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UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, DC 20549

FORM 10-K

(Mark One)

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

For the fiscal year ended December 31, 2019

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)	**(IRS Employer Identification No.)**
140 Kendrick Street, Building C East Needham, MA	**02494**
(Address of Principal Executive Offices)	**(Zip Code)**

(617)-928-5300

(Registrant's Telephone Number, Including Area Code)

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, $0.01 par value	**CHMA**	**NASDAQ Global Select Market**

Securities registered pursuant to Section 12(g) of the Act: None

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ☐ No ☒

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Exchange Act. Yes ☐ No ☒

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 every Interactive Data File required to be submitted 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 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. (Check one):

Large accelerated filer	☐	Accelerated filer	☒
Non-accelerated filer	☐	Smaller reporting company	☐
		Emerging growth company	☒

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

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

The aggregate market value of the registrant's common stock held by non-affiliates (without admitting that any person whose shares are not included in such calculation is an affiliate) as of June 28, 2019, was $192,861,371, based on the closing price of $7.47 of the registrant as reported on the NASDAQ Global Select Market on such date. As of March 9, 2020, there were 42,255,657 shares of common stock, $0.01 par value per share, outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

The registrant intends to file a definitive proxy statement pursuant to Regulation 14A within 120 days of the end of the fiscal year ended December 31, 2019. Portions of such definitive proxy statement are incorporated by reference into Part III of this Annual Report on Form 10-K.

CHIASMA, INC.
ANNUAL REPORT ON FORM 10-K
For the Year Ended December 31, 2019

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SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K, or this Annual Report, contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act, and is subject to the "safe harbor" created by those sections. Any statements about our expectations, beliefs, plans, objectives, assumptions or future events or performance are not historical facts and may be forward-looking. Some of the forward-looking statements can be identified by the use of forward-looking terms such as "believes," "expects," "may," "will," "should," "seek," "intends," "plans," "estimates," "projects," "anticipates," or other comparable terms.

Forward-looking statements in this Annual Report include, but are not limited to, statements about:

- our efforts to potentially obtain regulatory approval of octreotide capsules, conditionally trade-named MYCAPSSA®, in the United States;
- the timing of the regulatory review process, including our expectation that the FDA will respond to our NDA resubmission by the June 26, 2020 PDUFA date;
- our expected commercial launch timing of MYCAPSSA in the United States, if FDA approval is obtained;
- our ability to obtain supply of sufficient amounts of octreotide capsules to support our planned commercial launch in the United States, if FDA approval of our NDA is obtained, and for clinical trials;
- our development of octreotide capsules for the treatment of acromegaly;
- our efforts to potentially obtain regulatory approval in the European Union by conducting the ongoing MPOWERED Phase 3 clinical trial;
- the timing and receipt and announcement of top-line and other clinical data, including our ability to release top-line data from the MPOWERED trial in the fourth quarter of 2020;
- 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 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 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 commercialize or our TPE technology obsolete;
- 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; and
- our ability to continue as a going concern and estimates and expectations regarding our capital requirements, cash and expense levels and liquidity sources

These forward-looking statements are not exhaustive. These forward-looking statements involve risk and uncertainties. We cannot guarantee future results, levels of activity, performance or achievements, and you should not place undue reliance on our forward-looking statements. Our actual results may differ significantly from the results discussed in the forward-looking statements. Factors that might cause such a difference include, but are not limited to, those set forth in "Item 1A. Risk Factors" and elsewhere in this Annual Report. Except as may be required by law, we have no plans to update our forward-looking statements to reflect events or circumstances after the date of this Annual Report. We caution readers not to place undue reliance upon any such forward-looking statements, which speak only as of the date made. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we may make. No forward-looking statement is a guarantee of future performance.

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

Unless the context requires otherwise, references in this Annual Report to "Chiasma," "the Company," "we," "our," and "us" refer to Chiasma, Inc. and its subsidiaries.

PART I

Item 1. Business

Overview

We are a clinical, late-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. In January 2020, the U.S. Food and Drug Administration, or the FDA, accepted for review our New Drug Application, or NDA, for our oral octreotide capsules product candidate, conditionally trade-named MYCAPSSA®, for the maintenance treatment of adults with acromegaly. We resubmitted our NDA following positive results from our CHIASMA OPTIMAL Phase 3 clinical trial, which was conducted under a Special Protocol Assessment, or SPA, agreement with the FDA and designed to support FDA approval. The FDA assigned a Prescription Drug User-Fee Act, or PDUFA, target action date of June 26, 2020, which is a six-month review. Our primary focus is on developing and seeking the regulatory approval and subsequent commercialization of oral octreotide capsules, our sole TPE platform-based clinical product candidate, for the treatment of adult patients with acromegaly in the United States and European Union.

Acromegaly and Treatment Burden

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

Octreotide is an analog of somatostatin, a natural inhibitor of growth hormone secretion. The current standard of care for patients diagnosed with acromegaly and not otherwise cured by surgical removal of the pituitary tumor consists of lifelong, once-monthly injections of an extended release somatostatin analog, primarily octreotide or lanreotide. These products contain a viscous formulation and are typically administered by a healthcare professional with large-gauge needles into the muscle or deep subcutaneously, that is, deeply under the skin. While injectable somatostatin analogs are generally effective at reducing GH and IGF-1 levels and, therefore, providing disease control, the injections are associated with signification limitations and patient burdens, including suboptimal symptom control, especially as the treatment effects begin to wane near the end of the monthly cycle prior to the next injection, inconvenience, pain and other injection-related side effects. We believe that octreotide capsules, if approved by regulatory authorities, will be the first somatostatin analog available for oral administration. Octreotide capsules have been granted orphan designation in the United States and the European Union for the treatment of acromegaly. The worldwide market for injectable somatostatin analogs is approximately $2.8 billion annually, of which we estimate approximately $800 million represents annual sales for the treatment of acromegaly. We retain worldwide rights to develop and commercialize octreotide capsules with no royalty obligations to third parties.

Accepted New Drug Application for MYCAPSSA®

In July 2019, we announced positive top-line results from the CHIASMA OPTIMAL (Octreotide capsules vs. Placebo Treatment In MultinationAL centers), a Phase 3 clinical trial of octreotide capsules for the treatment of acromegaly conducted under a SPA agreement with the FDA and designed to support regulatory approval in the United States. Based on the positive results from the CHIASMA OPTIMAL trial, we resubmitted our NDA to the FDA in December 2019, seeking marketing approval of MYCAPSSA capsules as a maintenance therapy for adult patients with acromegaly. In January 2020, the FDA accepted for review the resubmission of our NDA as a complete response to deficiencies identified in the FDA's April 2016 complete response letter, or CRL, to our original NDA submission and assigned a PDUFA action date of June 26, 2020.

CHIASMA OPTIMAL

The CHIASMA OPTIMAL trial was a randomized, double-blind, placebo-controlled, nine-month clinical trial of octreotide capsules and enrolled 56 adult acromegaly patients whose disease was biochemically controlled by injectable somatostatin analogs based upon levels of IGF-1, a byproduct of increased GH levels caused by acromegaly (average IGF-1 £ 1.0 × upper limit of normal, or ULN). The patients also had confirmed active acromegaly following their last surgical intervention based upon an elevated IGF-1 at that time of ³ 1.3 × ULN. Patients were randomized on a 1:1 basis, to octreotide capsules or placebo. Patients were dose titrated from 40 mg per day (equaling one capsule in the morning and one capsule in the evening) to up to a maximum of 80 mg per day (equaling two capsules in the morning and two capsules in the evening). Patients who met the predefined withdrawal criteria, or discontinued from oral treatment for any reason, in either treatment arm during the course of the trial were considered treatment failures, reverted to their original treatment of injections and monitored for the remainder of the trial. The primary endpoint of the trial was the proportion of patients who maintained their biochemical response 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 × ULN (assessed at weeks 34 and 36). Hierarchical secondary endpoints that are expected to be considered by the FDA in evaluating the totality of evidence for octreotide capsules treatment effect include: proportion of patients who maintain growth hormone, or GH, response at week 36 compared to screening; time to loss of response: IGF-1 of 2 consecutive visits is > 1.0 × ULN; time to loss of response: IGF-1 of two consecutive visits is ³ 1.3 × ULN; and proportion of patients requiring rescue treatment.

In the CHIASMA OPTIMAL trial:

- The primary endpoint was met: 58% of the patients on octreotide capsules maintained their IGF-1 response compared to 19% of the patients on placebo (p = 0.008).

- All secondary endpoints were met.
  - 78% of patients treated with octreotide capsules maintained their GH levels below 2.5 ng/mL at the end of the core study compared to 30% of patients treated with placebo (p = 0.001).
  - Median time to loss of response (IGF-1 >1.0 × ULN) was not reached (>36 weeks) for patients treated with octreotide capsules compared to 16 weeks for patients treated with placebo (p <0.001).
  - Median time to loss of response (IGF-1 ³ 1.3 × ULN) was not reached (>36 weeks) for patients treated with octreotide capsules compared to 16 weeks for patients treated with placebo (p <0.001).
  - 25% of patients treated with octreotide capsules required rescue medication with injectable somatostatin analogs (octreotide LAR or lanreotide depot) anytime throughout the study compared to 68% of patients treated with placebo (p = 0.003).

Additionally, 75% of patients randomized to the octreotide capsules treatment arm completed the 36-week trial of which 90% elected to continue into the open label extension. Further, in a pre-specified exploratory endpoint, mean IGF-1 values across all 28 patients treated with octreotide capsules (including primary endpoint non-responders per protocol), remained within normal limits with a 0.97 x ULN at the end of oral treatment versus 1.69 x ULN at the end of treatment for the patients on placebo. For purposes of this analysis, the end of oral treatment value was the average of week 34 and week 36 values for all patients who completed the study on octreotide capsules or placebo and for those patients that required rescue medication, it was their last observed value prior to the use of rescue medication.

In the CHIASMA OPTIMAL trial, octreotide capsules appeared safe and well tolerated in the trial patient population. No new or unexpected safety signals were observed. The overall number of treatment emergent adverse events, or TEAEs, was comparable between the octreotide capsules and placebo treatment groups, 64% versus 54%, respectively. Two patients on octreotide capsules and one patient on placebo discontinued treatment due to TEAEs. Two patients on octreotide capsules and one patient on placebo had serious adverse events, or SAEs, assessed as not related to study drug. Severe TEAEs as well as TEAEs of special interest (acromegaly symptoms) were more common in placebo treated patients than in patients treated with octreotide capsules.

