CHIASMA, INC
Form 10-Q
August 10, 2017
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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, 2017

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, a smaller reporting company or an emerging growth company. See the definitions of large accelerated filer, accelerated filer, smaller reporting company, and emerging growth company in Rule 12b-2 of the Exchange Act.

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

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act.

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

As of August 7, 2017, there were 24,359,584 shares of the registrant s Common Stock, $0.01 par value per share, outstanding.

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CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Quarterly Report on Form 10-Q contains forward-looking statements. These statements include all matters that are not related to present facts or current conditions or that are not historical facts, including statements regarding our strategy, future operations, future financial position, future revenue, projected costs, prospects, plans, objectives of management and expected market growth. The words anticipate, believe, could, continue, should, predict, e expect, intend, may, plan, potentially, will, would, or the negative of these terms or other similar expressio 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, and our efforts to conduct and complete a new Phase 3 clinical trial of octreotide capsules in adult acromegaly patients per our agreement with the FDA under a Special Protocol Assessment, or SPA, to potentially enable us to resubmit our NDA to the U.S. Food and Drug Administration, or the FDA, in order to secure regulatory approval of octreotide capsules in acromegaly;

- our ability to preserve patients, sites and other resources necessary to enable us to simultaneously conduct two Phase 3 clinical trials in adult patients with acromegaly; one addressing the FDA s concerns raised in the CRL and agreed to in a SPA, and the other to seek regulatory approval from the European Medicines Agency, or EMA; and to produce data packages from each trial that could be suitable for submission in both the United States and Europe;

- any regulatory approvals that may be issued or denied by the FDA, the EMA 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 of octreotide capsules and the timing of the commencement and availability of data from these trials;

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 plans announced in June and August 2016; and

our estimates and expectations regarding our capital requirements, cash and expense levels and liquidity sources.

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.

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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.

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Chiasma, Inc.

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PART I FINANCIAL INFORMATION

Item 1. Financial Statements

Chiasma, Inc.

Condensed Consolidated Balance Sheets

	June 30, 2017 Unaudited	December 31, 2016
	(in thousands except share data)	
Assets		
Current Assets		
Cash and cash equivalents	$ 18,369	$ 37,013
Marketable securities	61,739	55,971
Prepaid expenses and other current assets	1,407	2,110
Total current assets	81,515	95,094
Property and equipment, net	607	683
Other assets	926	979
Total assets	$ 83,048	$ 96,756
Liabilities and Stockholders Equity		
Current liabilities		
Accounts payable	$ 2,015	$ 1,166
Accrued expenses	4,145	5,534
Other current liabilities	1,685	1,700
Total current liabilities	7,845	8,400
Long-term liabilities	1,102	2,631
Total liabilities	8,947	11,031
Commitments and Contingencies (Note 9)		
Stockholders equity:		
Common stock, $0.01 par value; authorized 125,000,000 shares at June 30, 2017 and December 31, 2016; issued and outstanding 24,359,584 shares at June 30, 2017 and December 31, 2016	244	244
Preferred stock, $0.01 par value; authorized 5,000,000 shares; none outstanding		
Additional paid-in capital	266,282	264,017
Accumulated other comprehensive loss	(24)	(9)
Accumulated deficit	(192,401)	(178,527)

Total stockholders equity	74,101	85,725
Total liabilities and stockholders equity	$ 83,048	$ 96,756

See accompanying notes to these unaudited condensed consolidated financial statements.

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Chiasma, Inc.

Condensed Consolidated Statements of Operations

(Unaudited)

	For the Three Months Ended June 30,		For the Six Months Ended June 30,	
	2017	2016	2017	2016
	(in thousands except share and per share data)			
Operating expenses:				
General and administrative	$ 2,641	$ 5,392	$ 5,101	$ 15,386
Research and development	4,279	14,779	8,934	22,005
Restructuring charges		6,537		6,537
Total operating expenses	6,920	26,708	14,035	43,928
Loss from operations	(6,920)	(26,708)	(14,035)	(43,928)
Other income, net	(204)	(121)	(364)	(250)
Loss before provision for income taxes	(6,716)	(26,587)	(13,671)	(43,678)
Provision for income taxes	138	76	203	165
Net loss	(6,854)	(26,663)	(13,874)	(43,843)
Earnings per share of common stock:				
Basic	$ (0.28)	$ (1.10)	$ (0.57)	$ (1.81)
Diluted	$ (0.28)	$ (1.10)	$ (0.57)	$ (1.81)
Weighted-average shares outstanding:				
Basic	24,359,584	24,321,069	24,359,584	24,279,580
Diluted	24,359,584	24,321,069	24,359,584	24,279,580

See accompanying notes to these unaudited condensed consolidated financial statements.

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Chiasma, Inc.

Condensed Consolidated Statements of Comprehensive Income (Loss)

(Unaudited)

	For the Three Months Ended June 30,		For the Six Months Ended June 30,	
	2017	2016	2017	2016
	(in thousands)			
Net loss	$ (6,854)	$ (26,663)	$ (13,874)	$ (43,843)
Other comprehensive income (loss):				
Unrealized gains (losses) on available for sale securities, net	7		(15)	115
Total other comprehensive income (loss)	7		(15)	115
Comprehensive loss	$ (6,847)	$ (26,663)	$ (13,889)	$ (43,728)

See accompanying notes to these unaudited condensed consolidated financial statements.

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Chiasma, Inc.

Condensed Consolidated Statements of Cash Flows

(Unaudited)

	Six Months Ended June 30,	
	2017	2016
	(in thousands)	
Operating Activities:		
Net loss	$ (13,874)	$ (43,843)
Adjustments to reconcile net loss to net cash provided by (used in) operating activities:		
Depreciation	79	153
Stock-based compensation	2,215	2,057
Amortization of premium (discount) on marketable securities, net	(134)	16
Provision for deferred income taxes	63	110
Non-cash interest expense	67	124
Non-cash restructuring charges		379
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	833	(333)
Accounts payable and accrued expenses	(670)	10,100
Other assets	(10)	(21)
Other current and long-term liabilities	139	1,522
Net cash used in operating activities	(11,292)	(29,736)
Investing Activities:		
Purchase of marketable securities	(55,831)	(78,941)
Maturities of marketable securities	50,182	101,606
Purchases of property and equipment	(3)	(2,384)
Net cash provided by (used in) investing activities	(5,652)	20,281
Financing Activities:		
Payment under license termination agreement	(1,700)	(1,700)
Exercise of warrants		5
Exercise of stock options		594
Net cash used in financing activities	(1,700)	(1,101)
Net decrease in cash and cash equivalents	(18,644)	(10,556)
Cash and cash equivalents, beginning of period	37,013	41,039
Cash and cash equivalents, end of period	$ 18,369	$ 30,483

See accompanying notes to these unaudited condensed consolidated financial statements.

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CHIASMA, INC.

Notes to Unaudited Condensed Consolidated Financial Statements

June 30, 2017

1. Description of Business and Summary of Significant Accounting Policies

Chiasma, Inc. is a clinical-stage 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 . We are focu on improving the lives of patients who face challenges associated with their existing treatments for rare and serious chronic disease. Employing our proprietary Transient Permeability Enhancer (TPE) technology platform, we seek to develop oral medications that are currently available only as injections. We are currently conducting an international Phase 3 clinical trial MPOWERED of oral octreotide capsules (conditionally trade-named MYCAPSSA) for the maintenance treatment of adult patients with acromegaly to support a potential submission of a Marketing Authorization Application (MAA) to the European Medicines Agency (the EMA). The MPOWERED trial is a global, randomized, open-label and active-controlled 15-month trial expected to enroll up to 150 adult acromegaly patients. We have also recently reached agreement with the United States Food and Drug Administration (the FDA or the Agency) on the design of a new Phase 3 clinical trial for oral octreotide capsules for the maintenance therapy of adult patients with acromegaly. The trial is designed to address the concerns previously raised in the FDA s Complete Response Letter (CRL) and was reached through Special Protocol Assessment (SPA) with the FDA which was received on August 4, 2017. The trial, referred to as OPTIMAL, is a randomized, double-blind, placebo-controlled, nine-month trial expected to enroll 50 adult acromegaly patients. Octreotide capsules, our sole TPE-based product candidate in clinical development, has been granted orphan designation in the United States and the European Union for the treatment of acromegaly. We retain worldwide rights to develop and commercialize octreotide capsules with no royalty obligations to third parties.

