an average of approximately 75 cases per million was determined, suggesting roughly 24,000 individuals with acromegaly in the United States. 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. We believe that approximately 8,000 adult acromegaly patients are chronically treated with somatostatin analogs in the United States. 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 octreotide capsules 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 octreotide capsules 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.

****Even if we receive regulatory approval of octreotide capsules, 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 octreotide capsules, if approved, will depend in large part on the willingness of physicians to prescribe these products to their patients. Octreotide capsules, if approved, will compete against products that have achieved broad recognition and acceptance among medical professionals. In order to achieve an acceptable level of prescriptions for octreotide capsules, if approved, 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 octreotide capsules, if approved, will depend on a number of factors, including:

- the clinical safety, efficacy, tolerability and other factors regarding octreotide capsules relative to injectable somatostatin analogs;
- the relative convenience, number of capsules that need to be taken, requirement to fast before and after each dose of octreotide capsules, and other factors affecting the ease of administration;
- the prevalence and severity of any adverse effects;
- the willingness of physicians to prescribe octreotide capsules 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 octreotide capsules 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 octreotide capsules may show utility;
- pricing and cost-effectiveness;
- the effectiveness of our or any future collaborators' sales and marketing, as well as disease education and awareness programs;
- limitations or warnings contained in labeling approved by the FDA or comparable foreign regulatory authorities;
- 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 octreotide capsules.

In addition, even if we obtain regulatory approvals, the timing or scope of any approvals may prohibit or reduce our ability to commercialize octreotide capsules successfully. For example, if the approval process takes too long, which is a greater likelihood as a result of the CRL from the FDA to our NDA, 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 be subject to restrictions or post-approval commitments that render octreotide capsules not commercially viable. For example, regulatory authorities may approve octreotide capsules for fewer or more limited indications than we request, may limit approved usage to narrower patient populations, may grant approval contingent on the performance of costly post-marketing clinical trials, or may approve octreotide capsules 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 octreotide capsules.

Even if octreotide capsules are approved, they 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 octreotide capsules and patients are transitioning from injected alternatives to octreotide capsules. Our efforts to educate the medical community, patients and third-party payors on the benefits of octreotide capsules 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.

Due to the recent restructuring, we no longer have a 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 octreotide capsules, if regulatory approvals are obtained.

As a result of our June 2016 restructuring action, we no longer have sales personnel and have a very limited number of marketing personnel. Based upon feedback provided by the FDA and our own analysis, we believe new or additional data will be required before the FDA would consider U.S. regulatory approval for the marketing and sale of octreotide capsules, which may require that we conduct one or more additional clinical trials.

Even if we are able to obtain regulatory approval, we cannot guarantee when that will occur or whether we will be successful in marketing octreotide capsules in the United States or any other jurisdiction. If we are not successful in recruiting of sales and marketing personnel on a timely basis, retaining the limited key personnel with commercial experience that we currently have on staff, or rebuilding a sales and marketing infrastructure, or if we do not successfully enter into appropriate collaboration arrangements, we will have difficulty commercializing octreotide capsules, if approved, 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 octreotide capsules 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 octreotide capsules 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 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 octreotide capsules 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 octreotide capsules 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 octreotide capsules 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 octreotide capsules and generate revenue.

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

Due to the recent restructuring, we no longer have a full medical affairs organization and, if we are unable to establish effective medical affairs capabilities in the United States and build or access them in Europe and other international markets, our business may suffer.

As a result of our June 2016 restructuring action, we no longer have a full medical affairs organization. Medical affairs personnel are responsible for a number of key activities within biopharmaceutical companies, which include, but are not limited to, providing expert advice to other functions within the organization, advising on medical education activities, reviewing promotional and non-promotional communications, supporting medical and scientific publications, reviewing grants for third-party continuing medical education events, and providing an important scientific point of contact for physicians and scientists who seek to partner with us or better understand our science.

Failure to successfully execute these activities could harm our business in the following ways:

- Our reputation among key physicians and scientists in acromegaly and other disease areas of interest to us may suffer;

- We may not be able to secure the advice and feedback of outside experts to help advance our knowledge and understanding of complex scientific and medical issues;
- Our commercial and corporate functions may not receive adequate medical and scientific information in the creation of their external communications, which could lead to inaccurate information being disseminated about the company, its product candidates, its disease areas of interest, or its other scientific endeavors;
- Our promotional, non-promotional, grants, and medical events review processes may not provide an effective control to ensure compliance with applicable laws, regulations and standards; and
- We may not successfully interact with European or other ex-U.S. healthcare professionals and scientists who could help the company execute plans for expansion into Europe or other international markets.