The CHIASMA OPTIMAL trial was conducted under a SPA agreement with the FDA, which indicates that the FDA agreed that the design and planned analysis of the CHIASMA OPTIMAL trial results adequately address the objectives necessary to support a regulatory submission. However, a SPA is not a guarantee of regulatory approval. We anticipate that the FDA will review the totality of the data collected from the CHIASMA OPTIMAL trial, including the primary and all secondary endpoints, together with certain data from our other clinical trials of octreotide capsules, including but not limited to data related to the loss of biochemical response when switching from injectable somatostatin analogs to octreotide capsules, in evaluating our NDA. We continue to believe that the data from the CHIASMA OPTIMAL trial alone is designed to address the clinical concerns raised by the FDA in its CRL to our original NDA submission and also that, with respect to our ongoing Phase 3 MPOWERED™ clinical trial (described below), the FDA only expects to review safety data from the MPOWERED trial as part of its review of our NDA resubmission. Any future requirement by the FDA to submit additional data, including the efficacy data from our MPOWERED clinical trial could delay or prevent the review or approval of our NDA.

MPOWERED™

We are also conducting an international Phase 3 clinical trial, referred to as MPOWERED (Maintenance of Acromegaly Patients with Octreotide Capsules Compared With Injections -Evaluation of REsponse Durability), of oral octreotide capsules for the maintenance treatment of adult patients with acromegaly to support regulatory approval in the European Union. The MPOWERED trial is designed to show parallel comparative safety and

effectiveness as required by the EMA. Initiated in March 2016, the MPOWERED trial is a randomized, open-label and active-controlled 15-month trial initially designed to enroll up to 150 patients. The European Medicines Agency, or EMA, requested that a minimum of at least 80 patients who are responders to octreotide capsules following the six-month run-in phase be randomized to either remain on octreotide capsules or return to injectable somatostatin receptor ligands (octreotide or lanreotide), and then followed for an additional nine months. We completed enrollment of 146 total patients in the MPOWERED trial in June 2019. In January 2020, the randomization of patients was completed. Of the 146 patients that entered the six-month run-in phase of the trial, 92 of these patients (or 63%) completed the run-in phase and were deemed to be responders to octreotide capsules per protocol (IGF-1 <1.3 x ULN and GH<2.5 ng/mL). Responders to octreotide capsules were randomized (2:3) per protocol to either go back to their original long-acting injectable somatostatin analog or remain on octreotide capsules at the dose identified during the run-in phase and then followed for an additional nine months.

The primary endpoint of the MPOWERED trial is the proportion of patients who are biochemically controlled throughout the randomized, controlled phase of the study, defined as a time weighted average of IGF-I < 1.3 ULN. In addition to measures of biochemical control, the MPOWERED trial is expected to provide data on the impact of treatment on acromegaly symptoms and patients' quality of life through multiple validated instruments. Secondary and exploratory endpoints are designed to explore overall health assessments and whether more patients experience maintenance or improvement of acromegaly symptoms between treatments, both individually and as an overall composite score. The trial is also designed to generate data on when patients experience their acromegaly symptoms and any interference with work productivity and the ability to perform regular activities of daily living. The impact of octreotide capsules versus injectable treatment is also expected to be measured from a standpoint of gastrointestinal adverse events and the burden of receiving injections in a healthcare setting versus the fasting requirements of MYCAPSSA capsules.

In late 2016, following the FDA's position that the MPOWERED trial would not be sufficient to address the concerns raised in the CRL, we modified certain elements of the MPOWERED trial in an effort to preserve patients, sites and other resources necessary to conduct the CHIASMA OPTIMAL Phase 3 trial, which was designed to address the FDA's concerns, and produce data packages suitable for submission in both the United States and the European Union. We expect to release top-line data from the MPOWERED trial in the fourth quarter of 2020. Subject to FDA approval of our NDA resubmission, if obtained, and assuming positive data from the MPOWERED trial, we expect to submit a marketing authorization application, or MAA, to the EMA in the first half of 2021 seeking marketing approval of MYCAPSSA capsules as a maintenance therapy for adult patients with acromegaly in the European Union.

Original NDA

We submitted our original NDA for octreotide capsules in June 2015 following the completion of a multinational, open-label Phase 3 clinical trial of oral octreotide capsules for the treatment of acromegaly in 2014. In April 2016, the FDA issued a CRL, which indicated that the review of our application was complete and 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 first 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.

Special Protocol Assessment

In August 2017, we reached agreement with the FDA under a SPA for a new Phase 3 clinical trial of octreotide capsules in adult acromegaly patients, designed to address the efficacy concerns previously raised in the CRL and support a potential resubmission of our NDA for octreotide capsules in acromegaly. In September 2017, we initiated the CHIASMA OPTIMAL trial, which was a randomized, double-blind, placebo-controlled, nine-month clinical trial conducted under the SPA. It enrolled 56 adult acromegaly patients (at least 20% of whom were required to be recruited from the United States) whose disease was biochemically controlled, based upon levels of IGF-1, on injectable somatostatin analogs at baseline (average IGF-1 £ 1.0 x ULN). The primary endpoint of the study was the proportion of patients who maintained 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 at weeks 34 and 36.

In May 2018, we reached further agreement with the FDA under a SPA Agreement Modification letter providing that the hierarchical secondary endpoints of the CHIASMA OPTIMAL trial that will be considered by the FDA in evaluating the totality of evidence for octreotide capsules treatment effect are:

- Proportion of patients who maintain GH response at week 36 compared to screening;
- Time to loss of response: IGF-1 > 1.0× ULN;
- Time to loss of response: IGF-1 > 1.3×ULN; and
- Proportion of patients requiring rescue treatment.

Manufacturing

We depend on third-party suppliers and contract manufacturing organizations, or CMOs, for all of our required raw materials and drug substance and to manufacture and package drug product for clinical use and commercial use, if we obtain marketing approval for MYCAPSSA capsules in the United States.

In order to have oral octreotide capsules available to support our planned commercial launch in the fourth quarter of 2020, we expect to submit for FDA review two prior approval manufacturing supplements to our NDA for our commercial sources of generic active pharmaceutical ingredient, or API, octreotide acetate. During 2020, we expect to have a total of three manufacturing sites qualified for commercial supply of API located in the United States, Israel and Switzerland.

The first manufacturing site, and the only one currently referenced in our NDA resubmission, is a small-scale manufacturing site of our secondary commercial API manufacturer. This site was also included in our original NDA. We do not currently plan to procure commercial API from this small-scale manufacturing site.

The second and third API manufacturing sites are larger-scale manufacturing sites that we plan to use to produce commercial supply of octreotide capsules. One of these sites is a new site affiliated with the small-scale manufacturing site currently referenced in the NDA resubmission, and the other site belongs to our primary commercial API manufacturer and was included in our original NDA. We did not reference these two larger-scale manufacturing sites in our recent NDA resubmission. At the time of our NDA resubmission, our primary commercial API manufacturer was in the process of resolving outstanding observations from a recent regulatory inspection of its site. To allow for further time to resolve the observations, we decided not to reference this site in our NDA resubmission. The inspection was closed by the regulator in February 2020. In addition, we did not reference the other larger-scale manufacturing site in our NDA resubmission because that allowed us to seek and obtain the FDA's designation of our NDA resubmission as a Class 2 resubmission. The benefit of a Class 2 designation is a six-month review cycle and, accordingly, the FDA assigned a June 26, 2020 PDUFA target date, which is a six-month review.

If we obtain marketing approval of octreotide capsules from the FDA, we expect to submit to the FDA a prior approval manufacturing supplement for each of these two larger-scale manufacturing sites to reference them in our NDA. In anticipation of FDA approval of our NDA resubmission, we are currently procuring API from these two larger-scale manufacturing sites. Subject to FDA's timely approvals of the NDA and either of the two planned prior approval manufacturing supplements, we expect to have oral octreotide capsules available to support our planned commercial launch in the fourth quarter of 2020.

In addition to these three manufacturing sites, we expect our primary commercial API manufacturer to scale-up and qualify a separate larger manufacturing site to meet our longer-term commercial requirements of octreotide acetate.

All excipients, or substances formulated together with the API, used in manufacture of octreotide capsules are obtained by our CMOs from third-party suppliers. The octreotide API is formulated with our TPE technology by a lyophilization service provider and filled into capsules and enteric-coated by another third-party CMO.

If we obtain marketing approval from the FDA, we plan to establish a distribution channel in the United States utilizing third-party logistics and one or more specialty pharmacies to distribute product directly to patients who have been prescribed octreotide capsules.

Commercial Readiness

We believe that approximately 8,000 adult acromegaly patients are chronically treated with somatostatin analogs in the United States, and that approximately 90% of these patients are managed by fewer than 1,000 patient care centers. Patients with acromegaly undergoing treatment in the United States are generally treated by endocrinologists at a small number of academic institutions with pituitary experts (pituitary centers), regional academic centers or hospital systems (regional referral centers) and some community endocrinologists. Accordingly, we believe that the U.S. market for MYCAPSSA capsules is addressable with a small orphan drug customer facing team ranging between 30 to 50 employees that includes case managers, sales representatives, nurse educators, and account managers. We began implementing commercial launch readiness plans in 2019 and in early 2020, in preparation for a potential commercial launch of MYCAPSSA capsules in the United States in the fourth quarter of 2020, including:

- expanding our organization with new key employees with expertise in marketing, sales, market access, patient services and product reimbursement and distribution in particular for rare diseases; and
- developing our commercial capabilities, including commencing the establishment of internal systems and infrastructure to support a commercial sales organization and patient-focused programs and appropriate quality systems and compliance policies and procedures.

We retain worldwide rights to develop and commercialize octreotide capsules with no royalty obligations to third parties. If approved, we plan to commercialize octreotide capsules ourselves in the United States and explore the strategic merits of collaboration opportunities for commercializing octreotide capsules in the European Union and the rest of the world.

Intellectual Property

Octreotide capsules are currently protected by issued patents lasting until at least 2029 in the United States, the European Union, United Kingdom, Japan and several other jurisdictions, and by pending patent applications in additional jurisdictions that will last until 2029, if granted. On March 26, 2019, a United States patent directed to specific methods of using octreotide capsules was granted. This patent will expire in 2036. We are also pursuing additional patent applications relating to particular uses, dosages and packaging for octreotide capsules.