Our New Drug Application (NDA) for octreotide capsules was filed in June 2015 and accepted for filing by the FDA in August 2015. In April 2016, the FDA issued a CRL, which indicated that the review for our application was complete and that our NDA was 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. In its CRL, the FDA advised us that it did not believe our NDA 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 site inspection, certain deficiencies were conveyed to the representative of one of our suppliers that would need to be resolved before approval. While the FDA did not note any safety concerns related to octreotide capsules in the CRL, it subsequently indicated in the June 2016 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, we discussed the concerns raised by the FDA in the CRL, and in the 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 potentially address some of the FDA s concerns. The OPTIMAL Phase 3 clinical trial protocol agreed to under SPA is designed to address the concerns raised by the FDA

in its CRL. We cannot provide any assurance that if we conduct the Phase 3 OPTIMAL clinical trial we will receive U.S. regulatory approval of octreotide capsules for acromegaly. If our efforts to address the concerns raised by the FDA in the CRL are unsuccessful in the new Phase 3 OPTIMAL clinical trial or if we fail to meet the primary or secondary endpoints in the trial, 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, which we are highly unlikely to pursue. We believe conducting a randomized, double-blind and controlled trial, with a placebo control, as agreed to in the SPA and incorporated in the OPTIMAL study design, may 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, if submitted, may also consume significant time.

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 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 with our ongoing international Phase 3 MPOWERED clinical trial of octreotide capsules in acromegaly to support potential regulatory approval in Europe and to initiate enrollment in the international Phase 3 OPTIMAL clinical trial of octreotide capsules in acromegaly in the second half of 2017 to support potential regulatory approval in the United States. In June and August 2016, we announced two separate corporate restructuring plans intended to focus our resources on the continued development of octreotide capsules for the maintenance treatment of adult acromegaly patients. We currently expect our existing cash, cash equivalents and marketable securities to fund our operations for at least one year after the date these condensed consolidated financial statements are issued. We expect to continue to incur significant operating losses for the foreseeable future.

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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 which resulted in a SPA agreement to the Phase 3 OPTIMAL trial design, 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 our planned development of octreotide capsules. Any of these actions could materially harm our business, results of operations and future prospects. Failure to obtain regulatory marketing approval of octreotide capsules in acromegaly will prevent us from commercializing the product candidate, which could raise significant concerns about our continued viability as a business.

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, 2016. 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 six months ended June 30, 2017 are not necessarily indicative of the operating results for the full year or for any other subsequent interim period.

Cash Equivalents

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 and 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 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. We routinely 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.

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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 we believe 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 February 2016, the Financial Accounting Standards Board 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 condensed consolidated financial statements and we currently expect that most of our operating lease commitments will be subject to the new standard and recognized as operating lease liabilities and right-of-use assets upon adoption.

2. Investments

Our investments consisted of the following as of June 30, 2017 and December 31, 2016:

	As of June 30, 2017			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
		($ in thousands)		
Money market funds	$ 16,706	$	$	$ 16,706
Corporate notes	25,410		(13)	25,397
Commercial paper	36,353	1	(12)	36,342
Total	$ 78,469	$ 1	$ (25)	$ 78,445

	As of December 31, 2016			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
		($ in thousands)		
Money market funds	$ 35,218	$	$	$ 35,218
Corporate notes	22,347		(7)	22,340
Commercial paper	33,633	7	(9)	33,631

Total	$ 91,198	$ 7	$ (16)	$ 91,189

As of June 30, 2017, 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, 2017 or 2016.

The fair values of our investments by classification in our condensed consolidated balance sheets as of June 30, 2017 and December 31, 2016 were as follows:

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	June 30, 2017	December 31, 2016
	($ in thousands)	
Cash and cash equivalents	$ 16,706	$ 35,218
Marketable securities	61,739	55,971
Total	$ 78,445	$ 91,189

Cash and cash equivalents in the table above exclude cash of $1.7 million and $1.8 million as of June 30, 2017 and December 31, 2016, 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:

	Fair Value Measurements at June 30, 2017			
	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)	Total
		($ in thousands)		
Cash equivalents:				
Money market funds	$ 16,706	$	$	$ 16,706
Total cash equivalents	$ 16,706	$	$	$ 16,706

Marketable securities:			
Corporate notes	$	$ 25,397	$ 25,397
Commercial paper		36,342	36,342
Total marketable securities		61,739	61,739
Total	$ 16,706	$ 61,739	$ 78,445

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	Fair Value Measurements at December 31, 2016			
	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)	Total
	($ in thousands)			
Cash equivalents:				
Money market funds	$ 35,218	$	$	$ 35,218
Total cash equivalents	$ 35,218	$	$	$ 35,218
Marketable securities:				
Corporate notes	$	$ 22,340	$	$ 22,340
Commercial paper		33,631		33,631
Total marketable securities		55,971		55,971
Total	$ 35,218	$ 55,971	$	$ 91,189

We did not have any Level 3 assets being measured at fair value on a recurring basis as of June 30, 2017 and December 31, 2016.

4. Earnings per Share of Common Stock

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, 2017 and 2016.

5. Accrued Expenses

As of June 30, 2017 and December 31, 2016, accrued expenses consisted of the following:

	June 30, 2017	December 31, 2016
	($ in thousands)	
Accrued general and administrative expenses	$ 639	$ 547
Accrued research and development expenses	2,138	2,107
Accrued payroll and employee benefits	1,311	2,597
Accrued restructuring costs	57	283
Total accrued expenses	$ 4,145	$ 5,534

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. Upon termination, Roche returned all rights and documentation granted under the agreement to us. 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 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 and the second $1.7 million payment in March 2017. 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. Warrants

As of December 31, 2016, there were 3,567,015 common stock warrants outstanding with exercise prices ranging from $0.09 per share to $9.13 per share. The warrants were issued at various points between October 2012 and February 2015 with expiration dates ranging from October 2022 through February 2025. There were no warrants exercised during the six months ended June 30, 2017. There were 3,567,015 outstanding warrants as of June 30, 2017.

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8. 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 initial public offering (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. In October 2016, the compensation committee of the board of directors determined there would be no increase to the shares reserved and available under the 2015 Stock Plan on January 1, 2017. As of June 30, 2017, the total number of shares authorized for stock award plans is 7,114,037 of which 3,179,265 remain available for grant. There are 3,642,537 stock options outstanding as of June 30, 2017.

Stock-based compensation for the three and six months ended June 30, 2017 and 2016 consisted of the following:

	Three Months Ended June 30,		Six Months Ended June 30,	
	2017	2016	2017	2016
	($ in thousands)			
General and administrative	$ 510	$ (106)	$ 865	$ 1,236
Research and development	986	403	1,350	821
Total	$ 1,496	$ 297	$ 2,215	$ 2,057

Primarily as result of the workforce reduction discussed in Note 10, approximately 766,000 options were forfeited during the three months ended June 30, 2016.

There were no exercises of stock options in the six months ended June 30, 2017. We issued approximately 289,000 shares of common stock following the exercise of underlying stock options in the six 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,	
	2017	2016
Expected volatility	74%	75%

Expected term (years)	5.63	6.20
Risk-free interest rate	1.79%	1.42%
Expected dividend yield	0%	0%

We issued approximately 104,000 option grants in the six months ended June 30, 2017. The weighted-average grant date fair value per share of options granted during the six months ended June 30, 2017 was $0.86. We issued approximately 1,164,000 option grants in 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.

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9. Commitments and Contingencies

We conduct certain of 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, 2017 and December 31, 2016. In conjunction with the facility leases, we provided bank guarantees in the aggregate amount of $0.5 million as security deposits at June 30, 2017, which were classified as other assets in the accompanying condensed consolidated balance sheets. At June 30, 2017, the minimum rental commitments under all non-cancelable operating leases with initial or remaining terms of more than one year was approximately $6.0 million through 2023.

Legal Proceedings

On June 9, 2016, Chiasma, Inc. and certain of our current and former 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 octreotide capsules and our ability to obtain FDA approval for the marketing and sale of octreotide capsules. In December 2016, a lead plaintiff was appointed in the case. An amended complaint was filed by the lead plaintiff on February 10, 2017 similarly challenging our statements regarding the Phase 3 clinical trial methodology and results, and our ability to obtain FDA approval for octreotide capsules, in violation of Sections 11 and 15 of the Securities Act of 1933. The amended complaint adds as defendants current and former members of our board of directors, as well as the investment banks that underwrote our initial public offering (IPO) on July 15, 2015. The lead plaintiff seeks to represent a class of all purchasers of our stock in our IPO. The plaintiff is seeking an unspecified amount of compensatory damages on behalf of himself and members of a putative shareholder class, including interest and reasonable costs and expenses incurred in litigating the action, and any other relief the court determines is appropriate. The defendants filed a motion to dismiss the amended complaint on March 27, 2017 and await a decision from the court following oral argument held on July 17, 2017. 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.