Even if we obtain marketing approval of octreotide capsules 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 octreotide capsules. Even if octreotide capsules are being marketed, the manufacture and marketing of octreotide capsules will be subject to ongoing regulation, including compliance with cGMPs, adverse event reporting requirements, guidance regarding the provision of reimbursement support and patient services, 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. Government investigation of these issues itself typically requires the expenditure of significant resources and can generate negative publicity, which could harm our business. 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. In recent years, 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 octreotide capsules 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 octreotide capsules, 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 octreotide capsules 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 octreotide capsules. For example, in its CRL, the FDA advised that, during a recent site inspection, certain deficiencies were conveyed to the representative of one of our suppliers that would need to be resolved before approval of our NDA for octreotide capsules.

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

Furthermore, in order to obtain approval of our product candidates, including octreotide capsules, 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 required testing 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, 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 manufacturing, 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 octreotide capsules 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 octreotide capsules 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 octreotide capsules and any future product candidates we may develop may be delayed and our business and results of operations may be harmed.

Octreotide capsules 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 octreotide capsules 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 octreotide capsules, if approved, and other products that we may develop. These third-party payors continually attempt to contain or reduce the costs of health care, such as 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 octreotide capsules are approved, we will seek to obtain reimbursement for octreotide capsules 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 enacted in 2010 with the passage of the Affordable Care Act, or the ACA. 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 octreotide capsules and our other potential products. Some of these changes and proposed changes could result in reduced reimbursement rates for octreotide capsules and our other potential products, which would adversely affect our business strategy, operations and financial results.

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

We expect that private insurers will consider the efficacy, cost effectiveness and safety of octreotide capsules, if approved, in determining whether to provide reimbursement for octreotide capsules 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 octreotide capsules, our business would be harmed if we do not receive approval of reimbursement of octreotide capsules 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 octreotide capsules.

Our business could also be harmed if governments, private insurers, Medicare, Medicaid or other reimbursing bodies or payors limit the indications for which octreotide capsules 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 octreotide capsules 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. In addition, even if we receive regulatory approval, the FDA may introduce significant restrictions to the label for octreotide capsules in an effort to address certain concerns raised in the CRL and End of Review meeting. Any such restrictions or potential reservations about efficacy expressed in the CRL within the medical community could significantly impact reimbursement, market adoption and commercial performance of octreotide capsules.

We expect to experience pricing pressures in connection with the sale of octreotide capsules 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 octreotide capsules, 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 octreotide capsules, if approved, we may 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, EMA and other health authority, as applicable, 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 octreotide capsules 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, or following receipt of the CRL to our NDA, 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, or in achieving economic terms that will be sufficiently favorable to justify development of one or more such future products.

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

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

- we may be unable to license or acquire the relevant product candidate or technology on terms that would allow us to make an appropriate return, or the financial terms required by the owners of those product candidates or technologies may be unfavorable enough to preclude successful development and commercialization for such products;
- companies that perceive us to be their competitors may be unwilling to assign or license their product rights to us;
- we may be unable to identify suitable products or product candidates within our areas of expertise; or
- our receipt of the CRL could reduce third-party confidence in our TPE platform and potentially make us a less attractive partner.

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 octreotide capsules 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 or the EMA 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 designation for octreotide capsules in acromegaly and may obtain orphan drug designation for octreotide capsules in other indications or for future product candidates we may develop, we may not obtain orphan drug exclusivity and any such exclusivity that we do obtain 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, if obtained. 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 octreotide capsules and any future product candidates we may develop for which we obtain marketing approval. Our arrangements with third-party payors and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may affect the business or financial arrangements and relationships through which we would market, sell and distribute our products. Even though we do not and will not control referrals of healthcare services or bill directly to Medicare, Medicaid or other third-party payors, federal and state healthcare laws and regulations pertaining to fraud and abuse and patients' rights are and will be applicable to our business. Restrictions under applicable federal and state healthcare laws and regulations that may affect our operations and expose us to areas of risk including the following:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons and entities from knowingly and willfully

soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made under a federal healthcare program such as Medicare and Medicaid;

- federal civil and criminal false claims laws and civil monetary penalty laws, which impose criminal and civil penalties, including through civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, including the Medicare and Medicaid programs, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program and also created federal criminal laws that prohibit knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statements in connection with the delivery of or payment for healthcare benefits, items or services;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, which also imposes obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of certain individually identifiable health information;
- the ACA 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 which 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 which 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 federal law, 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 ACA was 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"; and
- 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. If our product candidates are approved, we expect our branded pharmaceutical sales to constitute a small portion of the total federal health program pharmaceutical market, and therefore would not expect this annual assessment to have a material impact on our financial condition.

Despite initiatives to invalidate the ACA, 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 ACA, which provides federal premium tax credits to individuals purchasing coverage through health insurance exchanges. Additionally, there are legal challenges to the ACA in lower courts on other grounds.