Strategy

Our goal is to become a successful patient-focused biopharmaceutical company by developing and commercializing, ourselves or through others, octreotide capsules as a maintenance therapy for adult patients with acromegaly. Our strategy to pursue this goal includes the following elements:

- ***Obtain U.S. regulatory approval of octreotide capsules for the treatment of acromegaly.*** Based on the positive results from the CHIASMA OPTIMAL trial, in December 2019, we resubmitted our NDA seeking approval of MYCAPSSA capsules as a maintenance therapy for adult patients with acromegaly to the FDA. In January 2020, the FDA accepted for review the resubmission of the NDA as a complete response to deficiencies identified in the CRL to our original NDA and assigned an action date of June 26, 2020 under the PDUFA.
- ***Commercialize octreotide capsules in the United States***. We expect to commercialize MYCAPSSA capsules in the United States if marketing approval is granted by the FDA. We believe that the U.S. market for MYCAPSSA capsules is addressable with a small, specialty orphan drug sales force. During 2019 and early 2020, we began implementing commercial launch readiness plans in anticipation of a potential U.S. marketing approval of MYCAPSSA capsules. Subject to the timely approval by the FDA of our NDA and either of the planned prior approval manufacturing supplements, we expect to launch the sale of MYCAPSSA capsules in the United States during the fourth quarter of 2020. In anticipation of receiving marketing approval from the FDA, we are building a focused in-house sales and marketing organization to identify pituitary specialists and community endocrinologists who comprise the top prescribers of therapies for acromegaly and are preparing to market octreotide capsules, if approved, to these physicians.
- ***Obtain European Union regulatory approval of octreotide capsules for the treatment of acromegaly.*** To support approval in the European Union, we initiated the Phase 3 MPOWERED clinical trial in March 2016, with a protocol that has been accepted by the EMA, to evaluate the comparative safety and efficacy of octreotide capsules in adult acromegaly patients. We currently expect to release top-line data from this trial in the fourth quarter of 2020, and assuming favorable results, and pending FDA approval of our NDA resubmission, we expect to submit our MAA to the EMA in the first half of 2021 to potentially secure approval in the European Union for MYCAPSSA capsules.
- ***Explore collaboration opportunities in the European Union and the rest of the world for octreotide capsules in acromegaly.*** At the appropriate time, we plan to explore one or more collaborations to commercialize octreotide capsules in acromegaly outside of the United States. However, depending on our evaluation of the strategic merits of these collaboration opportunities, we may decide to retain commercial rights in key markets and undertake commercialization preparation and activities ourselves, if required regulatory approvals are obtained.
- ***Generate real-world data on acromegaly treatments.*** We began enrolling patients in the first industry-sponsored disease state registry for acromegaly in the United States known as the Management of Acromegaly, or MACRO, Registry. The MACRO Registry is designed to enroll patients from over 40 planned clinical sites in the United States and collect real-world data on treatment burden and effectiveness of various acromegaly treatments.

Our Product Candidate, Octreotide Capsules (MYCAPSSA®) in Acromegaly

Product Candidate Overview

Octreotide capsules are a novel oral formulation of octreotide developed utilizing our TPE platform. We are developing octreotide capsules as a liquid-filled solid gelatin capsule formulation which is intended to be taken twice a day. We expect that acromegaly patients who are prescribed octreotide capsules, if approved, will receive a 28-day supply of capsules, which may be stored at room temperature by the patient for up to one month. Based on the aggregate data from our completed clinical trials and the randomization rate of responders per protocol

following the six-month run-in phase of our Phase 3 MPOWERED clinical trial, we believe octreotide capsules have the potential to induce biochemical response (inhibition of GH and IGF-1) while also potentially improving symptoms and reducing the burden of disease and treatment in patients afflicted with acromegaly.

Our product candidate, octreotide capsules, has completed two Phase 3 clinical trials for the treatment of acromegaly and 11 pharmacology and pharmacokinetic (PK) Phase 1 studies. In August 2015, our NDA for octreotide capsules as a maintenance therapy for acromegaly in the United States was accepted by the FDA for filing. In April 2016, the FDA issued a CRL to our NDA. In the 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 be 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 December 2016, we were informed that the supplier referred to in the CRL had recently received its Establishment Inspection Report, or EIR, from the FDA. In September 2017, we initiated a Phase 3 clinical trial for oral octreotide capsules for the maintenance therapy of adult patients with acromegaly following our agreement with the FDA on the design of the trial, reached through a SPA agreement in August 2017. The trial, referred to as CHIASMA OPTIMAL, was a randomized, double-blind, placebo-controlled, nine-month trial that enrolled 56 adult acromegaly patients and was designed to address the concerns raised in the CRL and support regulatory approval of octreotide capsules in the United States. In July 2019, we announced positive top-line results from the CHIASMA OPTIMAL trial. We resubmitted our NDA to the FDA in December 2019, seeking marketing approval of MYCAPSSA capsules as a maintenance therapy for adult patients with acromegaly. In January 2020, the FDA accepted for review the resubmission of our NDA as a complete response to deficiencies identified in the CRL and assigned a PDUFA action date of June 26, 2020.

The EMA has advised us that a clinical trial demonstrating non-inferiority of octreotide capsules compared to injectable somatostatin analogs as active controls will be required prior to regulatory approval in the European Union. We agreed on the Phase 3 clinical trial protocol with the EMA and, in March 2016, we initiated an international Phase 3 clinical trial, referred to as MPOWERED, of oral octreotide capsules for the maintenance treatment of adult patients with acromegaly to support regulatory approval in the European Union. In late 2016, following the FDA's position that the MPOWERED clinical trial will not be sufficient to address the concerns in the CRL, we modified certain elements of the MPOWERED trial in an effort to preserve patients, sites and other resources necessary to conduct the CHIASMA OPTIMAL 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. The EMA requested that a minimum of at least 80 patients who are responders to octreotide capsules following the six-month run-in phase be randomized to either remain on octreotide capsules or return to injectable somatostatin receptor ligands (octreotide or lanreotide), and then followed for an additional nine months. In October 2018, 80 patients were randomized following the six-month run-in phase in the MPOWERED trial. Further, in October 2018, we elected to resume enrollment in the trial in an effort to enroll up to 15 additional patients exclusively located in the United States in order to gain further U.S. investigator and patient experience with octreotide capsules. We completed enrollment of 146 total patients in the MPOWERED trial in June 2019. In January 2020, the randomization of patients was completed. Of the 146 patients that entered the six-month run-in phase of the trial, 92 of these patients (or 63%) completed the run-in phase and were deemed to be responders to octreotide capsules per protocol. We expect to release top-line data from the MPOWERED trial in the fourth quarter of 2020. Subject to FDA approval of our NDA resubmission, if obtained, and assuming positive data from the MPOWERED trial, we expect to submit our MAA to the EMA in the first half of 2021 seeking marketing approval of MYCAPSSA capsules as a maintenance therapy for adult patients with acromegaly in the European Union.

Overview of Acromegaly

Acromegaly results from the overproduction of GH, most often due to the growth of a benign tumor in the pituitary gland in middle-aged adults. GH, in turn, stimulates the production of IGF-1 in the liver which stimulates the growth of bones and other tissues. Progression of acromegaly can result in significant health problems such as hypertension, enlargement of the heart, or cardiomyopathy, sleep apnea, type-2 diabetes, and abnormal growths in the colon and uterus. Acromegaly is associated with a number of symptoms, some acute, such as headaches, joint pain and fatigue, and some long-term, such as enlarged hands, feet and internal organs, as well as altered facial features. Because acromegaly is uncommon and physical changes occur gradually, the condition is often not recognized immediately, sometimes not for years. If not treated promptly, acromegaly can lead to serious illness and is associated with premature death, primarily due to cardiovascular disease. However, both surgical and drug treatments are available for acromegaly that can reduce the risk of complications and premature death and significantly improve symptom control.

Surgery is often the first line of therapy for acromegaly and, in most cases, surgical removal of the pituitary tumor can result in normalization of GH and IGF-1 levels. In many other cases, however, the levels of GH remain elevated even after surgery due to residual tumor and many patients therefore also require a therapeutic intervention. The body's natural inhibitor of excess GH secretion is somatostatin, a peptide hormone. Octreotide and lanreotide, analogs of somatostatin with a significantly longer half-life in the blood than natural somatostatin, have achieved widespread adoption by physicians treating patients afflicted with acromegaly. These somatostatin analogs are routinely administered by injection by a healthcare professional. If not administered with proper technique, the injection may not effectively deliver the medication. There is currently no oral formulation of a somatostatin analog on the market.

Incidence and Prevalence of Acromegaly and Current Treatment Landscape

We believe there are an estimated 69,000 individuals with acromegaly in the major markets (United States, European Union, Japan, Australia and Canada). 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 13 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, 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. Data from a 2017 study by Lavrentaki et. al. suggest that the global prevalence of acromegaly may be between 28 and 137 cases per million people.

According to publicly available financial reports, injectable forms of octreotide and lanreotide generated worldwide sales of approximately $2.8 billion annually in 2019 for the treatment of acromegaly, neuroendocrine tumors and some other smaller indications. We believe approximately $800 million of this total represents the annual sales for the treatment of acromegaly. The great majority of these sales come from once-monthly long acting formulations that must be administered by intramuscular or deep subcutaneous injections with large-gauge needles. Although we are targeting acromegaly with octreotide capsules, we believe that this product candidate, if approved in acromegaly, has the potential to become a standard of care in other indications currently treated with injectable somatostatin analogs.

Current Therapeutic Options and Their Limitations

For acromegaly patients not cured by surgery, the current standard of care involves injectable somatostatin analogs. These therapies are associated with significant patient limitations and burdens. Currently, the first therapeutic treatment options are octreotide LAR, marketed by Novartis AG, or Novartis, which is administered monthly and intramuscularly using a large gauge needle, and lanreotide depot, another long-acting analog of

somatostatin marketed by Ipsen SA, or Ipsen, which is administered monthly using a deep subcutaneous injection. Immediate release octreotide, while available, is more rarely used. For patients not controlled on these somatostatin analogs, the typical second line of treatment options (which may also be acceptably used as first line therapy) includes pegvisomant daily injections, marketed by Pfizer, Inc., or Pfizer, and pasireotide LAR, which is another somatostatin analog marketed by Recordati, which is administered monthly via intramuscular injection.