10. 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. In August 2016, we announced a second corporate restructuring plan, including an immediate reduction of approximately 44% of our remaining workforce. In aggregate, these restructuring plans resulted in a reduction to our workforce of more than 60% since May 1, 2016. As a result of the August reduction in force, we no longer required the research lab and additional office space of the Israel facility and we were able to early terminate the Israel lease in November 2016. Accordingly, during the year ended December 31, 2016, we recorded restructuring charges totaling $8.2 million which consisted of employee severance benefits and related costs of $2.2 million, manufacturing commitment-related suspension fees of $4.5 million, non-cash restructuring charges of $0.8 million resulting from the impairment of leasehold improvements of $1.7 million offset by the forgiveness of tenant allowances received under the lease of $0.9 million and non-cash restructuring charges related to the impairment of previously capitalized commercial software and laboratory equipment of $0.7 million.

The components of our restructuring charges during the three and six months ended June 30, 2016 are as follows:

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

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Activity related to accrued restructuring costs is as follows:

	For the Six Months Ended June 30, 2017 ($ in thousands)
Balance at beginning of year	$ 283
Plus:	
Current year restructuring costs	
Less:	
Payment of employee severance costs	226
Payment of manufacturing suspension fees	
Non-cash restructuring charges	
Balance at end of period	$ 57

The accrued restructuring costs as of June 30, 2017 were paid in July 2017.

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Item 2. 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, 2016. Some of the information contained in this discussion and analysis or set forth elsewhere in this Quarterly Report on Form 10-Q, including information with respect to our plans and strategy for our business and related financing, includes forward-looking statements that involve risks and uncertainties. As a result of many factors, including those factors set forth in the Risk Factors section of this Quarterly Report on Form 10-Q and our prior filings with the SEC, our actual results could differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.

Overview

We are a clinical-stage biopharmaceutical company focused on improving the lives of patients who face challenges associated with their existing treatments for rare and serious chronic disease. Employing our proprietary Transient Permeability Enhancer, or TPE, technology platform, we seek to develop oral medications that are currently available only as injections. We are currently conducting an international Phase 3 clinical trial MPOWERED of oral octreotide capsules, conditionally trade-named MYCAPSSA and referred to herein as octreotide capsules, for the maintenance treatment of adult patients with acromegaly to support a potential submission of a Marketing Authorization Application, or MAA, to the European Medicines Agency, or EMA. The MPOWERED trial is a global, randomized, open-label and active-controlled 15-month trial expected to enroll up to 150 adult acromegaly patients. We have also recently reached agreement with the United States Food and Drug Administration, or the FDA or the Agency on the design of a new Phase 3 clinical trial for oral octreotide capsules for the maintenance therapy of adult patients with acromegaly. The trial is designed to address the concerns previously raised in the FDA s Complete Response Letter, or CRL, and was reached through Special Protocol Assessment, or SPA, with the FDA. The trial, referred to as OPTIMAL, is a randomized, double-blind, placebo-controlled, nine-month trial expected to enroll 50 adult acromegaly patients. We believe octreotide capsules, if approved by regulatory authorities, may be the first somatostatin analog available for oral administration to patients with acromegaly. Octreotide capsules, our sole TPE-based product candidate in clinical development, has been granted orphan designation in the United States and the European Union for the treatment of acromegaly. We retain worldwide rights to develop and commercialize octreotide capsules with no royalty obligations to third parties.

Our New Drug Application, or NDA, for octreotide capsules was filed in June 2015 and accepted for filing by the FDA, in August 2015. In April 2016, the FDA issued a CRL which indicated that the review for our application was complete and that our NDA was 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. In its CRL, the FDA advised us that it did not believe our NDA 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 site inspection, certain deficiencies were conveyed to the representative of one of our suppliers that would need to be resolved before approval. While the FDA did not note any safety concerns related to octreotide capsules in the CRL, it subsequently indicated in the June 2016 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.

On August 4, 2017, we reached agreement with the FDA under a SPA of a new Phase 3 clinical trial of octreotide capsules in adult acromegaly patients to potentially enable us to resubmit the NDA in order to secure regulatory approval of octreotide capsules in acromegaly. The trial, referred to as OPTIMAL (Octreotide capsules vs. Placebo Treatment In MultinationAL centers), that we plan to conduct is a randomized, double-blind, placebo-controlled, nine-month clinical trial in 50 adult acromegaly patients (at least 20% of whom must be recruited from the United States) whose disease is biochemically controlled, based upon levels of insulin-like growth factor, IGF-1, a byproduct of increased growth hormone, or GH, levels caused by acromegaly, on injectable somatostatin analogs at baseline (average IGF-1 £1.0 x upper limit of normal (ULN)). The patients must also have confirmed active acromegaly following their last surgical intervention based upon an elevated IGF-1 at that time of ≥1.3 x ULN. The trial will be randomized on a 1:1 basis to octreotide capsules or placebo. Patients will be dose titrated from 40mg per day to up to a maximum of 80mg per day, equaling two capsules in the morning and two capsules in the evening. Patients meeting predefined biochemical failure criteria during the course of the trial will revert to their original treatment of injections and will be monitored for the remainder of the trial. The primary endpoint of the study is the proportion of patients who maintain their biochemical response compared to placebo at the end of the nine-month double-blind, placebo controlled period as measured using the average of the last two IGF-1 levels £1.0 x ULN. Secondary endpoints that will be considered by the FDA in evaluating the totality of evidence for octreotide capsules treatment effect include:

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Proportion of patients who maintain GH response at week 36, compared to screening.

Time to loss of response: IGF-1 > 1×ULN

Time to loss of response: IGF-1 > 1.3×ULN

Change from screening to end of treatment in mean growth hormone (GH).

Change in IGF-1 (ULN), from baseline to end of treatment.

An open-label extension phase is planned following the nine-month study, which could enable patients who completed the randomized phase to continue receiving octreotide capsules and for the company to collect long-term safety information. The results of the extension phase are not required as the basis for an efficacy claim.

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 historical revenue has been related to one license agreement, which has been terminated. Since our inception and through June 30, 2017, 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, 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, 2017, our consolidated cash, cash equivalents and marketable securities were $80.1 million, of which $0.6 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 $13.9 million for the six months ended June 30, 2017 and $61.1 million for the year ended December 31, 2016. As of June 30, 2017, we had an accumulated deficit of $192.4 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 MPOWERED clinical trial of octreotide capsules in acromegaly that we initiated in March 2016 to support potential regulatory approval in Europe and plan to initiate our Phase 3 OPTIMAL clinical trial of octreotide capsules in acromegaly in the second half of 2017 to support potential regulatory approval in the United States. We expect the release of top-line OPTIMAL data by the end of 2019 and we expect the release of top-line MPOWERED data in 2020. Clinical development timelines, the probability of success and development costs can differ materially from expectations.

In June and August 2016, we announced two separate corporate restructuring plans intended to focus our resources on the continued development of octreotide capsules for the maintenance treatment of adult acromegaly patients. As a result of the August 2016 reduction in workforce, we eliminated our research and discovery functions and are currently not investing in those areas. 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 and debt financings, and we may also opportunistically consider 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 and made the second $1.7 million payment in March 2017. Other than these payments, we have no further financial or operational obligations to Roche.

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Financial Overview

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 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 included 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 of clinical trial material, manufacturing process development and validation regulatory and clinical activities, and our TPE platform. We expense research and development costs as incurred.

As a result of the August 2016 reduction in workforce, we eliminated our research and discovery functions and are currently not investing in those areas. We continue to invest in the clinical development of octreotide capsules. 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 MPOWERED clinical trial of octreotide capsules in acromegaly that we initiated in March 2016 to support potential regulatory approval in Europe. We also plan to initiate our Phase 3 OPTIMAL clinical trial of octreotide capsules in acromegaly in the second half of 2017 to support potential regulatory approval in the United States. The successful development of octreotide capsules is highly uncertain. We estimate the total direct cost of the OPTIMAL clinical trial to be between $18.0 million and $20.0 million and the remaining costs of the MPOWERED clinical trial to be between $15.0 million and $17.0 million.