The full effects of the ACA cannot be known until it is fully implemented through regulations or guidance issued by CMS and other federal and state healthcare agencies. The financial impact of the ACA 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. Although it is too early to determine the full effect of the ACA, 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.

In addition, other legislative changes have been proposed and adopted in the United States since the ACA 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 octreotide capsules, 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 octreotide capsules 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 octreotide capsules 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 octreotide capsules and any future product candidates we may develop, but we may be unable to obtain commercially reasonable product liability insurance for our product candidates, if approved for marketing. Large judgments have been awarded in class action lawsuits based on drugs that had unanticipated side effects. A successful product liability claim or series of claims brought against us, particularly if judgments exceed our insurance coverage, could decrease our cash and harm our business. In addition, we may not be able to maintain sufficient insurance coverage at an acceptable cost or otherwise to protect against potential product liability claims, which could prevent or inhibit the commercial production and sale of our products.

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

Risks Related to Our Reliance on Third Parties

****We are, and expect to be for the foreseeable future, dependent on a limited number of third parties to manufacture octreotide capsules.***

We do not currently have, nor do we plan to acquire, the capability or infrastructure to manufacture the API in octreotide capsules 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 an affiliate of Teva API, Inc., and Bachem Americas Inc. in the United States as our suppliers of the generic API, octreotide acetate. All excipients, or substances formulated together with the API that are used in the manufacture of octreotide capsules, are readily available. The octreotide API is lyophilized, formulated with our TPE technology, filled into capsules and enteric-coated by Lyophilization Services of New England Inc., or LSNE, 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 octreotide capsules are evaluated by the FDA. 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 API and finished drug products. These cGMP regulations cover all aspects of the manufacturing, testing, quality control and record keeping relating to octreotide capsules. 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, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory approval of or market octreotide capsules, if approved. For example, in its CRL, the FDA advised that, during a recent site inspection, certain deficiencies were conveyed to the representative of one of our suppliers that would need to be resolved before approval of our NDA for octreotide capsules.

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 octreotide capsules, 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 octreotide capsules.

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 octreotide capsules product or should cease doing business with us, we could experience significant interruptions in the supply of octreotide capsules or may not be able to create a supply of octreotide capsules at all. Were we to encounter manufacturing issues, our ability to produce a sufficient supply of octreotide capsules 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 octreotide capsules 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 octreotide capsules if we decided to transfer the manufacture of octreotide capsules 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, if our products receive marketing approval, result in lost sales. Additionally, we rely on third parties to supply the raw materials needed to manufacture our product candidates. 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 manufacturers caused by problems at suppliers could delay shipment of octreotide capsules and, if approved for marketing, 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 octreotide capsules over time, particularly following the recent suspension of our commercial commitments to certain of our manufacturers following the receipt of the CRL. If the manufacturing costs of octreotide capsules remain at current levels, these costs may significantly impact our operating results. In order to reduce costs, we may need to develop and implement process improvements. However, in order to do so, we will need, from time to time, to notify or make submissions with regulatory authorities, and the improvements may be subject to approval by such regulatory authorities. We cannot be sure that we will receive these necessary approvals or that these approvals will be granted in a timely fashion. We also cannot guarantee that we will be able to enhance and optimize output in our commercial manufacturing process. If we cannot enhance and optimize output, we may not be able to reduce our costs over time.

We have recently established commercial manufacturing agreements with Teva API, Inc. for the API in octreotide capsules and with LSNE for certain testing and lyophilization services. In anticipation of the approval of our NDA by FDA on the PDUFA date, we made substantial commercial production commitments to these manufacturers via binding rolling forecasts. Following our receipt of the CRL, we indefinitely suspended our commercial production commitments to Teva API, Inc. and LSNE, which resulted in aggregate financial penalties to us of approximately $4.7 million. In the future, if octreotide capsules are approved, we may not be able to reach or maintain agreements containing terms that are acceptable to us with our commercial manufacturers.

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.

****An important part of our strategy is to seek to enter into licensing or collaboration agreements with respect to octreotide capsules 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 octreotide capsules and any future product candidates we may develop 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. Our receipt of the CRL from the FDA may cause potential collaborators to assign a lower probability to our regulatory success of octreotide capsules which could reduce the likelihood of our ability to enter into a collaboration on favorable terms, if at all. 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 octreotide capsules. As a result, we assumed responsibility for the further development and commercialization of octreotide capsules and will receive no additional funding from Roche for this purpose.

Further, our potential future collaborators may develop alternative products or pursue alternative technologies either on their own or in collaboration with others, including our competitors, and the priorities or focus of our collaborators may shift such that our product candidates receive less attention or resources than we would like, or they may be terminated altogether. Any such actions by our potential future collaborators may harm our business prospects and ability to earn revenues. In addition, we could have disputes with our potential future collaborators, such as the interpretation of terms in our agreements. Any such disagreements could lead to delays in the development or commercialization of our product candidates or could result in time-consuming and expensive litigation or arbitration, which may not be resolved in our favor.