Current Injectable Treatment Options for Acromegaly

Product	Company	Route	Needle (length/gauge)	Status
Octreotide LAR	Novartis	Intramuscular	1.5”/19 or 20 G	Marketed
Lanreotide Depot	Ipsen	Deep Subcutaneous	0.79”/18 or 19 G	Marketed
Pasireotide LAR	Recordati	Intramuscular	1.5”/20 G	Marketed
Pegvisomant	Pfizer	Subcutaneous	1”/21-27 G	Marketed

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

- ***Suboptimal control.*** In a published patient-reported outcomes survey that we conducted in 195 acromegaly patients receiving injected somatostatin analogs, or our patient survey, 52% of patients reported that the treatment effects begin to wane near the end of the monthly cycle prior to the next injection, and 32% of controlled patients still experienced some symptoms.
- ***Pain.*** Injections with somatostatin analogs require a large-gauge needle to slowly inject a viscous solution into the muscle or deep into subcutaneous tissue. Patients report these injections to be very painful. Often, this pain persists for several days after the injection. In our patient survey, 70% of patients said they experienced pain during the injection and approximately half of these patients experienced continuing pain days later.
- ***Injection-site reactions.*** Patients frequently experience hardness, nodules and swelling at the site of the injection as well as bruising and inflammation.
- ***Lack of convenience.*** The treatment effectiveness is dependent on proper delivery technique and thus the injections are typically administered by a healthcare professional. The monthly injection schedule for injectable somatostatin analogs and the associated travel to the healthcare provider is inconvenient for many patients.
- ***Emotional impact.*** In our patient survey, 36% of patients said that they felt a loss of independence due to the requirement for chronic injections that typically require them to visit a healthcare professional.
- ***Lost work days.*** In our patient survey, 16% of patients said that the treatment burden associated with the injectable therapies caused them to regularly miss work for injections. These patients missed an average of 11 days a year.

Utilizing the Acromegaly Treatment Satisfaction Questionnaire, or Acro-TSQ, a patient-reported symptom assessment tool developed and copyrighted by us, screening data from 70 eligible patients in the MPOWERED trial who treated their acromegaly with octreotide LAR or lanreotide depot were collected and analyzed in 2018. The findings include:

- ***Ongoing symptoms.*** 66% of patients reported ongoing acromegaly symptoms, of which 83% reported some symptoms “all the time.”
- ***Worsening symptoms.*** 50% indicated some symptoms worsen towards the end of the monthly injection interval.
- ***Interference with life.*** Symptoms interfered with daily life (91%) and leisure activities (86%).

- ***GI side effects.*** More than 50% reported gastrointestinal, or GI, side effects (median duration five days following each injection) that interfered with daily life.
- ***Worsening GI effects.*** GI side effects were worse in patients with more active symptoms but did not correlate with IGF-1 levels or treatment dose.

A cross-sectional online study was conducted to understand the experience of acromegaly patients treated with somatostatin analog injections in the United States with stable disease (no change to SSA-based treatment in the past 12 months) and to compare patients' perception with those of their healthcare provider, or HCP. Patients completed an online survey focusing on disease characteristics and management; symptoms; adverse reactions; general health; and the Acro-TSQ. Patients were also asked to provide contact information for their treating HCP who were contacted and asked to participate in a telephone interview about their patient and complete applicable portions of the Acro-TSQ. A total of 105 patients completed the online survey and 47 HCPs completed the interview.

Preliminary data from 65 acromegaly patients enrolled in this study were analyzed to understand the disease and treatment burden. The findings included:

- ***Symptoms*****.** 78% reported headaches, 80% reported fatigue/weakness, 69% had excessive sweating, 85% had joint pain, 83% had soft tissues swelling, 63% had carpal tunnel symptoms, 54% had vision problems, 66% reported snoring, and 86% reported forgetfulness, and short-term memory loss or feeling in a daze (referred to as "acro-fog");
- ***Injection Site Reactions***. A significant number of patients (>30%; range: 31% to 41%) reported that the severity of their injection site reactions was moderate to severe;
- ***GI Side Effects***. 66% experienced GI side effects, lasting on average 11 days. 91% reported GI side effects affected daily life, 93% said they interfered with leisure activities, and 91% reported they interfered with work; and
- ***Bother.*** Patients were bothered by the amount of time they experienced symptoms (100%), bothered by injection site reactions during the first few days (74%), the need to schedule injections (65%), and having to travel for injections (85%).

Data from this study were also utilized to understand how HCPs perceive their acromegaly patients' treatment outcomes. A total of 30 HCPs (of the total of 47), who treated patients who were biochemically controlled (of the total of 105 patients), were interviewed. The key findings included:

- ***Symptom Control.*** HCPs reported 27% of their patients were symptomatically well-controlled and 73% were partially controlled;
- ***Symptoms.*** HCPs reported that a majority of their patients experienced fatigue/weakness/feeling tired (87%), joint pain (70%), and headaches (60%). 43% of their patients reported soft tissue swelling and 47% reported acro-fog; and
- ***General Health.*** HCPs gave patients a mean general health rating of 73 (out of 100, where 100 is the best health possible).

Additional data on this study for all 47 acromegaly patients and their designated HCP included:

- ***Symptoms reported by patients.*** 81% reported acro-fog, 81% reported joint pain, 79% reported soft tissue swelling, 77% reported fatigue/weakness, and 72% reported headaches;
- ***Symptoms reported by HCPs.*** 92% of their patients report fatigue/weakness/tired, 75% report joint pain, and 62% report headaches; and
- ***Concordance between patients and HCPs:*** There was poor agreement between patients and HCPs on the frequency, severity, and pattern of symptoms, as well as on the severity of injection site reactions and on multiple portions of the Acro-TSQ. In general, patients reported symptoms and injection site reactions more often and with higher frequency than HCPs.

Since injectable somatostatin analogs are used in other diseases beyond acromegaly, these limitations and burdens are also associated with the treatment of the other indications. If approved in acromegaly, we believe oral octreotide capsules have the potential to become a standard of care in these other indications.

Clinical Program for Octreotide Capsules in Acromegaly

United States Regulatory Pathway

We are seeking regulatory approval of octreotide capsules for the maintenance therapy of acromegaly in the United States utilizing the FDA's 505(b)(2) regulatory pathway. The 505(b)(2) pathway enables us to rely, in part, on the FDA's prior findings of safety and efficacy of an approved product, or published literature, in support of an NDA. In the case of octreotide capsules in acromegaly, the approved product to which our original NDA submission referred is the short-acting subcutaneous injectable formulation of octreotide that was the original product approved by the FDA before the long-acting formulation was developed. Since this formulation of octreotide was approved by the FDA in generic form and is therefore no longer proprietary, we are not aware of any third party from which we would be required to obtain any license or acquire any rights to commercialize octreotide capsules, if approved. As described in more detail below, we have completed two Phase 3 clinical trials and a series of Phase 1 clinical trials, including a trial to demonstrate that the systemic octreotide exposure from octreotide capsules, developed utilizing our TPE technology, is comparable to that of octreotide administered in the short-acting subcutaneous injectable formulation as well as a Phase 1 clinical trial to evaluate the bioactivity of octreotide capsules in healthy subjects.

In April 2016, the FDA issued a CRL to our original NDA. In the 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 be 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 December 2016, we were informed that the supplier had recently received its Establishment Inspection Report, or EIR, from the FDA. The receipt of the EIR is an indication that the FDA has concluded its inspection of the supplier and as of the date of its report considers outstanding deficiencies resolved. In June 2016, we participated in an End of Review meeting with the FDA where the FDA reiterated its concerns raised in the CRL. In the minutes from the End of Review Meeting, the FDA indicated that some of its concerns could potentially be addressed through a placebo-controlled study design.

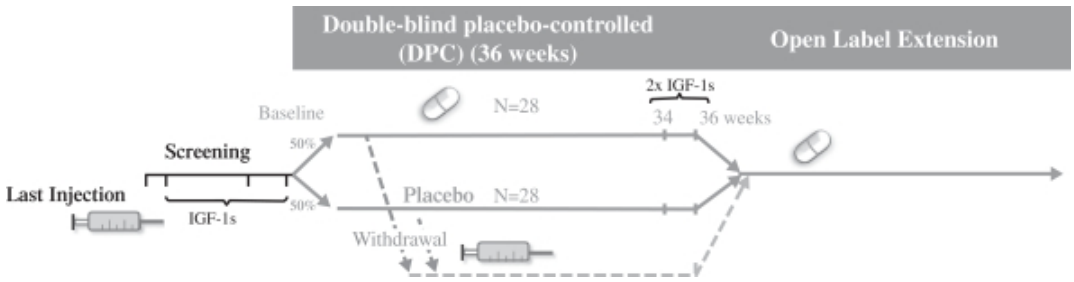
Special Protocol Assessment and CHIASMA OPTIMAL Phase 3 Clinical Trial

In August 2017, we reached agreement with the FDA under a SPA of a new Phase 3 clinical trial of octreotide capsules in adult acromegaly patients, designed to address the concerns previously raised in the CRL and support a potential resubmission of our NDA for octreotide capsules in acromegaly. The CHIASMA OPTIMAL trial, which we initiated in September 2017, was a randomized, double-blind, placebo-controlled, nine-month clinical trial conducted under the SPA. It enrolled 56 adult acromegaly patients (at least 20% of whom must be recruited from the United States) whose disease was biochemically controlled, based upon levels of insulin-like growth factor, IGF-1, a byproduct of increased GH levels caused by acromegaly, on injectable somatostatin analogs at baseline (average IGF-1 £ 1.0 x ULN). The patients were required to have confirmed active acromegaly following their last surgical intervention based upon an elevated IGF-1 at that time of ³ 1.3 x ULN. The patients in the trial were randomized on a 1:1 basis to octreotide capsules or placebo. Patients were dose titrated from 40 mg per day to up to a maximum of 80 mg per day, equaling two capsules in the morning and two capsules in the evening. Similar to the requirements of our first completed Phase 3 clinical trial and the MPOWERED trial, patients were required to take octreotide capsules at least one hour prior to a meal or two hours after a meal.