General and Administrative

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

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. Following the June 2016 restructuring plan and the termination of primarily all of our commercial personnel, these expenses were significantly reduced throughout 2016. Our marketing expenses in 2017 have been immaterial to date and are expected to continue to be immaterial.

Restructuring Charges

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

Other Income, Net

Other income, net consists mainly of interest income earned on our investments, net of interest incurred on our obligation related to the acquisition of API and trade name MYCAPSSA from Roche.

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.

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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, 2016. There have been no material changes in our critical accounting policies during the three and six months ended June 30, 2017. 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, include 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, 2017 and 2016

Research and Development

The following is a comparison of research and development expenses for the three and six months ended June 30, 2017 and 2016:

	Three Months Ended June 30,				Six Months Ended June 30,			
	2017	2016	$ Change	% Change	2017	2016	$ Change	% Change
	($ in thousands)							
Research and development	$ 4,279	$ 14,779	$ (10,500)	(71%)	$ 8,934	$ 22,005	$ (13,071)	(59%)

For the three months ended June 30, 2017, our total research and development expenses decreased by $10.5 million to $4.3 million. For the six months ended June 30, 2017, our total research and development expenses decreased by $13.1 million to $8.9 million. The decreases were primarily due to approximately $7.4 million of API purchases during the three months ended June 30, 2016 and pre-commercial manufacturing validation activities in 2016, that did not reoccur in 2017, as well as reduced compensation-related costs and other research and development program efforts following the reductions of force in June and August 2016. In addition, clinical trial costs decreased by $0.8 million and $0.2 million for the three and six months ended June 30, 2017 as compared to June 30, 2016, respectively.

General and Administrative

The following is a comparison of general and administrative expenses for the three and six months ended June 30, 2017 and 2016:

	Three Months Ended June 30,				Six Months Ended June 30,			
	2017	2016	$ Change	% Change	2017	2016	$ Change	% Change
	($ in thousands)							

General and administrative	$ 2,641	$ 5,392	$ (2,751)	(51%)	$ 5,101	$ 15,386	$ (10,285)	(67%)

For the three months ended June 30, 2017, our general and administrative expenses decreased by $2.8 million to $2.6 million. For the six months ended June 30, 2017, our general and administrative expenses decreased by $10.3 million to $5.1 million. These decreases were primarily due to the reduction in pre-commercial activity expenditures following the CRL, as well as the June and August 2016 reductions in force of substantially all of our commercial personnel and certain administrative functions.

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 commitment-related suspension fees of $4.7 million. There were no restructuring charges in the six months ended June 30, 2017.

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Other Income, net

Other income totaled $0.4 million for the six months ended June 30, 2017, compared to other income of $0.3 million for the same period in 2016. The improvement was driven by interest income generated from increased yields on our cash equivalents and marketable securities and a decrease in the imputed interest expense associated with the 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, 2017, representing an effective tax rate of (1.5%), as compared to a tax provision of $0.2 million for the six months ended June 30, 2016, representing an effective tax rate of (0.4%).

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, 2017, 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, 2017, our cash and cash equivalents were $18.4 million, of which $0.6 million was held by our Israeli subsidiary. In addition, as of June 30, 2017, we have $61.7 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 clinical trial costs (including the international Phase 3 MPOWERED clinical trial that we initiated in March 2016 to support anticipated European regulatory approval of octreotide capsules and the international Phase 3 OPTIMAL clinical trial that we plan to initiate in the second half of 2017 to support United States regulatory approval of octreotide capsules following the receipt of SPA on August 4, 2017 from the FDA), manufacturing of octreotide capsules for market consumption, if approved, 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 development services, legal and other regulatory expenses, and other general operating costs. As of June 30, 2017, we estimate the total direct cost of the OPTIMAL clinical trial to be between $18.0 million and $20.0 million and the remaining costs of the MPOWERED clinical trial to be between $15.0 million and $17.0 million.

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 octreotide capsules for the potential maintenance treatment of adult acromegaly patients. This plan included a reduction of approximately 33% of our workforce at the time, including substantially all of our commercial personnel. In August 2016, we announced a second corporate restructuring plan that included the reduction of approximately 44% of our remaining workforce. In aggregate, these restructuring plans resulted in a reduction to our workforce of more than 60% since May 1, 2016. We currently expect

our existing cash, cash equivalents and marketable securities will be sufficient to fund our operations through the anticipated release of top-line data from the Phase 3 OPTIMAL trial by the end of 2019 while supporting the MPOWERED trial in parallel. We cannot estimate the actual amounts necessary to successfully complete the development and commercialization of octreotide capsules, if at all, 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 the development and regulatory review of octreotide capsules;
- the progress and results of our ongoing clinical trial of octreotide capsules or any future clinical trials or studies we may conduct;
- 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;

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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 and debt financings and we may opportunistically consider 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 current or future product candidates, exploratory programs, technologies or future revenue streams 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 of octreotide capsules or grant rights to develop and market future potential 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, 2017 and 2016:

	Six Months Ended June 30,	
	2017	2016
	($ in thousands)	
Cash flows provided by (used in):		
Operating activities	$ (11,292)	$ (29,736)
Investing activities	(5,652)	20,281
Financing activities	(1,700)	(1,101)

Operating Activities

Net cash used in operating activities was $11.3 million for the six months ended June 30, 2017, and primarily consisted of $13.9 million in net loss, adjusted for non-cash items of $2.3 million (primarily stock-based compensation). 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 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). The primary driver for the decrease in our operating spending during the six months ended June 30, 2017 compared to the six months ended June 30, 2016 was the implementation of our two corporate restructuring plans following the receipt of the CRL in April 2016, which indefinitely suspended our pre-commercial marketing expenditures and significantly reduced our compensation-related expenses associated with the expansion of our U.S. office, all in anticipation of FDA s approval of octreotide capsules in April 2016, which did not occur.

Investing Activities

Net cash used in investing activities was $5.7 million for the six months ended June 30, 2017, primarily related to the purchase of marketable securities, compared to $20.3 million in cash provided by investing activities for the six months ended June 30, 2016, primarily related to the maturity of marketable securities which was partially offset by fixed asset purchases of $2.4 million.

Financing Activities

Net cash used in financing activities was $1.7 million during the six months ended June 30, 2017, related to the second $1.7 million installment payment related to the termination of the Roche license agreement. For the six months ended June 30, 2016, net cash used in financing activities was $1.1 million, 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.

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Contractual Obligations

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, 2017 or December 31, 2016. In conjunction with the facility leases, we provided bank guarantees in the aggregate amount of $0.5 million as security deposits at June 30, 2017, which were classified as other assets in the accompanying condensed consolidated balance sheets. At June 30, 2017, the minimum rental commitments under all non-cancelable operating leases with initial or remaining terms of more than one year was approximately $6.0 million through 2023.

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, 2017, we had $18.4 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, 2017, we had $61.7 million of marketable securities consisting of short-term corporate notes and commercial paper. 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 $0.2 million. As of June 30, 2017, 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 2%, 21% and 7%, respectively. As of June 30, 2017, we held $0.6 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 has concluded based upon the evaluation described above that, as of June 30, 2017, our disclosure controls and procedures were effective at the reasonable assurance level.

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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, 2017, 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 current and former 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 octreotide capsules and our ability to obtain FDA approval for the marketing and sale of octreotide capsules. In December 2016, a lead plaintiff was appointed in the case. An amended complaint was filed by the lead plaintiff on February 10, 2017 similarly challenging our statements regarding the Phase 3 clinical trial methodology and results, and our ability to obtain FDA approval for octreotide capsules, in violation of Sections 11 and 15 of the Securities Act of 1933. The amended complaint adds as defendants current and former members of our board of directors, as well as the investment banks that underwrote our initial public offering (IPO) on July 15, 2015. The lead plaintiff seeks to represent a class of all purchasers of our stock in to our IPO. The plaintiff is seeking an unspecified amount of compensatory damages on behalf of himself and members of a putative shareholder class, including interest and reasonable costs and expenses incurred in litigating the action, and any other relief the court determines is appropriate. The defendants filed a motion to dismiss the amended complaint on March 27, 2017 and await a decision from the court following oral argument held on July 17, 2017. 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 our receipt of the Special Protocol Assessment agreement, or SPA, on August 4, 2017 from the U.S. Food and Drug Administration, or FDA, regarding our planned OPTIMAL Phase 3 clinical trial of octreotide capsules for the maintenance treatment of U.S. adult patients with acromegaly, 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, 2016, as filed with the SEC. If any such risks or uncertainties actually occur, our business, financial condition or operating results could differ materially from the plans, projections and other forward-looking statements included in the section titled Management s Discussion and Analysis of Financial Condition and Results of Operations and elsewhere in this report and in our other public filings. The trading price of our common stock could decline due to

any of these risks, and as a result, you may lose all or part of your investment.