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 octreotide capsules or any future candidates we may develop could be delayed or not obtained at all.

We do not have the ability to conduct 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 clinical programs for octreotide capsules 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 octreotide capsules 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 primarily through proceeds from sales of our common stock, 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 $106.5 million after deducting underwriting discounts and commissions and offering expenses payable by us. From our inception through June 30, 2016, we had received net proceeds of $267.9 million from such transactions, including amounts raised in the IPO. As of June 30, 2016, our cash and cash equivalents and marketable securities were $115.6 million. Since inception, we have incurred significant operating losses. Our net loss was $43.8 million for the six months ended June 30, 2016, respectively, and $35.9 million for the year ended December 31, 2015. As of June 30, 2016, we had an accumulated deficit of $161.3 million.

We have no products approved for commercialization and have never generated any product revenue. We expect to incur operating losses for at least 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. In June 2016, in light of the CRL, we announced a corporate restructuring plan intended to focus our resources on the continued development of Mycapssa for the maintenance treatment of adult acromegaly patients. This plan included a reduction of approximately 33% of our workforce, including substantially all of our commercial personnel. We continue to revisit all areas of investment and resources to potentially enable further reductions in our expenses and extend our cash runway. We plan to issue guidance regarding our cash forecasts, planned product development activities and expenditures after we have determined our path forward and conducted these analyses. We currently expect our existing cash, cash equivalents and marketable securities to fund our operations through at least 2017. In addition, we will incur additional costs associated with operating as a public company. As a result of these and other factors, we expect to continue to incur significant 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.

We have not generated 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 octreotide capsules 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 octreotide capsules or any future product candidates are 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 octreotide capsules, including undertaking nonclinical studies and conducting clinical trials. Octreotide capsules are our only current product candidate for which we have conducted clinical trials, we have completed only a single later-stage clinical trial to date with this product candidate, and the FDA has strongly recommended that we complete a randomized, double-blind and controlled clinical study of octreotide capsules. 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 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 will 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 likely require additional capital that we have not yet secured. In the short term, we expect to continue to conduct an additional Phase 3 clinical trial of octreotide capsules to treat acromegaly required for European regulatory approval. In June 2016, following our receipt of the CRL and the End of Review meeting, we announced a corporate restructuring plan intended to focus the company's resources on the continued development of Mycapssa for the maintenance treatment of adult acromegaly patients. We continue to revisit all areas of investment and resources to potentially enable further reductions in our expenses and extend our cash runway. We plan to issue updated guidance regarding our cash forecasts, planned product development activities and expenditures after we have determined our path forward and conducted these analyses.

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:

- our efforts to obtain FDA approval of octreotide capsules in acromegaly, especially if we are required to conduct a randomized, double-blinded and controlled clinical trial as the FDA strongly recommended in the CRL;
- the amount of our future operating losses;
- the timing of approvals, if any, of octreotide capsules in additional jurisdictions;
- the need and cost of conducting one or more additional clinical trials for octreotide capsules and our other drug candidates;
- the amount of our research and development, marketing, selling and general and administrative expenses;
- the extent to which we enter into, maintain, and derive revenues from licensing agreements, including potential agreements to out-license octreotide capsules, research and other collaborations, joint ventures and other business arrangements;
- our success in integrating product candidates, technologies or companies that we may acquire; and
- regulatory changes and technological developments in our markets.

General market conditions or the market price of our common stock may not support capital-raising transactions, such as an additional public or private offering of our common stock or other securities. In addition, our ability to raise additional capital may be dependent upon our stock being quoted on The NASDAQ Global Select Market or upon obtaining stockholder approval. There can be no assurance that we will be able to satisfy the criteria for continued listing on The NASDAQ Global Select Market or that we will be able to obtain stockholder approval if it is necessary. If we are unable to obtain additional funds on a timely basis or on terms favorable to us, we may be required to cease or reduce certain research and development projects, to sell some or all of our technology or assets 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. The terms of any debt facility may involve significant cash payment obligations as well as covenants and specific financial ratios that may restrict our ability to commercialize octreotide capsules 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, the ownership interest of our existing stockholders will be diluted, and the terms may include liquidation or other preferences that adversely affect the rights of our existing stockholders. 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 and scientific personnel. As of August 1, 2016, and following our restructuring plan announced in June 2016, we had a total of 41 full-time employees. 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, Tara McCarthy, our General Counsel, and Mark J. Fitzpatrick, our Chief Financial Officer. These executives have significant research and development, regulatory industry, sales and marketing, operational, and/or corporate finance and legal experience. Our recent receipt of a CRL from the FDA related to our NDA may make the retention of these individuals, other principal members of our management team and key employees more challenging. The loss of any executive, other principal member of our management team or key employee could impair our ability to identify, develop and market new products and conduct successful operations.