Patients who met predefined withdrawal criteria or withdraw from oral treatment in either treatment arm for any reason during the course of the trial were considered treatment failures; those patients were offered their original treatment of injections and monitored for the remainder of the trial. The primary endpoint of the study was 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. In May 2018, we reached further agreement with the FDA under a SPA Agreement Modification letter providing that the hierarchical secondary endpoints that will be considered by the FDA in evaluating the totality of evidence for octreotide capsules treatment effect are:

- Proportion of patients who maintain GH response at week 36 compared to screening;
- Time to loss of response: IGF-1 > 1.0×ULN;
- Time to loss of response: IGF-1 > 1.3×ULN; and
- Proportion of patients requiring rescue treatment.

CHIASMA OPTIMAL Phase 3 Clinical Trial Design



We initiated the CHIASMA OPTIMAL trial in September 2017 and activated more than 50 clinical sites dedicated to the CHIASMA OPTIMAL trial. In July 2019, we announced positive top-line results from the CHIASMA OPTIMAL trial. In the trial:

- The primary endpoint was met: 58% of the patients on octreotide capsules maintained their IGF-1 response compared to 19% of the patients on placebo (p = 0.008). P-value is a conventional statistical method for measuring the statistical significance of clinical results. A p-value of 0.05 or less is generally considered to represent statistical significance, meaning that there is a less than 1-in-20 likelihood that the observed results occurred by chance.
- All secondary endpoints were met.
  - 78% of patients treated with octreotide capsules maintained their GH levels below 2.5 ng/mL at the end of the core study compared to 30% of patients treated with placebo (p = 0.001).
  - Median time to loss of response (IGF-1 >1.0 × ULN) was not reached (>36 weeks) for patients treated with octreotide capsules compared to 16 weeks for patients treated with placebo (p <0.001).
  - Median time to loss of response (IGF-1 ³ 1.3 × ULN) was not reached (>36 weeks) for patients treated with octreotide capsules compared to 16 weeks for patients treated with placebo (p <0.001).
  - 25% of patients treated with octreotide capsules required rescue medication with injectable somatostatin analogs (octreotide LAR or lanreotide depot) anytime throughout the study compared to 68% of patients treated with placebo (p = 0.003).

Additionally, 75% of patients on octreotide capsules completed the trial of which 90% elected to continue into the open label extension. However, the results of the extension phase are not required as the basis for an efficacy claim. In addition, in a pre-specified exploratory endpoint, mean IGF-1 values across all 28 patients treated with octreotide capsules (including primary endpoint non-responders per protocol), remained within normal limits with a 0.97 x ULN at the end of oral treatment versus 1.69 x ULN at the end of treatment for the patients on placebo.

In the CHIASMA OPTIMAL trial, octreotide capsules appeared safe and well tolerated in the trial patient population. No new or unexpected safety signals were observed. The overall number of treatment emergent adverse events, or TEAEs, was comparable between the octreotide capsules and placebo treatment groups, 64% versus 54%, respectively. Two patients on octreotide capsules and one patient on placebo discontinued treatment due to TEAEs. Two patients on octreotide capsules and one patient on placebo had serious adverse events, or SAEs, assessed as not related to study drug. Severe TEAEs as well as TEAEs of special interest (acromegaly symptoms) were more common in placebo treated patients than in patients treated with octreotide capsules. The following table summarizes the safety data observed in the CHIASMA OPTIMAL trial:

	Octreotide Capsules		Placebo	
Subjects with:	**n**	**%**	**n**	**%**
At least one TEAE	28	100.0	27	96.4
Treatment-Related TEAE	18	64.3	15	53.6
SAEs	2	7.1	1	3.6
Treatment-Related SAEs	0	0.0	0	0.0
Severe TEAEs	3	10.7	7	25.0
TEAE Leading to Study Drug Discontinuation	2	7.1	1	3.6
TEAEs of Special Interest (acromegaly symptoms)	15	53.6	26	92.9

Accepted New Drug Application for MYCAPSSA®

Based on the positive results from the CHIASMA OPTIMAL trial, in December 2019, we resubmitted our NDA seeking approval of MYCAPSSA capsules as a maintenance therapy for adult patients with acromegaly to the FDA. In January 2020, the FDA accepted for review the resubmission of the NDA as a complete response to deficiencies identified in the CRL to our original NDA and assigned an action date of June 26, 2020 under the PDUFA.

The CHIASMA OPTIMAL trial was conducted under SPA agreement with the FDA, which indicates that the FDA agreed that the design and planned analysis of the CHIASMA OPTIMAL trial results adequately address the objectives necessary to support a regulatory submission. However, a SPA is not a guarantee of regulatory approval. We anticipate that the FDA will review the totality of the data collected from the CHIASMA OPTIMAL trial, including the primary and all secondary endpoints, together with certain data from our other clinical trials of octreotide capsules, including but not limited to data related to the loss of biochemical response when switching from injectable somatostatin analogs to octreotide capsules, in evaluating our NDA. We continue to believe that the data from the CHIASMA OPTIMAL trial alone is designed to address the clinical concerns raised by the FDA in its CRL to our original NDA submission and also that, with respect to our ongoing Phase 3 MPOWERED clinical trial, the FDA only expects to review safety data from the MPOWERED trial as part of its review of our NDA resubmission. Any future requirement by the FDA to submit additional data, including the efficacy data from our MPOWERED clinical trial may delay or prevent the review or approval of our NDA. While we believe our NDA resubmission includes a compelling data package, there can be no assurance that the data collected from the CHIASMA OPTIMAL trial will be sufficient to support approval of our NDA.

European Regulatory Pathway

We also plan to seek regulatory approval of octreotide capsules for the treatment of acromegaly in the European Union utilizing the hybrid application pathway. In addition to the clinical data we previously submitted to the

FDA in 2015, the EMA has advised us that a clinical trial demonstrating non-inferiority of octreotide capsules compared to injectable somatostatin analogs as active controls will be required prior to regulatory approval by EMA. We also anticipate that the EMA will expect to review the safety and efficacy data from the CHIASMA OPTIMAL trial in any MAA we may file. Our MPOWERED Phase 3 clinical trial protocol has been accepted by the EMA and we initiated this trial in March 2016.

MPOWERED Phase 3 Clinical Trial

Comparative effectiveness is an important regulatory consideration in the European Union. After agreeing to the clinical trial protocol with the EMA, we initiated an international Phase 3 clinical trial of octreotide capsules in acromegaly in March 2016 to show parallel comparative safety and effectiveness.

This trial is called MPOWERED, **M**aintenance of Acromegaly **P**atients with **O**ctreotide Capsules Compared **W**ith Injections -**E**valuation of **RE**sponse **D**urability. This trial is an open-label, randomized, active-controlled study of octreotide capsules in patients who have been classified in the study as responders to a once-a-month injectable somatostatin analog based on criteria comparable to the criteria utilized in our first Phase 3 clinical trial. This trial is intended to demonstrate non-inferiority, comparing efficacy responses as between two randomized groups of patients who demonstrated response to octreotide capsules and was initially to enroll up to 150 patients. In July 2018, we completed the enrollment of 135 adult acromegaly patients into the run-in phase of the MPOWERED trial. The EMA requested that a minimum of at least 80 patients who are responders to octreotide capsules following the six-month run-in phase be randomized to either remain on octreotide capsules or return to injectable somatostatin receptor ligands (octreotide or lanreotide), and then followed for an additional nine months. In October 2018, 80 patients were randomized following the six-month run-in phase in the MPOWERED trial. Further, in October 2018, we elected to resume enrollment in the trial in an effort to enroll up to 15 additional patients exclusively located in the United States in order to gain further U.S. investigator and patient experience with octreotide capsules. In June 2019, we completed enrollment of 146 total patients in the trial in the United States, Europe, Russia and other foreign countries. Each patient initially receives a daily dose of 40 mg of octreotide capsules, which is increased up to a maximum of 80 mg daily dose if lower doses are not effective. Similar to the requirements of our first completed Phase 3 clinical trial and the CHIASMA OPTIMAL trial, patients are required to take octreotide capsules at least one hour prior to a meal or two hours after a meal.

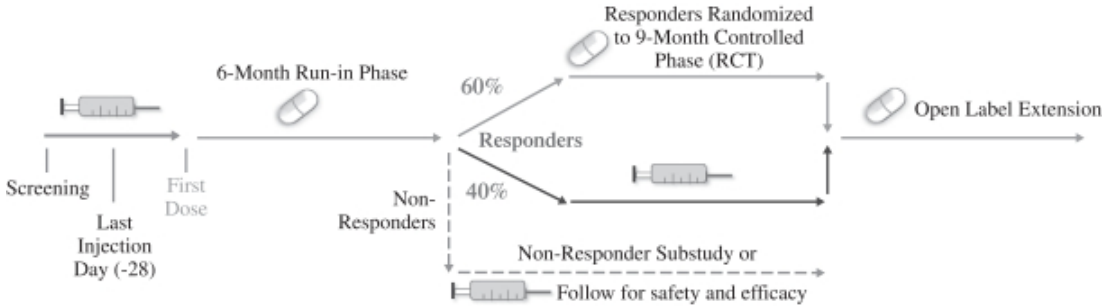
The primary efficacy endpoint for this trial is the proportion of patients who are biochemically controlled throughout the nine-month randomized-controlled phase measuring IGF-1 with responders defined as patients who achieve an IGF-1 level less than 1.3 times the ULN adjusted for age, the same IGF-1 efficacy criteria utilized in our first, completed Phase 3 clinical trial. Measurements of IGF-1 will be taken throughout the randomized phase of the trial and a time weighted average of these biochemical measures will be calculated. In addition, assessment of symptom control and patient reported outcomes are expected to be reported. The primary endpoint of the MPOWERED trial is the proportion of patients who are biochemically controlled throughout the randomized, controlled phase of the study, defined as a time weighted average of IGF-I < 1.3 ULN. In addition to measures of biochemical control, the MPOWERED trial is expected to provide data on the impact of treatment on acromegaly symptoms and patients' quality of life through multiple validated instruments. Secondary and exploratory endpoints are designed to explore overall health assessments and whether more patients experience maintenance or improvement of acromegaly symptoms between treatments, both individually and as an overall composite score. The trial is also designed to generate data on when patients experience their acromegaly symptoms and any interference with work productivity and the ability to perform regular activities of daily living. The impact of octreotide capsules versus injectable treatment is also expected to be measured from a standpoint of gastrointestinal adverse events and the burden of receiving injections in a healthcare setting versus the fasting requirements of MYCAPSSA capsules.