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

In light of our receipt of a Complete Response Letter, or CRL, from the FDA in April 2016 regarding our New Drug Application, or NDA, for octreotide capsules for the maintenance treatment of U.S. adult patients with acromegaly, our participation in an End of Review Meeting and several additional interactions with the FDA, and despite our receipt of the SPA for our planned OPTIMAL Phase 3 clinical trial, the approvability of octreotide capsules is uncertain and we may never obtain regulatory approval in the United States.

In June 2015, we submitted an NDA to the FDA for the marketing and sale of octreotide capsules 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 was complete and the NDA was not ready for approval in its present form. In its CRL, the FDA advised us that it did not believe our application provided

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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 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 octreotide capsules in the CRL, it subsequently indicated in the minutes from our June 2016 End of Review meeting 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 End of Review meeting we discussed the concerns raised by the FDA in the CRL, and in the 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. On August 4, 2017, we reached agreement with FDA under its Special Protocol Assessment, or SPA, procedures of a new Phase 3 clinical trial of octreotide capsules in adult acromegaly patients which includes a placebo control, which trial, if successful, could potentially enable us to resubmit the NDA. We refer to this new Phase 3 trial using the acronym OPTIMAL. We currently estimate that we will report top-line data from this planned Phase 3 clinical trial by the end of 2019 and that the NDA, if resubmitted, will qualify for a 6-month review period, but the duration of the trial and time provided for the NDA review, if submitted, could take longer. We may not have sufficient capital resources to fully fund this new trial, or any additional trials that the FDA may require as a condition to approval. We cannot provide any assurance that if we conduct this new Phase 3 clinical trial we will receive U.S. regulatory approval of octreotide capsules for acromegaly.

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 first 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 first 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 first 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 first 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 in the CRL are unsuccessful in our new planned Phase 3 OPTIMAL clinical trial or if we fail to meet the primary or secondary endpoints in the trial, 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, which we are highly unlikely to pursue.

Even though our planned Phase 3 OPTIMAL trial is being conducted under a SPA agreed to with the FDA, we cannot guarantee that the design of, or data collected from, this trial or any of our clinical trials will be sufficient to support filing or approval of an NDA.

In the context of a Phase 3 clinical trial, the purpose of a SPA is to reach agreement with the FDA on the protocol design and size of the trial that may form the primary basis of an efficacy claim in support of an NDA. In requesting a SPA agreement, a sponsor asks focused questions on specific issues relating to the protocol, protocol design, study conduct, study goals and data analysis. However, according to draft regulatory guidance, a SPA agreement does not indicate FDA concurrence on every protocol detail. Absence of an FDA comment on a particular aspect of a trial does not necessarily indicate agreement if the sponsor did not specifically ask about that aspect. Moreover, a SPA is not a guarantee of approval, even if the trial is successful. A SPA is not binding on the FDA and may be rescinded if, for example, the FDA identifies a safety concern related to the product or its pharmacological class, if the FDA and the scientific community recognize a paradigm shift in disease diagnosis or management, if the relevant data, assumptions or information provided by the sponsor in the SPA submission are found to be false or misstated or omit relevant facts, or if the sponsor fails to follow the protocol that was agreed upon with the FDA. A SPA may be modified with the written agreement of the FDA and the trial sponsor and, according to draft regulatory guidance, minor issues can be resolved through additional correspondence and protocol amendments after the trial begins. However, the FDA retains significant latitude and discretion in interpreting the terms of a SPA agreement, the significance of protocol amendments, if necessary after the trial begins, and the data and results from the applicable clinical trial.

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Further, the results from the OPTIMAL trial, a double-blind, placebo controlled clinical trial, may not be sufficiently robust to support the filing or approval of an NDA. It should be noted that the design of the OPTIMAL trial is different in important ways from the design of both our current MPOWERED clinical trial and our completed Phase 3 clinical trial. For example, in contrast to our completed Phase 3 clinical trial, which did not have a placebo arm, the OPTIMAL trial design calls for the randomization of 50% of study patients to placebo capsules, the effect of which we cannot predict. We believe conducting a randomized, double-blind and controlled trial, with a placebo control may be particularly challenging. For example, it may be difficult to identify patients with acromegaly willing to enroll in a trial with this design. In our completed Phase 3 clinical trial we used IGF-1 < 1.3 times the upper limit of normal as a screening eligibility criteria and the threshold for response whereas in our OPTIMAL trial we plan to use IGF-1 £ 1.0 times the upper limit of normal. The OPTIMAL trial is also expected to have a small sample size and therefore missing data, which might be only a few measurements, may raise questions about data quality and may, ultimately, invalidate the trial results. In light of these new trial design elements, even if we achieve a clinical response consistent with or similar to what we believe we achieved in our completed Phase 3 clinical trial, we may fail to achieve the primary or secondary endpoints of the OPTIMAL trial.

We anticipate that both primary and secondary endpoints in the OPTIMAL trial will be taken into account by the FDA in evaluating the totality of evidence for octreotide capsules treatment effect, and mere achievement of the primary endpoint alone may not be sufficient to support approval. Not all endpoints measured may be supportive of octreotide capsules efficacy or safety, particularly those secondary endpoints which measure the biochemical response at the end of the trial of patients taking octreotide capsules as compared to patients rescued by injectable somatostatin analogs. The OPTIMAL trial, as agreed to under SPA, contains secondary endpoints requiring a true intent to treat analysis, or what the FDA refers to as an estimand, that will allow the FDA to compare the difference between treatment arms for all randomized patients at the end of the nine-month, double-blind controlled period, regardless of therapy. As such, the statistical analysis plan requires a biochemical comparison (secondary endpoints measuring both growth hormone and IGF-1) of the patients randomized to octreotide capsules versus patients randomized to placebo at the end of the nine-month, double-blind placebo controlled period, even if those patients require injectable somatostatin analog rescue therapy during the trial. We believe that as many as 90% or more of the patients randomized to placebo could require injectable somatostatin analog rescue therapy during the trial and that octreotide capsules are not likely to demonstrate superiority over injectable somatostatin analogs when evaluated using these secondary endpoint analyses, even if we achieve a statistically significant result of octreotide capsules versus placebo as assessed by the primary endpoint of the trial. Our trial design includes as exploratory endpoints the last observed biochemical values (measuring both growth hormone and IGF-1) prior to rescue by injectable somatostatin analogs, which is more likely to demonstrate a statistically significant result for octreotide capsules if we also achieve a statistically significant result as assessed by the primary endpoint. We expect to continue to evaluate the estimand-related secondary endpoints included in the statistical analysis plan for the OPTIMAL trial. We anticipate that the FDA will review the totality of the data collected from the OPTIMAL trial, including both primary and secondary endpoints and whether the data collected is sufficiently robust to support the interpretability of these analyses, in determining whether to approve our NDA, if submitted, for the marketing and sale of octreotide capsules. There can be no assurance that the data collected from the OPTIMAL trial will be sufficient to support approval of our NDA, if submitted, for the marketing and sale of octreotide capsules.

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 clinical-stage biopharmaceutical company with no products approved by regulatory authorities or available for commercial sale. As a result, our potential to generate future revenues is currently dependent upon our ability to obtain regulatory approval and achieve commercial success of octreotide capsules for the treatment of acromegaly in the United States, Europe and other countries. Our receipt of a CRL from the FDA to our NDA for octreotide capsules

and the requirement to conduct an additional Phase 3 clinical trial to address the concerns raised in the CRL has resulted, and will continue to 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, if approved, in an effort to address the concerns it raised in the CRL and the End of Review meeting or to address findings in the planned OPTIMAL trial. Any such restrictions or concerns about efficacy within the medical community could significantly impact market adoption and commercial performance of octreotide capsules, even if we are able obtain regulatory approval to commercialize in the United States in the future.