In addition, if octreotide capsules are approved, our growth will require us to hire a significant number of qualified technical, commercial, medical 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 octreotide capsules, if approved, 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 you that, following an acquisition, we will achieve the revenues or specific net income that justifies the acquisition.

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

We are engaged in the biopharmaceutical field, which is characterized by extensive research efforts and rapid technological progress. New developments in research are expected to continue at a rapid pace in both industry and academia. We cannot assure you that research and discoveries by others will not render some or all of our programs or product candidates uncompetitive or obsolete. The longer-term success of our business depends upon our ability to utilize our TPE platform to develop and commercialize oral forms of therapies that are currently only available in injectable or other non-absorbable forms. We cannot assure you that unforeseen problems will not develop with our TPE technology or applications or that any commercially feasible products will ultimately be developed by us.

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

We are exposed to the risk that our employees, independent contractors, consultants, commercial partners, principal investigators, CROs and vendors may engage in fraudulent conduct or other misconduct, including intentional failures to comply with FDA regulations or similar regulations of comparable foreign regulatory authorities, to provide accurate information to the FDA or comparable foreign regulatory authorities, to comply with manufacturing standards we have established, to comply with federal and state healthcare fraud and abuse laws and regulations and similar laws and regulations established and enforced by comparable foreign regulatory authorities, and to report financial information or data accurately or disclose unauthorized activities to us. The misconduct of our employees and contractors could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. 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 clinical trials that we may consider 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 octreotide capsules and any future product candidates we may develop could be delayed.

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

Our operations could be subject to earthquakes, power shortages, telecommunications failures, water shortages, floods, hurricanes, typhoons, fires, extreme weather conditions, medical epidemics, military conflicts, acts of terrorism and other natural or man-made disasters or business interruptions. Some of our operations are in Israel, which has a history of certain conflicts. The occurrence of any business disruptions could seriously harm our operations and financial condition and increase our costs and expenses. We rely on third-party manufacturers to produce octreotide capsules. Our ability to obtain clinical supplies of octreotide capsules 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. An 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 octreotide capsules 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.

Security breaches and other disruptions could compromise our information and expose us to liability, which would cause our business and reputation to suffer.

We collect and store sensitive data, including intellectual property, our proprietary business information and that of our manufacturers, business partners, healthcare professionals and patients. This includes, where required or permitted by applicable laws, personally identifiable information. The secure maintenance of this information is critical to our operations and business strategy. Despite our security measures, our information technology and infrastructure may be vulnerable to attacks by hackers or breached due to employee error, malfeasance or other disruptions. Any such breach could compromise our networks and the information stored there could be accessed, publicly disclosed, lost or stolen. Any such access, disclosure or other loss of information could result in legal claims or proceedings, liability under laws that protect the privacy of personal information, disrupt our operations, and damage our reputation which could adversely affect our business.

****Compliance with changing European privacy laws could require us to incur significant costs or experience significant business disruption and failure to so comply could result in an adverse impact on our business.***

In Europe, Directive 95/46/EC of the European Parliament and of the Council of 24 October 1995 on the protection of individuals with regard to the processing of personal data and on the free movement of such data, or the Directive, has required European Union member states to implement data protection laws to meet the strict privacy requirements of the Directive. Among other requirements, the Directive regulates transfers of personally identifiable data that is subject to the Directive, or Personal Data, to countries such as the United States, that have not been found to provide adequate protection to such Personal Data. We have not in the past and cannot in the future rely upon adherence to the U.S. Department of Commerce's Safe Harbor Privacy Principles and compliance with the U.S.-EU and U.S.-Swiss Safe Harbor Frameworks as agreed to and set forth by the U.S. Department of Commerce, and the European Union and Switzerland, which established a means for legitimating the transfer of Personal Data by data controllers in the European Economic Area, or the EEA, to the United States. As a result of the October 6, 2015 European Union Court of Justice, or ECJ, opinion in Case C-362/14 (*Schrems v. Data Protection Commissioner*) regarding the adequacy of the U.S.-EU Safe Harbor Framework, the U.S. – EU Safe Harbor Framework is no longer deemed to be a valid method of compliance with requirements set forth in the Directive (and member states' implementations thereof) regarding the transfer of Personal Data outside of the EEA.