In January 2020, the randomization of patients was completed. Of the 146 patients that entered the six-month run-in phase of the trial, 92 of these patients (or 63%) completed the run-in phase and were deemed to be responders to octreotide capsules per protocol (IGF-1 <1.3 x ULN and GH<2.5 ng/mL). Responders to octreotide

capsules were randomized (2:3) per protocol to either go back to their original long-acting injectable somatostatin analog or remain on octreotide capsules at the appropriate dose identified during the run-in phase and then followed for an additional nine months. After completing the randomized controlled phase, patients are offered the opportunity to participate in a withdrawal phase sub-study to assess evidence of active disease and the requirement for long term treatment. We expect that all eligible patients will have the option of entering an extension phase during which period these patients would receive octreotide capsules at the dose identified during the run-in phase.

Patients who did not respond during the run-in phase did not enter the randomized phase but were switched back to long-acting injectable somatostatin analog and followed for an additional three months or, in selected centers, were offered the opportunity to determine if they can respond to a combination of octreotide capsules with a second oral agent called cabergoline. Cabergoline is used for the treatment of mild acromegaly. It has a different mechanism of action and publications have suggested it may have an additive effect to somatostatin analogs. This sub-study, which the EMA did not accept as part of the final protocol for comparative effectiveness, is unlikely to be sufficient to gain regulatory approval for the combination of both drugs but may provide useful information to physicians.

MPOWERED Phase 3 Design to Support EMA Application



In late 2016, the FDA advised us that the MPOWERED clinical trial will not be sufficient to address the concerns identified by the FDA in the CRL. Consequently, we modified certain elements of the MPOWERED study in an effort to preserve patients, sites and other resources necessary to conduct the CHIASMA OPTIMAL trial, which was designed to address the FDA's concerns, and produce data packages that could be suitable for submission in both the United States and the European Union. We completed enrollment in the MPOWERED trial in June 2019 and expect to release top-line data from the trial in the fourth quarter of 2020. Subject to FDA approval of our NDA resubmission, if obtained, and assuming positive data from the MPOWERED trial, we expect to submit our MAA to the EMA in the first half of 2021 seeking marketing approval of MYCAPSSA as a maintenance therapy for adult patients with acromegaly in the European Union.

First Completed Phase 3 Clinical Trial

In March 2012, we initiated a Phase 3 multi-center, open-label, baseline-controlled clinical trial to evaluate the safety and efficacy of octreotide capsules in patients with acromegaly who responded to and tolerated treatment with somatostatin analogs. We completed this trial in November 2014 and the results were published in the *Journal of Clinical Endocrinology & Metabolism* in February 2015 and presented at the Endocrine Society's Annual Meeting in March 2015. In addition, the results were submitted with our original NDA for octreotide capsules in June 2015. In the CRL to our NDA, the FDA expressed concerns regarding certain aspects of the company's 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 the minutes from our End of Review Meeting, the FDA indicated that some of its concerns could potentially be addressed through a placebo-controlled study design, which we have sought to address with the CHIASMA OPTIMAL trial.

Trial Design

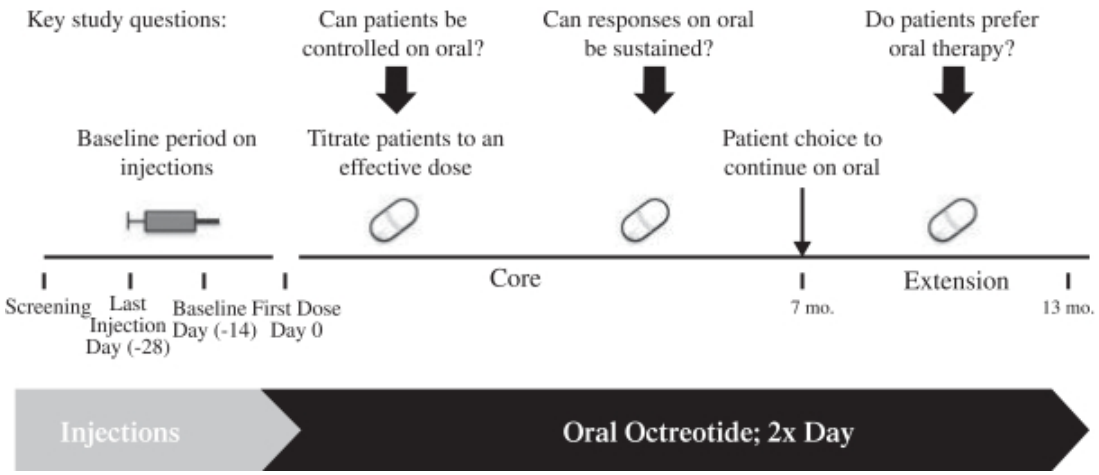
A total of 155 patients with acromegaly, each of whom was classified according to the study parameters as a responder to a long-acting injectable somatostatin analog, were enrolled in the trial. Two weeks after their last monthly injection of the long-acting injectable somatostatin analog, patients were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

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

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

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

Completed Phase 3 Clinical Trial Design



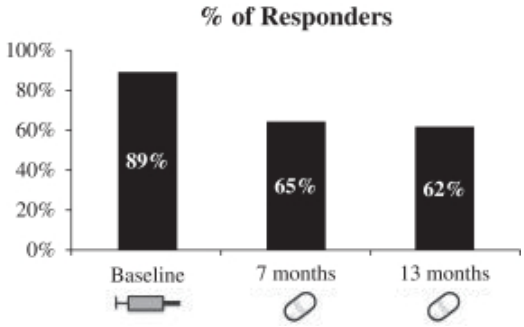
Trial Results

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

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

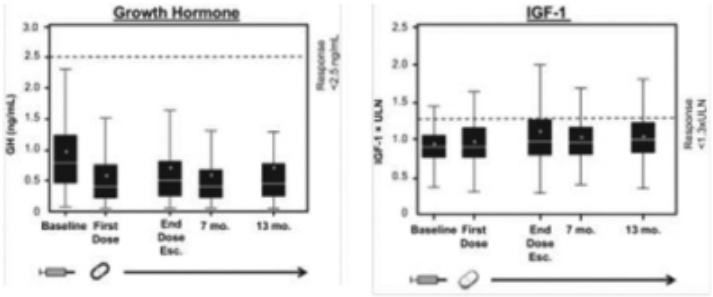
Applying a last-observation carried forward, or LOCF, methodology, 65% of patients in the mITT group were classified as responders at the end of the seven-month core treatment phase, which was the primary endpoint for the trial. Applying a worst-case imputation method, whereby all patients who withdrew from the study prematurely (regardless of reason) are treated as non-responders, 53% of patients were classified as responders at the end of the seven-month core treatment phase. By the end of the six-month extension phase, or 13 months after first dosing, utilizing LOCF the responder rate was 62% in the mITT group. Of the 110 patients who completed the dose-escalation phase, and therefore received an optimized dose of octreotide capsules, 75% were classified as responders. For all 151 patients included in the mITT group, the responder rate on long-acting injectable somatostatin analogs was 89% at baseline, prior to initiation of octreotide capsules. Endocrinologists indicated to us that effectiveness in at least 50% of patients treated would be sufficient for an oral treatment to generally be prescribed by physicians.

Overall Phase 3 Response in mITT Group vs. Baseline



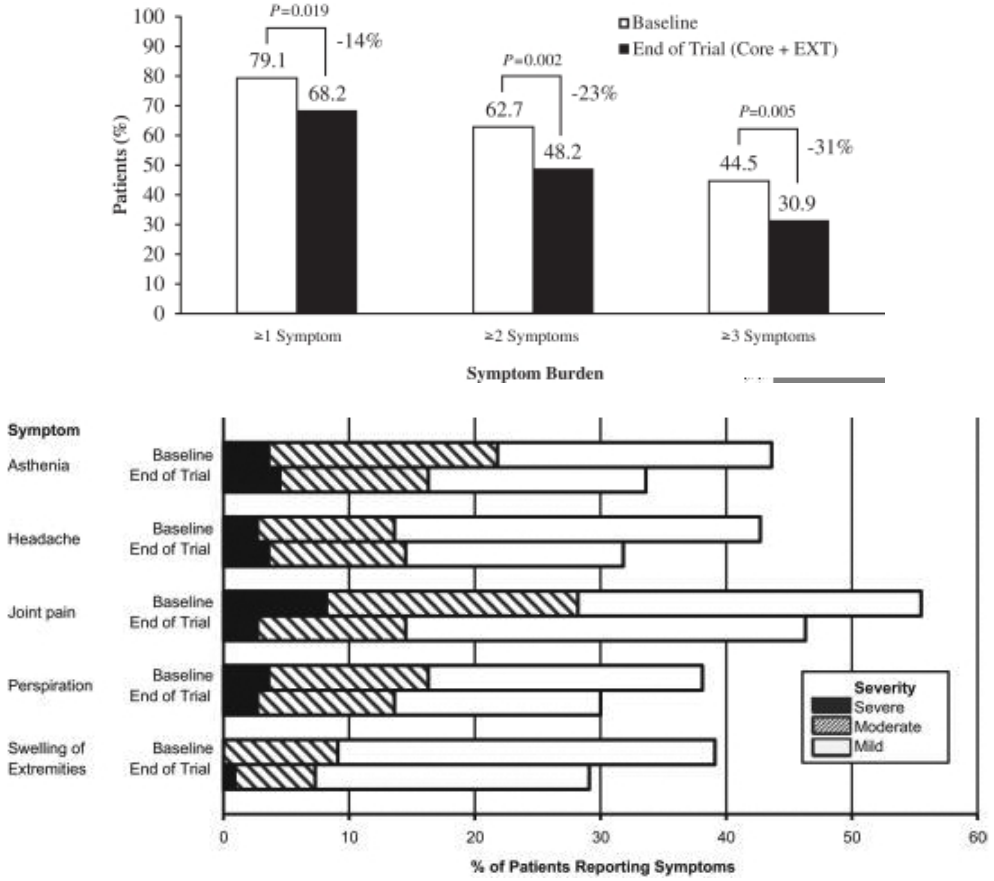
We further assessed the quality of the responses to octreotide capsules in the patients studied. The quality of the patient responses on octreotide capsules was comparable to the quality of the responses on injectable therapies. In the mITT group, mean GH levels for patients on octreotide capsules were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

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



We also assessed control of acromegaly symptoms, the incidence of symptoms, and the severity and number of symptoms in patients using octreotide capsules in a retrospective analysis performed after completion of the trial. At baseline, 81% of patients in the mITT group, the majority of whom were classified as responders, still had acromegaly symptoms, such as headaches, excessive perspiration, muscle weakness and/or joint pain and swelling. Patients who completed 13 months of treatment reported significantly fewer acromegaly symptoms at the conclusion of the trial than at the time of their baseline screening, and this result was statistically significant, with p-values of less than 0.020. There was also a reduction in the severity of symptoms reported. In addition, a questionnaire conducted in a subset of the patients in the clinical trial reported that breakthrough symptoms of acromegaly were experienced by 36% of patients receiving injections at baseline compared to 22% at 13 months on octreotide capsules.