In addition, we have incurred and expect to continue to incur significant expenses and to utilize virtually all of our efforts and financial resources as we continue to pursue the approval of octreotide capsules in the United States and Europe. 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 taking 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.

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We may also fail to develop future product candidates, especially since we terminated our research personnel in connection with the August 2016 restructuring plan. As a result, we 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 further declines to our market value and stock price.

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, raise future capital, or continue as a standalone business could be materially impaired.

In June 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 second Phase 3 trial to evaluate the non-inferiority of octreotide capsules to injectable somatostatin analogs in adult patients with acromegaly. This clinical trial, which is referred to as MPOWERED and was initiated in March 2016, is an open-label, randomized, active-controlled study that is currently anticipated to include up to 150 patients in the European Union, Russia, the United States and certain other countries. This clinical trial is currently designed to show comparative effectiveness as required by the EMA, to support submission of a marketing authorization application, or MAA, and approval. The FDA has advised us that positive data from the ongoing MPOWERED clinical trial, if obtained, will not be sufficient to address the concerns identified by the FDA in the CRL. Shortly following the receipt of this advice, we commenced the SPA process with FDA for the new planned Phase 3 OPTIMAL clinical trial. The FDA may never approve an octreotide capsules NDA, if resubmitted following the OPTIMAL trial, our ongoing MPOWERED Phase 3 clinical trial may not be successful, or acceptable to the EMA to support regulatory approval in Europe, the CRL or data produced from the OPTIMAL trial 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.

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 our ability to obtain regulatory approval, are not successful for the acromegaly indication or are delayed, or if adequate demand for octreotide capsules is not generated, our business and ability to generate revenues will be materially harmed. Failure to obtain regulatory marketing approval of octreotide capsules in acromegaly will prevent us from commercializing the product candidate, which could raise significant concerns about our continued viability

as a business.

The success of octreotide capsules will depend on the receipt of regulatory approval, and the issuance 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;

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- 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, as was the case with the FDA s review of our completed Phase 3 clinical trial contained in the NDA, or that any current or 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.

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 if resubmitted following the planned OPTIMAL trial will continue to rely, and we intend that our 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, initiated or planned, such as the OPTIMAL trial. The relevant regulatory authorities also may determine that we have not provided sufficient data to justify reliance on prior investigations involving the approved immediate-release injectable octreotide product.

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In addition, notwithstanding the approval of many products by the FDA pursuant to Section 505(b)(2), in the past some pharmaceutical companies and others have objected to the FDA s interpretation of Section 505(b)(2). For example, parties have filed citizen petitions objecting to the FDA approving a Section 505(b)(2) NDA on 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, and our current and future clinical trials may not be successful. 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. In the CRL and subsequent End of Review meeting minutes, the FDA strongly recommended that we conduct a randomized, double-blind and controlled trial, and introduced the concept of a placebo control as a design element that could potentially address some of the FDA s concerns. We acknowledged FDA s feedback contained in the CRL and in the End of Review meeting minutes, and plan to conduct a third Phase 3 clinical trial, called the OPTIMAL trial, under the FDA s SPA procedures, which trial we plan to initiate in the second half of 2017. We may also eventually initiate clinical trials of octreotide capsules in indications other than acromegaly, 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. The results of our completed clinical trials for octreotide capsules in acromegaly do not ensure that future clinical trials, including the MPOWERED Phase 3 trial required to support EMA approval, the planned OPTIMAL trial or other trials required by the FDA, or clinical trials for other indications, will also generate comparable results. Among other considerations, these trials may be designed in a way that is different from our completed clinical trials. 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 as used in our first Phase 3 clinical trial of IGF-1 < 1.3 times the upper

limit of normal as the threshold for response while the FDA agreed that we use IGF-1 £ 1.0 times the upper limit of normal in the OPTIMAL trial. The fact that we have not used such endpoints previously for regulatory submissions introduces an additional level of uncertainty in the outcome of the MPOWERED and OPTIMAL Phase 3 clinical trials, or for other studies using this methodology for assessing the success of our product candidate. Further, the OPTIMAL trial design calls for the randomization of 50% of study patients to placebo capsules, the effect of which we cannot accurately estimate. 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 MPOWERED Phase 3 clinical trial in acromegaly to support regulatory approval in Europe or our planned OPTIMAL Phase 3 clinical trial in acromegaly to support regulatory approval in the United States, or clinical trials for other indications, if any, 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 acromegaly, or any other indication, if studied. 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,

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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 and we expect to rely on a similar hybrid application pathway for the MAA that we plan to submit in Europe. 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 or EMA to approve octreotide capsules for the treatment of acromegaly or any other indication that may be specified in future NDA or MAA 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, or vice versa.

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, cause our market value and stock price to fall and jeopardize our viability as a business.

Delays in the completion of the Phase 3 MPOWERED 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, including the planned OPTIMAL trial which we expect to initiate in the second half of 2017, 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 MPOWERED Phase 3 clinical trial to extend the control period from six months to nine months. The final protocol accepted by EMA therefore dictated that additional time will be needed 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 the MPOWERED Phase 3 trial or the planned OPTIMAL Phase 3 trial will be completed on schedule, if at all, or will be successful. In light of the FDA s position that the MPOWERED clinical trial will not be sufficient to address the concerns in the CRL, in late 2016 we modified certain elements of the MPOWERED trial in an effort to preserve patients, sites and other resources necessary to conduct the planned OPTIMAL Phase 3 trial. The modifications to the MPOWERED trial will delay the expected timing of an MAA filing with the EMA, which we previously estimated to occur in 2019, and we now expect top-line data from the MPOWERED study in 2020. The completion of the MPOWERED or OPTIMAL Phase 3 trials or other clinical trials that may be conducted can be delayed for a number of other 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, and our planned OPTIMAL trial may be particularly difficult to enroll given the placebo-controlled design;

a facility manufacturing octreotide acetate, octreotide capsules, placebo 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 acromegaly or any of the indications for which we may develop octreotide capsules or potential product candidates, or participating in competing clinical trials;

difficulty in maintaining contact with patients after treatment, resulting in incomplete or missing 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;

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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;

the inability to enroll patients who participated in prior clinical trial in our current or planned clinical trials; or

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

Product development costs for octreotide capsules in acromegaly 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.

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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, and we may not have sufficient capital on hand or the ability to raise additional capital to cover such costs, delays in advancing octreotide capsules or any of future product candidates we may develop, delays in testing the effectiveness of future product candidates, if any, 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 Russia, 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 Europe. The same limitation is true for our planned OPTIMAL trial. Further, in light of the FDA s position that the MPOWERED clinical trial will not be sufficient to address the concerns in the CRL, we have modified certain elements of the MPOWERED trial in an effort to preserve patients, sites and other resources necessary to conduct the planned OPTIMAL Phase 3 trial. Further, the issuance of the CRL by FDA may negatively impact physician or patient attitudes towards octreotide capsules which could significantly delay enrollment in both MPOWERED and OPTIMAL trials or any future trials. In addition, conducting a randomized, double-blind and controlled trial in the United States, as strongly recommended by the FDA in the CRL and End of Review meeting minutes, and as planned for in the OPTIMAL trial, may be particularly challenging as we believe it may be difficult to identify patients with acromegaly willing to enroll in a trial with this design, and we believe such a trial could take a number of years to complete and submit to FDA for review. We expect to conduct the MPOWERED and OPTIMAL Phase 3 trials simultaneously, and as such, we will have two active clinical trials competing for the same or similar pools of patients and enrollment in either trial, or both trials, could be negatively impacted.

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, such as in the planned OPTIMAL trial;

possibility of being randomized back to current injectable therapies, such as in the MPOWERED study, or rescued back to current injectable therapies following a loss of biochemical and symptom control, such as in the planned OPTIMAL trial;

proximity and availability of clinical trial sites for prospective patients;

availability of competing therapies and clinical trials;

perceptions of patients and healthcare providers as to the potential advantages of the drug being studied in relation to other available therapies, including any new drugs that may be approved for the indications we are investigating;

efforts to facilitate timely enrollment of patients in clinical trials;

patient referral practices of physicians; and

ability to monitor patients adequately during and after treatment.

If we have difficulty enrolling a sufficient number of patients to conduct our clinical trials or our clinical trials produce incomplete data, 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

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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, 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, there would be significant doubts about our viability as a standalone business.

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 potential products or the manufacturing facilities for our potential 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.