In February 2016, negotiators from Europe and the United States reached political agreement on a successor to the Safe Harbor framework that is being referred to as the EU-US Privacy Shield and a draft adequacy decision was presented by the European Commission on February 29, 2016. On April 13, 2016, the Article 29 Working Party, a body made up of a representative from the data protection authority of each EU member State, expressed "strong concerns" about the adequacy of the EU-US Privacy Shield. In its

opinion on the draft adequacy decision, the Working Party noted that the framework does not incorporate some of the key principles of the EU data protection regime. Accordingly, the EU-US Privacy Shield was subject to further negotiations and revisions. On May 26, 2016 the European Parliament adopted a resolution and on July 8, 2016 the European Member States representatives approved the final version of the EU-US Privacy Shield, paving the way for the adoption of the decision by the European Commission. On July 12, 2016, the U.S. Department of Commerce announced that the EU-US Privacy Shield program would be open to registrants as of August 1, 2016. However, there continue to be concerns about whether the EU-US Privacy Shield will face additional challenges (as the Safe Harbor framework did). We expect that for the immediate future, we will continue to face uncertainty as to whether our efforts to comply with our obligations under European privacy laws will be sufficient. If we are investigated by a European data protection authority, we may face fines and other penalties. Any such investigation or charges by European data protection authorities could have a negative effect on our existing business.

The Directive will be replaced in time with the recently adopted European General Data Protection Regulation, which will enter into force on May 25, 2018, and which will impose additional obligations and risk upon our business and which will increase substantially the penalties to which we could be subject in the event of any non-compliance, including fines of up to 10,000,000 Euros or up to 2% of the total worldwide annual turnover for certain comparatively minor offenses, or up to 20,000,000 Euros or up to 4% of the total worldwide annual turnover for more serious offenses. We may incur substantial expense in complying with the new obligations to be imposed by the European General Data Protection Regulation and we may be required to make significant changes in our business operations.

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."

Risks Related to Our Intellectual Property

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

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

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

selling competing products. If there are material defects in the form or preparation of our patents or patent applications, such patents or applications may be invalid or unenforceable. Moreover, our competitors may independently develop equivalent knowledge, methods, and know-how. Any of these outcomes could impair our ability to prevent competition from third parties, which may have an adverse impact on our business, financial condition, and operating results.

The patent positions of biotechnology and pharmaceutical companies generally are highly uncertain, involve complex legal and factual questions and have in recent years been the subject of much litigation. As a result, the issuance, scope, validity, enforceability and commercial value of any patents that issue, are highly uncertain. The steps we have taken to protect our proprietary rights may not be adequate to preclude misappropriation of our proprietary information or infringement of our intellectual property rights, both inside and outside the United States. Further, the examination process may require us to narrow the claims of pending patent applications, which may limit the scope of patent protection that may be obtained if these applications issue. The rights that may be granted under future issued patents may not provide us with the proprietary protection or competitive advantages we are seeking. If we are unable to obtain and maintain patent protection for our technology and products, or if the scope of the patent protection obtained is not sufficient, our competitors could develop and commercialize technology and products similar or superior to ours, and our ability to successfully commercialize our technology and products may be impaired.

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

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

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

Competitors may infringe our patents or the patents of our licensors. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time consuming. In a patent litigation in the United States, defendant counterclaims alleging invalidity or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, for example, lack of novelty, obviousness or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO, or made a misleading statement, during prosecution. The outcome following legal assertions of invalidity and unenforceability during patent litigation is unpredictable. A court may decide that a patent of ours or our licensors is not valid or is unenforceable, or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. With respect to the validity question, for example, we cannot be certain that no invalidating prior art exists. An adverse result in any litigation or defense proceedings could put one or more of our patents at risk of being invalidated, found unenforceable, or interpreted narrowly, and it could put our patent applications at risk of not issuing. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. If a defendant were to prevail on a legal assertion of invalidity or unenforceability, we would lose at least part, and perhaps all, of the patent protection on one or more of our products or certain aspects of our platform technology. Such a loss of patent protection could have an adverse impact on our business.

Interference proceedings brought by the USPTO may be necessary to determine the priority of inventions with respect to our patents and patent applications or those of our collaborators or licensors. An unfavorable outcome could require us to cease using the technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if a prevailing party does not offer us a license on terms that are acceptable to us. Litigation or interference proceedings may fail and, even if successful, may result in substantial costs and distraction of our management and other employees. We may not be able to prevent, alone or with our licensors, misappropriation of our proprietary rights, particularly in countries where the laws may not protect those rights as fully as in the United States. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock.

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

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

Filing, prosecuting and defending patents on octreotide capsules 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.

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.

Octreotide capsules 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 octreotide capsules 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 octreotide capsules, 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 octreotide capsules from being marketed. Any patent-related legal action against our collaborators or us claiming damages and seeking to enjoin commercial activities relating to octreotide capsules or our processes could subject us to potential liability for damages and require us to obtain a license to continue to manufacture or market octreotide capsules 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 octreotide capsules 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 octreotide capsules or a future product candidate, which could harm our business, financial condition and operating results.