Reduced Number of Acromegaly Symptoms at Conclusion of Phase 3 Trial
(Fixed Dose Population (n = 110))



The safety profile of octreotide capsules in the trial was consistent with the known safety profile of octreotide and the disease burden of acromegaly, with the most common adverse events observed in the gastrointestinal system, such as nausea and diarrhea, the nervous system, such as headaches, and the musculoskeletal system, such as joint pain, but without adverse injection-site reactions. No new or unexpected safety signals were observed in the study. While the FDA did not note any safety concerns related to octreotide capsules in the CRL, it subsequently indicated in the End of Review meeting minutes that the size, duration, dropout rate and absence of a control group in this Phase 3 clinical trial were factors limiting an overall safety assessment.

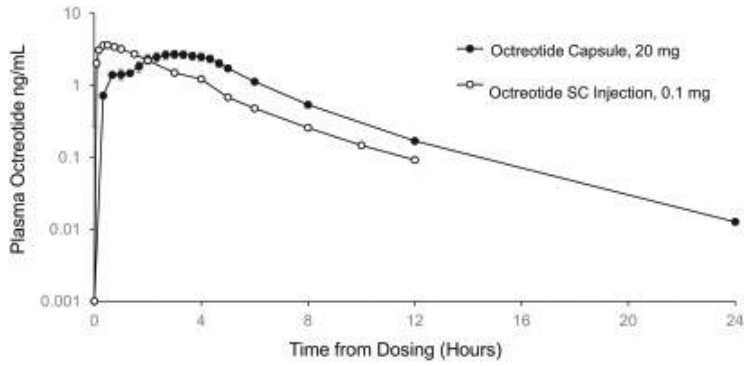
We only performed statistical analysis on the symptom reductions for this Phase 3 trial of octreotide capsules in acromegaly and did not perform statistical analysis related to the biochemistry, specifically the reduction in GH and IGF-1 levels.

Completed Phase 1 Clinical Trials of Octreotide Capsules

Together with a group of academic collaborators, we conducted a series of Phase 1 clinical trials to demonstrate that the bioavailability of octreotide capsules, developed utilizing our TPE technology, is comparable to the bioavailability of octreotide administered in the short-acting subcutaneous, or sc, formulation. These trials

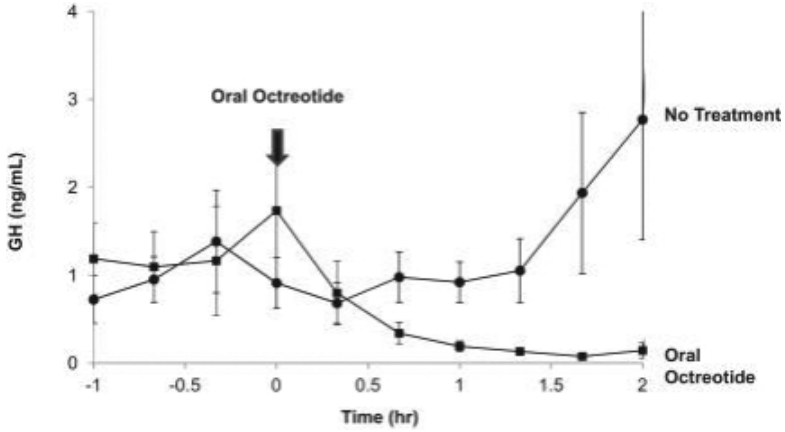
demonstrated similar pharmacokinetics for octreotide capsules and octreotide 0.1 mg sc injection and that a 20 mg oral dose of octreotide capsules produced systemic exposure comparable to octreotide 0.1 mg sc injection in healthy volunteers. There was no effect of route of administration on octreotide elimination, and the mean elimination half-life (t1/2) was comparable with the two treatments. However, these studies also demonstrated that the bioavailability of octreotide capsules is approximately 90% lower when it is taken with a high-fat meal rather than in the fasted state. Accordingly, our CHIASMA OPTIMAL and MPOWERED clinical trials require patients to take octreotide capsules at least one hour prior to a meal or two hours after a meal.

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



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

Suppression of GH Levels in Healthy Volunteers



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

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

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

Other Potential Indications for Octreotide Capsules

If we receive regulatory approval for octreotide capsules in acromegaly, we plan to pursue the development of octreotide capsules in at least one other indication. At this time, we do not currently have the personnel or financing to simultaneously pursue the development of octreotide capsules in indications other than acromegaly.

Our Proprietary Transient Permeability Enhancer Technology Platform

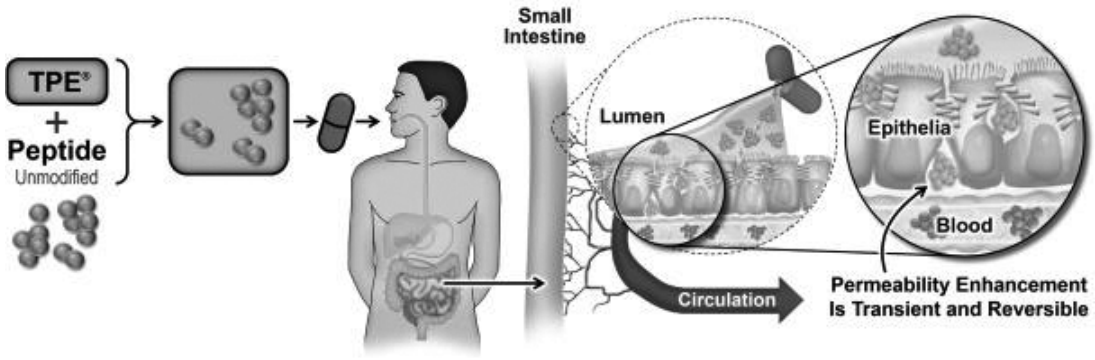
Our Transient Permeability Enhancer, or TPE®, technology is a proprietary platform, developed internally by us, that enhances the absorption through the intestinal wall of drugs that otherwise would not be absorbed efficiently by that route. Using our TPE technology, we can transiently and reversibly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

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

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

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

Our TPE Platform



Although not sufficiently staffed or financed to do so, if octreotide capsules are approved in acromegaly, we may seek to use our TPE platform to develop other oral medications to help improve the lives of patients suffering from other debilitating diseases that are currently being treated with injectable therapies. If we pursue new peptide-based drugs to develop using our TPE platform, to potentially reduce the development time and expenses and overall level of investment required, where possible, we may focus our efforts on drugs for which we may utilize the FDA's 505(b)(2) regulatory pathway in the United States and the hybrid application pathway in the European Union. In March 2017, the Tufts Center for the Study of Drug Development reported that the FDA's 505(b)(2) regulatory pathway for new drug applications in the United States has not led to shorter approval times. With octreotide capsules, we brought a TPE-based product candidate from concept to the first clinical trial within 18 months and then initiated our first Phase 3 clinical trial approximately two years later.

Prior License Agreement with Roche

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

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

Commercialization Strategy

We retain worldwide rights to develop and commercialize octreotide capsules with no royalty obligations to third parties. If approved, we expect to commercialize octreotide capsules ourselves in the United States employing a strategy that differentiates our product and is tailored to the needs of patients and their physicians. We believe

that approximately 8,000 adult acromegaly patients are chronically treated with somatostatin analogs in the United States, and that approximately 90% of these patients are managed by fewer than 1,000 patient care centers. Patients with acromegaly undergoing treatment in the United States are generally treated by endocrinologists at a small number of academic institutions with pituitary experts (pituitary centers), regional academic centers or hospital systems (regional referral centers) and some community endocrinologists. Accordingly, we believe that the U.S. market for MYCAPSSA capsules is addressable with a small orphan drug customer facing team ranging between 30 to 50 employees that includes case managers, sales representatives, nurse educators, and account managers. During 2019 and early 2020, in preparation for a potential commercial launch of MYCAPSSA capsules in the United States during the fourth quarter of 2020, pending the approval by the FDA of our NDA and either of the planned prior approval manufacturing supplements, we began implementing commercial launch readiness plans, including (i) expanding our organization with new key employees with expertise in marketing, sales, market access, patient services and product reimbursement and distribution in particular for rare diseases and (ii) developing our commercial capabilities, including commencing the establishment of internal systems and infrastructure to support a commercial sales organization and patient-focused programs and appropriate quality systems and compliance policies and procedures. In anticipation of receiving marketing approval from the FDA, we are building a focused in-house sales and marketing organization to identify pituitary specialists and community endocrinologists who comprise the top prescribers of therapies for acromegaly and are preparing to market octreotide capsules to these physicians.

Prior to the receipt of the CRL, we conducted market research with endocrinologists, nurses and patients with acromegaly and other pre-commercial activities in the United States to better understand satisfaction levels and key unmet needs with respect to current treatments for acromegaly and to build awareness of octreotide capsules. In surveys commissioned by us, more than 80% of patients with acromegaly expressed a preference for an oral treatment, and endocrinologists surveyed predicted that an oral treatment would ultimately become the preferred treatment option. Endocrinologists indicated that effectiveness in at least 50% of patients treated would be sufficient for an oral treatment to generally be prescribed by physicians. To assess the attitudes of commercial third-party payors toward reimbursement for octreotide capsules, in 2019 and 2020 we conducted two separate research projects with payers and pharmacy benefit managers, or PBMs to determine likely coverage and access for octreotide capsules. The project results indicated that oral octreotide would be covered similarly to injectable somatostatin analog products assuming pricing and any contracting was in a range comparable to existing therapies. Additional U.S. payor and pricing research, among other considerations, may be conducted to inform our pricing and commercialization strategy if our NDA for octreotide capsules in acromegaly is approved.