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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. If approved, we expect octreotide capsules will face competition from established drugs and major brand names and also generic versions of these 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 first 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. Camurus AB is also developing, in partnership with Novartis, CAM2029, a product candidate that according to published reports will enter into Phase 3 clinical studies in acromegaly in 2017. Ipsen SA markets lanreotide, another long-acting analog of somatostatin, like octreotide, which is administered monthly using a deep subcutaneous injection, and is further studying in clinical trials a prolonged release formulation of lanreotide which could be administered, if successful, once every three months. 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:

- develop our product candidate and demonstrate that it is 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.

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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 them 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.

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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 and our plans to conduct the OPTIMAL Phase 3 trial prior to any resubmission of 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 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 our corporate restructuring in June 2016, we no longer have a sales and marketing organization and, as a company, have not commercialized any products. If we are able to secure regulatory approval for octreotide capsules in acromegaly, but 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.

As a result of our June 2016 restructuring action, we essentially no longer have sales and marketing personnel. Based upon feedback provided by the FDA in the CRL and End of Review meeting minutes, as well as through the SPA process, new or additional data will be required before the FDA would consider U.S. regulatory approval for the marketing and sale of octreotide capsules in acromegaly, which requires that we conduct the planned OPTIMAL Phase 3 trial and possibly 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 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.

If pursued by us, expansion of our business into the European Union and other international markets will require significant management attention and additional financial resources. We may 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;

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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 or 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 both in the United States and internationally. We do not have any experience in a commercial launch in the United States, Europe or elsewhere.

Due to our corporate restructuring in 2016, we no longer have a 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 and except for Dr. William Ludlam, our Senior Vice President of both clinical and medical affairs, we no longer have a 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.

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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 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. Although we were informed that the supplier received an Establishment Inspection Report, or EIR, from FDA, indicating that the FDA has concluded its inspection of the supplier and as of the date of its report considers outstanding deficiencies resolved, we expect that our suppliers will be subject to additional regulatory inspections in the future, including in connection with the FDA s review of any NDA we may submit in the future, if any, seeking approval of octreotide capsules in acromegaly. There can be no assurances that our suppliers will pass all future inspections, the failure of which could result in delays to our ability to receive regulatory approval 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.

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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. 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. If approved, we will 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 NDA approval, if obtained, and 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, our business will be harmed and we may not have sufficient resources to continue as a standalone company.

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 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 initiation or completion of an ongoing clinical trial, receipt of marketing approval, or a commercial launch of a product. The achievement 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 strategic decisions on trial design and modifications thereto in an effort to preserve patients, sites and other resources necessary to conduct the planned OPTIMAL Phase 3 trial addressing the FDA s concerns and produce data packages that could be suitable for submission in both the United States and the European Union;
- 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, if approved, 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, if approved, 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 subsequent products that we may develop, if any. 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.

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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 any other potential products we may pursue. Some of these changes and proposed changes could result in reduced reimbursement rates for octreotide capsules and any other potential products we may pursue, 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, End of Review meeting or the agency s review of the OPTIMAL trial or any future clinical trials we may conduct. Any such restrictions or potential reservations about efficacy expressed by the FDA or 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, if required regulatory approvals are obtained, 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 expand the approved uses of octreotide capsules beyond acromegaly, if approved and 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 expand the approved uses of octreotide capsules beyond acromegaly, if approved, and utilize our proprietary Transient Permeability Enhancer, or TPE, technology platform to develop and commercialize other 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 in acromegaly, if approved, we may pursue development of octreotide capsules for other indications or develop other product candidates alone or in collaboration with other parties. Because we eliminated substantially all of our research and discovery functions during the August 2016 reduction in workforce, we do not currently have the

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internal capacity to develop any new product candidates. We also may never be able to identify other peptide drugs or poorly absorbed small-molecule drugs that can successfully be developed into product candidates utilizing our TPE platform, let alone receive regulatory approval of such product candidates, and we may never be able to engage in licensing transactions that enable a third party to utilize TPE in the development of future product candidates.

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, and we are not currently investing in such research programs. As a result, we may not be able to successfully identify any future product candidates or new indications for octreotide capsules.

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, which we do not currently contemplate, may impair our ability to continue development and commercialization of octreotide capsules for the treatment of acromegaly and other indications, if pursued, 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 octreotide capsules in other indications besides acromegaly or other product candidates, these product candidates may never demonstrate sufficient safety and efficacy to be approved by the FDA or other regulatory authorities.

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.

As a result of the elimination of substantially all of our research functions, we are currently unable to develop future potential products through internal research programs. Therefore, we may consider expanding the scope of future potential product candidates by licensing injectable or poorly absorbed drugs from third parties or licensing our TPE technology to 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. For example, 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 research, 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 do not currently have dedicated research or business development personnel on staff;

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.

We do not have sufficient human and financial resources to develop suitable potential product candidates through internal research programs, we may not have the resources to obtain rights from third parties, and we may not be able to license our TPE technology to third parties for development of future product candidates, 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

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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 potential 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 a potential future product candidate of ours receives an orphan drug designation and 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 paying 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;

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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

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 octreotide capsules or any of our future potential 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.

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Some of the provisions of the ACA have yet to be fully implemented, while certain provisions have been subject to judicial and Congressional challenges. In January 2017, Congress voted to adopt a budget resolution for fiscal year 2017, that while not a law, is widely viewed as the first step toward the passage of legislation that would repeal certain aspects of the ACA. Further, on January 20, 2017, President Trump signed an Executive Order directing federal agencies with authorities and responsibilities under the ACA waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal burden on states or a cost, fee, tax, penalty or regulatory burden on individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. Congress also could consider subsequent legislation to repeal or replace elements of the ACA. Thus, the full impact of the ACA, or any law replacing elements of it, and the political uncertainty regarding any repeal and replacement on the ACA, on our business remains unclear.

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 2025 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. 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.

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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 and other regulatory bodies. 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 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. Although we were informed that the supplier received an EIR from the FDA, indicating that the FDA has concluded its inspection of the supplier and as of the date of its report considers outstanding deficiencies resolved, we expect that our suppliers will be subject to additional regulatory inspections in the future, including in connection with the FDA s review of any NDA we may submit in the future, if any, seeking approval of octreotide capsules in acromegaly. There can be no assurances that our suppliers will pass all future inspections, the failure of which could result in delays to our ability to receive regulatory approval 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 effectively 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 octreotide capsules. 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.

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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 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 future 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 previously 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 April 2016 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 $4.5 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 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 development and production efforts, which could harm our business, prospects, financial condition or results of operations.

****An important part of our strategy may be to enter into licensing or collaboration agreements with respect to octreotide capsules and future product candidates, if any, 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 candidate 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.

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

We rely, and will rely in the future, on third parties to conduct our 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 clinical programs for octreotide capsules, 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 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 clinical trials are not our employees, and, we cannot control whether or not they devote sufficient time and resources to our ongoing clinical 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 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 initial public offering, or 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 December 31, 2016, we had received net proceeds of $267.9 million from such transactions, including amounts raised in the IPO. As of June 30, 2017, our cash, cash equivalents and marketable securities were $80.1 million. Since inception, we have incurred significant operating losses. Our net loss was $13.9 million for the six months ended June 30, 2017 and $61.1 million for the year ended December 31, 2016. As of June 30, 2017, we had an accumulated deficit of $192.4 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 octreotide capsules and pursuit of regulatory approval in the United States and Europe for the maintenance treatment of adult acromegaly patients. This plan included a reduction of approximately 33% of our workforce in June 2016, including substantially all of our commercial personnel. In August 2016, we announced a second corporate restructuring plan which further reduced our workforce by approximately 44%, primarily in our research and administrative functions. In aggregate, these restructuring plans resulted in a reduction to our workforce of more than 60% since May 1, 2016. We currently expect our existing cash, cash equivalents and marketable securities will be sufficient to fund our operations through the anticipated release of top-line data from the Phase 3 OPTIMAL trial by the end of 2019 while supporting the MPOWERED trial in parallel. In addition, we will incur additional costs associated with operating as a public

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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, when we will become profitable, if at all, or whether we will have the funds necessary to continue as a standalone business in the long term.