A number of companies, including several major pharmaceutical companies, have conducted research on pharmaceutical uses of somatostatin analogs, which resulted in the filing of many patent applications related to this research. If we were to challenge the validity of these or any issued U.S. patent in court, we would need to overcome a statutory presumption of validity that attaches to every U.S. patent. This means that, in order to prevail, we would have to present clear and convincing evidence as to the invalidity of the patent's claims. If we were to challenge the validity of these or any issued U.S. patent in an administrative trial before the Patent Trial and Appeal Board in the USPTO, we would have to prove that the claims are unpatentable by a preponderance of the evidence. There is no assurance that a jury and/or court would find in our favor on questions of infringement, validity or enforceability.

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

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

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. Our planned move out of our Jerusalem location in 2016 may also negatively impact the local tax benefits we have received by operating there.

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 affecting 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. 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. Instability in the region may lead to deterioration of the political relationships that exist between Israel and these countries and has raised concerns regarding security in the region and the potential for armed conflict. Our commercial insurance does not cover losses that may occur as a result of an event associated with the security situation in the Middle East. Any losses or damages incurred by us could have an adverse effect on our business. Any armed conflicts, terrorist activities or political instability in the region could materially and adversely affect our business, financial condition and results of operations.

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

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

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

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

Risks Related to Our Common Stock

****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, 2016, we had federal net operating loss, or NOL, carryforwards of approximately $101.7 million. The federal NOL carryforwards expire at various dates through 2036. At June 30, 2016, 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 Series E Preferred Stock 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, 2016, our executive officers, directors and principal stockholders collectively controlled approximately 62.8% 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. 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.

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:

- our interactions with the FDA regarding our NDA for octreotide capsules in acromegaly;
- the commencement, enrollment or results of our ongoing Phase 3 clinical trial of octreotide capsules or any future clinical trials we may conduct, or changes in the development status of octreotide capsules or any other product candidates we may develop;
- any delay in our regulatory filings for octreotide capsules 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 octreotide capsules, such as occurred on April 15, 2016 with the FDA's CRL to our NDA;
- changes in laws or regulations applicable to octreotide capsules 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 octreotide capsules or any other future product candidates, if approved;
- our ability to obtain coverage and adequate reimbursement from third-party payors for octreotide capsules or any other future product candidates, if approved;
- unanticipated serious safety concerns related to the use of octreotide capsules or any other future product candidates;
- our ability to effectively manage our growth or restructuring;
- 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;
- 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 are recently the subject of securities litigation, which is expensive and may divert our management's attention.

On June 9, 2016, Chiasma, Inc. and certain of our officers were named as defendants in a purported federal securities class action lawsuit filed in the United States District Court for the District of Massachusetts, styled *Gerneth v. Chiasma, Inc., et al*. This lawsuit challenges our public statements regarding our Phase 3 clinical trial methodology for Mycapssa (octreotide) capsules and our ability to obtain FDA approval for the marketing and sale of Mycapssa, in violation of Sections 10(b) and 20(a) of the Securities Exchange Act of 1934, as amended, and Rule 10b-5 promulgated thereunder, and Sections 11 and 15 of the Securities Act of 1933, as amended. The plaintiff seeks to represent a class consisting of all purchasers of our common stock from July 15, 2015 to April 17, 2016. We believe this lawsuit is meritless and intend to vigorously defend against it. At this time, no assessment can be made as to the likely outcome of this lawsuit or whether the outcome will be material to us.

This litigation may result in substantial costs and divert our management's attention from other business concerns, which could seriously harm our business. We may not be successful in defending this claim and cannot provide assurance that insurance proceeds will be sufficient to cover any liability under such claims.

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 cash 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 cash dividends on any of our classes of capital stock to date and we currently intend to retain our future earnings, if any, to fund the development and growth of our business. As a result, capital appreciation, if any, of our common stock will be your sole source of gain for the foreseeable future. Consequently, in the foreseeable future, you will likely only experience a gain from your investment in our common stock if the price of our common stock increases.

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

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

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, as amended, or the Exchange Act, the Sarbanes-

Oxley Act and the rules and regulations of the stock market on which our common stock is listed. The Sarbanes-Oxley Act requires, among other things, that we maintain effective disclosure controls and procedures and internal control over financial reporting. Commencing with our fiscal year ending December 31, 2016, we must perform system and process evaluation and testing of our internal control over financial reporting to allow management to report on the effectiveness of our internal control over financial reporting in our Form 10-K filing for that year, as required by Section 404 of the Sarbanes-Oxley Act. This will require that we incur substantial additional professional fees and 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.

In addition, if, as a result of restructuring the company, we increase our reliance on contractors for important business functions, it may be more difficult to collect, analyze and report the information we are obligated to disclose as a public company and this could result in a material misstatement or omission in our disclosures.

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, the trading price of our common stock could decline significantly. As of June 30, 2016, we had 24,356,697 outstanding shares of common stock, assuming no exercise of outstanding options or warrants.

In addition, the 4,210,999 shares subject to outstanding options under our stock option plans, the 2,613,690 shares reserved for future issuance under our stock option plans and the 3,567,015 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, holders of approximately 16,543,995 shares of our common stock 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.

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. Since our IPO, four securities analysts have initiated coverage on our company. Since these coverage initiations, and following the receipt of the CRL to our NDA from the FDA, each of these analysts has downgraded their ratings on and lowered their price targets for our stock, and one has since dropped coverage. In the event that one or more of the analysts who cover us further downgrades our stock or publish inaccurate or unfavorable research about our business, our trading price would likely decline. If one or more of these remaining 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

Recent Sales of Unregistered Securities

None.

Issuer Purchases of Equity Securities

In the quarter ended June 30, 2016, we did not repurchase any shares of our common stock.

Use of Proceeds from Initial Public Offering of Common Stock

On July 21, 2015, we completed the sale of 7,319,750 shares of our common stock (inclusive of 954,750 shares of common stock sold by us pursuant to the full exercise of an option granted to the underwriters) in our IPO at a price to the public of $16.00 per share. The offer and sale of the shares in our IPO 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 15, 2015, and Form S-1MEF (File No. 333-205691), which was filed with the SEC on July 15, 2015 and automatically effective upon filing. Following the sale of the shares in connection with the closing of our IPO, 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 for the offering. William Blair & Company, L.L.C. and Oppenheimer & Co. Inc. acted as co-managers.

We raised approximately $106.5 million in net proceeds after deducting underwriting discounts and commissions and offering expenses payable by us. Through June 30, 2016, 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. We invested the funds received in cash equivalents and other short-term investments in accordance with our investment policy.

In June 2016, following our receipt of the CRL and the End of Review meeting, we announced a corporate restructuring plan intended to focus our resources on the continued development of Mycapssa for the maintenance treatment of adult acromegaly patients. We continue to revisit all areas of investment and resources to potentially enable further reductions to our expenses and extend our cash runway.

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.

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 11, 2016

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

August 11, 2016

By: /s/ Mark J. Fitzpatrick
Mark J. Fitzpatrick
Chief Financial Officer
(Principal Financial and Accounting Officer)

Table of Contents

EXHIBIT INDEX

Exhibit No.	Description	Incorporated by Reference to: Form or Schedule	Exhibit No.	Filing Date with SEC	SEC File Number
31.1*	Certification of Principal Executive Officer pursuant to Exchange Act rules 13a-14 or 15d-14, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.				
31.2*	Certification of Principal Financial Officer pursuant to Exchange Act rules 13a-14 or 15d-14, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.				
32.1+	Certification of Principal Executive Officer and Principal Financial Officer pursuant 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.				
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.

Exhibit 31.1

Certification

I, Mark Leuchtenberger, certify that:

1. I have reviewed this quarterly report on Form 10-Q for the period ended June 30, 2016 of Chiasma, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) for the registrant and have:

   a. Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   b. (Paragraph omitted pursuant to SEC Release Nos. 33-8238/34-47986 and 33-8392/34-49313);

   c. Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   d. Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on my most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   a. All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   b. Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: August 11, 2016

/s/ Mark Leuchtenberger

Mark Leuchtenberger
President, Chief Executive Officer and Director
(Principal Executive Officer)

Exhibit 31.2

Certification

I, Mark J. Fitzpatrick, certify that:

1. I have reviewed this quarterly report on Form 10-Q for the period ended June 30, 2016 of Chiasma, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) for the registrant and have:

   a. Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   b. (Paragraph omitted pursuant to SEC Release Nos. 33-8238/34-47986 and 33-8392/34-49313);

   c. Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   d. Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on my most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   a. All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   b. Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: August 11, 2016

/s/ Mark J. Fitzpatrick
Mark J. Fitzpatrick
Chief Financial Officer
(Principal Financial and Accounting Officer)

Exhibit 32.1

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the quarterly report on Form 10-Q of Chiasma, Inc. (the "Company") for the period ended June 30, 2016, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), each of the undersigned officers hereby certify, pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, 18 U.S.C. Section 1350, that to his knowledge:

1) the Report which this statement accompanies fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended; and

2) the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: August 11, 2016

/s/ Mark Leuchtenberger
Mark Leuchtenberger
President, Chief Executive Officer and Director
(Principal Executive Officer)

Date: August 11, 2016

/s/ Mark J. Fitzpatrick
Mark J. Fitzpatrick
Chief Financial Officer
(Principal Financial and Accounting Officer)