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 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 Phase 3 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, which we plan to conduct in the Phase 3 OPTIMAL trial. 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. If we are successful in obtaining marketing approval of octreotide capsules in acromegaly, 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 operations, which may be difficult to obtain and restrict our operations and would result in additional dilution to our stockholders.***

Our business will require additional capital that we have not yet secured. In the short term, we expect to continue to conduct our second Phase 3 clinical trial of octreotide capsules to treat acromegaly MPOWERED required for European regulatory approval, and we plan to initiate our third Phase 3 clinical trial of octreotide capsules to treat acromegaly OPTIMAL in the second half of 2017 to potentially secure approval in the United States for octreotide capsules. In June and August of 2016, following our receipt of the CRL and the End of Review meeting, we announced corporate restructuring plans intended to focus our resources on the continued development of octreotide capsules for the maintenance treatment of adult acromegaly patients.

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, and to conduct a randomized, double-blinded and controlled Phase 3 clinical trial as the FDA strongly recommended in the CRL and that we plan to conduct under the OPTIMAL protocol agreed to in the SPA;

- the amount of our future operating losses;

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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 any future 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 development of octreotide capsules, 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 develop and commercialize octreotide capsules or any future product candidates or operate our business. Any of these actions could raise substantial doubt about our ability to continue as a going concern and have a material adverse effect on our business, financial condition and results of operations.

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 development personnel. As of June 30, 2017, we have a total of 17 full-time employees. In September 2016, following our restructuring actions, we announced that our Chief Financial Officer, Mark Fitzpatrick, was appointed to the role of Chief Executive Officer. Roni Mamluk, our former Chief Development Officer, who has been employed by us since 2006 ended her full-time employment with us on March 31, 2017, and transitioned to a board of director member of both our subsidiary, Chiasma (Israel), Ltd., and Chiasma, Inc. 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. These executives have significant research and development, regulatory, industry, operational, and/or corporate finance experience. Our receipt of a CRL from the FDA related to our NDA and expected octreotide capsules clinical development timelines 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, key employee or member of our board of directors could impair our ability to develop and commercialize octreotide capsules, if approved, and identify, develop and market new products and conduct successful operations.

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In addition, if octreotide capsules are approved, we will likely need 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 octreotide capsules or future product candidates we may develop uncompetitive or obsolete. The longer-term success of our business depends upon our ability to develop octreotide capsules for other approved indications and utilize our TPE platform to develop and commercialize oral forms of therapies that are currently only available in injectable or other non-absorbable forms, which strategy assumes we first obtain regulatory approval of octreotide capsules in acromegaly. 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

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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 and those of our clinical service providers 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 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.

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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. We conducted a self-assessment and subsequently self-certified under the Privacy Shield Framework in September 2016, and received a notice of acceptance of our self-certification in October 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

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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.

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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 polypeptide containing capsules including 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,

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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 candidate is in clinical trials, we believe that the use of our product candidate in these 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 current and any future product candidates progress toward commercialization, the possibility of a patent infringement claim against us increases. There can be no assurance that our current and any future 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 development efforts and limit our ability to continue our operations.

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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 or any future product candidates 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 development activities 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.

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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.

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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 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 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 (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 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, and our current separation agreements with Israeli employees who have left our company include a waiver of all claims, rights or payments under Israeli law, we may still 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 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 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, it is difficult (and may even be impossible) to

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enforce these agreements or any part thereof against our Israeli employees unless it can be shown that there are special circumstances in any particular case. 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, 2017, we had federal net operating loss, or NOL, carryforwards of approximately $140.7 million. The federal NOL carryforwards expire at various dates through 2036. At June 30, 2017, 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 2016 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 2014. In addition, future changes in our stock ownership, which may be outside of our control, may trigger an ownership change, as may future equity acquisitions that have equity as a component and of the purchase price. If additional ownership changes occur in the future, our ability to utilize our net operating losses to offset income if we attain profitability may be limited.

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

As of June 30, 2017, our executive officers, directors and principal stockholders collectively controlled approximately 64.3% of our outstanding common stock, excluding any shares of common stock that such persons may have the right to acquire upon exercise of outstanding options or warrants. As a result, these stockholders, if they act together, will be able to influence our management and affairs and all matters requiring stockholder approval, including the election of directors and approval of significant corporate transactions.

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

Provisions of Delaware law and our amended and restated certificate of incorporation and amended and restated bylaws, may discourage, delay or prevent a merger, acquisition or other change in control that stockholders may consider favorable, including transactions in which stockholders might otherwise receive a premium for their shares. These provisions may also prevent or delay attempts by stockholders to replace or remove our current management or members of our board of directors. These provisions include:

a classified board of directors;

limitations on the removal of directors;

advance notice requirements for stockholder proposals and nominations;

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

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

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

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

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

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

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

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

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

On July 21, 2015, we completed the sale of 7,319,750 shares of our common stock in our IPO, at a price to the public of $16.00 per share. Since shares of our common stock were sold in our IPO, our stock price has reached a high of $30.52 per share and a low of $1.25 per share through July 31, 2017. There has been a public market for our common stock for only a relatively 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 product candidate, octreotide capsules in acromegaly;
- the enrollment and results of our MPOWERED and planned OPTIMAL Phase 3 clinical trials 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, including the planned OPTIMAL Phase 3 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 of clinical trial material or 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;

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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 operations or changes in organizational structure;

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 current and former 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 octreotide capsules and our ability to obtain FDA approval for the marketing and sale of octreotide capsules. In December 2016, a lead plaintiff was appointed in the case. An amended complaint was filed by the lead plaintiff on February 10, 2017 similarly challenging our statements regarding the Phase 3 clinical trial methodology and results, and our ability to obtain FDA approval for octreotide capsules, in violation of Sections 11 and 15 of the Securities Act of 1933. The amended complaint adds as defendants current and former members of our board of directors, as well as the investment banks that underwrote our IPO on July 15, 2015. The lead plaintiff seeks to represent a class of all purchasers of our stock in our IPO. The plaintiff is seeking an unspecified amount of compensatory damages on behalf of himself and members of a putative shareholder class, including interest and reasonable costs and expenses incurred in litigating the action, and any other relief the court determines is appropriate. The defendants filed a motion to dismiss the amended complaint on March 27, 2017 and await a decision from the court following oral argument held on July 17, 2017. 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.

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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 these claims 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

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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 March 2017 and future Form 10-K filings, as required by Section 404 of the Sarbanes-Oxley Act. This requires 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, 2017, we had 24,359,584 outstanding shares of common stock, assuming no exercise of outstanding options or warrants.

In addition, the 3,642,537 shares subject to outstanding options under our stock option plans, the 3,179,265 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 three have since dropped coverage. In the event that one or more analysts who now, or in the

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future, cover us further downgrades our stock or publishes inaccurate or unfavorable research about our business, our trading price would likely decline. If one or more analysts, now or in the future, cease coverage of our company or fail to publish reports on us regularly, demand for our stock could decrease, which might cause our trading price and trading volume to decline.

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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, 2017, 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. We invested the funds received in cash equivalents and other short-term investments in accordance with our investment policy.

In June 2016 and August 2016, we announced two separate corporate restructuring plans intended to focus our resources on the continued development of octreotide capsules for the maintenance treatment of adult acromegaly patients. As a result of the August 2016 reduction in workforce, we eliminated our research and discovery functions and are currently not significantly investing in those areas.

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 clinical trial costs (including the international Phase 3 MPOWERED clinical trial that we initiated in March 2016 to support anticipated European regulatory approval of octreotide capsules and our planned international Phase 3 OPTIMAL clinical trial that we plan to initiate in the second half of 2017 to support United States regulatory approval of octreotide capsules following the receipt of SPA on August 4, 2017 from the FDA), manufacturing of octreotide capsules for market consumption, if approved, 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 development services, legal and other regulatory expenses, and other general operating costs.

Item 6. Exhibits

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

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SIGNATURES

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

CHIASMA, INC.

August 10, 2017

By: /s/ Mark J. Fitzpatrick
Mark J. Fitzpatrick
President, Chief Executive Officer and Director

(Principal Executive Officer and Principal Financial Officer)

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EXHIBIT INDEX

Exhibit No.	Description	Incorporated by Reference to: Form or Schedule	Exhibit No.	Filing Date with SEC	SEC File Number
10.1	Separation Agreement by and between Chiasma (Israel) Ltd. and Roni Mamluk, Ph.D., effective as of March 31, 2017	8-K	10.1	June 19, 2017	001-37500
10.2	Director Agreement by and between Chiasma (Israel) Ltd. and Roni Mamluk, Ph.D., effective as of April 1, 2017	8-K	10.2	June 19, 2017	001-37500
31.1*	Certification of Principal Executive Officer and 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.
Indicates a management contract or compensation plan, contract or arrangement.
\+ 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.