We believe that the potential clinical benefits of oral octreotide capsules and preferences of patients and healthcare professionals for an oral therapy together with our planned patient-centric approach could enable octreotide capsules, if approved, to change the standard of pharmacological care in the management of patients with acromegaly.

Subject to FDA approval of our NDA resubmission and assuming positive data in our ongoing Phase 3 MPOWERED clinical trial, we plan to submit an MAA to the EMA in the first half of 2021 seeking authorization to commercialize octreotide capsules in the European Union as a maintenance therapy for adult patients with acromegaly. We plan to explore the strategic merits of collaboration opportunities for commercializing octreotide capsules in the European Union and the rest of the world in order to maximize the availability of the product candidate, if approved, to patients. However, depending on our evaluation of the strategic merits of these collaboration opportunities, we may decide to retain commercial rights in key markets.

Manufacturing

We depend on third-party suppliers and contract manufacturing organizations, or CMOs, for all of our required raw materials and drug substance and to manufacture and package drug product for clinical use and commercial use, if approved. We have qualified Novetide Ltd., a subsidiary of Teva API Pharmaceuticals Industries (TAPI) Ltd., in Israel, and Bachem Americas Inc., in the United States, as suppliers of the generic active pharmaceutical ingredient, or API, octreotide acetate.

In order to have oral octreotide capsules available to support our planned commercial launch in the fourth quarter of 2020, we expect to submit for FDA review two prior approval manufacturing supplements to our NDA for our commercial sources of generic active pharmaceutical ingredient, or API, octreotide acetate. During 2020, we expect to have a total of three manufacturing sites qualified for commercial supply of API located in the United States, Israel and Switzerland.

The first manufacturing site, and the only one currently referenced in our NDA resubmission, is a small-scale manufacturing site of our secondary commercial API manufacturer. This site was also included in our original NDA. We do not currently plan to procure commercial API from this small-scale manufacturing site.

The second and third API manufacturing sites are larger-scale manufacturing sites that we plan to use to produce commercial supply of octreotide capsules. One of these sites is a new site affiliated with the small-scale manufacturing site currently referenced in the NDA resubmission, and the other site belongs to our primary commercial API manufacturer and was included in our original NDA. We did not reference these two larger-scale manufacturing sites in our recent NDA resubmission. At the time of our NDA resubmission, our primary commercial API manufacturer was in the process of resolving outstanding observations from a recent regulatory inspection of its site. To allow for further time to resolve the observations, we decided not to reference this site in our NDA resubmission. The inspection was closed by the regulator in February 2020. In addition, we did not reference the other larger-scale manufacturing site in our NDA resubmission because that allowed us to seek and obtain the FDA's designation of our NDA resubmission as a Class 2 resubmission. The benefit of a Class 2 designation is a six-month review cycle and, accordingly, the FDA assigned a June 26, 2020 PDUFA target date, which is a six-month review.

If we obtain marketing approval of octreotide capsules from the FDA, we expect to submit to the FDA a prior approval manufacturing supplement for each of these two larger-scale manufacturing sites to reference them in our NDA. In anticipation of FDA approval of our NDA resubmission, we are currently procuring API from these two larger-scale manufacturing sites. Subject to FDA's timely approvals of the NDA and either of the two planned prior approval manufacturing supplements, we expect to have oral octreotide capsules available to support our planned commercial launch in the fourth quarter of 2020.

In addition to these three manufacturing sites, we expect our primary commercial API manufacturer to scale-up and qualify a separate larger manufacturing site to meet our longer-term commercial requirements of octreotide acetate.

All excipients, or substances formulated together with the API, used in manufacture of octreotide capsules are obtained by our CMOs from third-party suppliers. The octreotide API is formulated with our TPE technology by Lyophilization Services of New England Inc. and filled into capsules, enteric-coated and blister packed by Capsugel, a division of Lonza, in Scotland. Almac Pharma Services Limited in Northern Ireland provides finished packaging and release services. All manufacturers periodically undergo inspections by regulatory authorities.

Octreotide capsules are intended to be refrigerated and our NDA includes stability information supporting 36 months under these storage conditions. We have also obtained data regarding additional one-month storage at room temperature. The FDA has previously indicated that the testing parameters for our control strategy and product release and stability specifications are acceptable. The manufacturing process for the API has been validated at both of our API manufacturers and octreotide capsules manufactured at our CMOs as well as final product packaging has also been validated. In the 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. In December 2016, we were informed that the supplier had recently received its EIR from the FDA. The receipt of the EIR is an indication 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 our NDA resubmission seeking approval of octreotide capsules in acromegaly or the prior approval manufacturing

supplements to the NDA that we expect to submit following the expected June 26, 2020 PDUFA date, if our NDA is approved.

If we obtain marketing approval for MYCAPSSA capsules from the FDA, we plan to establish a distribution channel in the United States utilizing third-party logistics and one or more specialty pharmacies to distribute product directly to patients who have been prescribed octreotide capsules.

Competition

Our industry is highly competitive and subject to rapid and significant technological change as researchers learn more about diseases and develop new technologies and treatments. Our potential competitors include primarily large pharmaceutical, biotechnology companies and specialty pharmaceutical companies. Key competitive factors affecting the commercial success of octreotide capsules, if approved, 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.

The standards of care for patients suffering from acromegaly all involve injectable therapies, other than cabergoline, an oral agent used for the treatment of mild acromegaly. Novartis markets octreotide LAR, which is administered monthly and intramuscularly using a large gauge needle. Ipsen markets lanreotide, another long-acting analog of somatostatin, like octreotide, which is administered monthly using a deep subcutaneous injection. Both therapies, which are most frequently the first drug treatment options for patients, involve side effects related to the injections and inconvenience due to the timing and requirements of the injections. Pfizer markets pegvisomant daily injections and Recordati markets pasireotide LAR, which is another somatostatin analog administered via intramuscular injection. Pegvisomant daily injections and pasireotide LAR are significantly more costly than injectable octreotide and lanreotide. The label for pasireotide LAR includes a warning about hyperglycemia and diabetes, which can sometimes be severe. The label advises healthcare professionals administering pasireotide LAR to monitor glucose levels periodically during therapy and to monitor glucose levels more frequently in the months that follow initiation or discontinuation of therapy and following dose adjustment. Generic versions of these drugs may also bring additional competition to the treatment landscape. For example, while octreotide LAR and lanreotide currently have no generic competitors in the United States, generic versions are available in some markets in the EU. In addition, we are aware of other companies involved in early-stage nonclinical and clinical studies of similar somatostatin analogs, but most involve administration via injection. Most notably, Camurus AB is developing CAM2029, a subcutaneous octreotide depot for the potential treatment of neuroendocrine tumors and acromegaly. Camurus AB received FDA approval of its IND in June 2019 to initiate a Phase 3 acromegaly trial. MidaTech Pharma PLC also conducted its first in human study and also recently initiated a Phase 1 study of Q-Octreotide (MTD201), Midatech's injectable treatment for acromegaly built on its Q-Sphera sustained release platform technology. In 2019, Crinetics Pharmaceuticals, Inc. announced the initiation of two Phase 2 clinical trials to evaluate the safety and efficacy of CRN00808 in acromegaly patients. CRN00808 is a nonpeptide somatostatin agonist designed to be taken orally once per day. In May 2017, Dauntless Pharmaceuticals, Inc., a privately held biopharmaceutical company, announced positive results from its two-part, Phase 1 pharmacokinetic/pharmacodynamic study evaluating DP1038, a novel formulation of octreotide acetate for intranasal administration. In 2018, Ionis Pharmaceuticals initiated a Phase 2 trial of IONIS-GHR-L_{Rx}, its growth hormone receptor antagonist to control growth hormone production in acromegaly patients. In January 2020, Rani Therapeutics (RaniPill™ capsule containing octreotide) announced the completion of a Phase 1 study in 58 healthy volunteers, indicating that the RaniPill performed as designed. Per published reports, Rani Therapeutics plans to conduct a head-to-head study in acromegaly patients and demonstrate equivalence or non-inferiority to the injectable version of octreotide sc. We are also aware that Strongbridge Biopharm (valdoreotide, or COR-005) may also be actively developing products for the maintenance treatment of acromegaly. If any or a combination of the other product candidates in development for acromegaly receive regulatory approval in a similar timeframe as, our octreotide capsules, or demonstrate superior clinical results to octreotide capsules, we may encounter significant difficulties with our commercial launch of octreotide capsules, if approved.

Many of our existing or potential competitors have substantially greater financial, technical and human resources than we do and significantly greater experience in the discovery and development of product candidates, obtaining FDA and other regulatory approvals of products and the commercialization of those products. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a small number of our competitors. Accordingly, our competitors may be more successful than we may be in obtaining FDA approval of drugs and achieving widespread market acceptance. Our competitors' drugs, or drugs they may develop in the future, may be more effective, or more effectively marketed and sold, than any drug we may commercialize and may render 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. 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, will be adversely affected.

Intellectual Property

We strive to protect the proprietary technology that we believe is important to our business, including seeking and maintaining patents intended to cover our product candidates and compositions, their methods of use and processes for their manufacture, and any other aspects of inventions that are commercially important to the development of our business. We also rely on trade secrets to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection.

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

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

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

Patents

As of March 9, 2020, our patent portfolio includes a total of eight utility patents issued in the United States; patents issued in foreign jurisdictions; patent applications pending in the United States; and patent applications

pending in various foreign jurisdictions. Some of these patents and patent applications include narrow and broad claims directed to polypeptide compositions including octreotide compositions formulated with our TPE technology; capsules containing such compositions; methods of treatment using such compositions; and methods of making various compositions with our TPE technology. This patent family includes three issued U.S. patents with claims directed to enteric-coated oral dosage form comprising octreotide compositions, capsules containing octreotide compositions, and methods of treating various conditions with related octreotide compositions. Other patents in this family have issued in Australia, Canada, China, Europe, Hong Kong, Israel, Japan, Korea, Mexico, New Zealand, Russia, South Africa, and the United Kingdom, and patent applications are pending in other jurisdictions, including Brazil, Canada, China, Europe, Israel and Korea, Mexico, Russia, Australia, and Japan. Patents in this family are expected to expire in 2029, absent any adjustments or extensions. This patent family includes an issued U.S. patent with claims relating to enteric-coated oral dosage form comprising polypeptide compositions.

We also own a family of patent applications directed to a dosage regimen for octreotide and also directed to methods of treating acromegaly with certain octreotide-containing compositions and dosage regimens, which has entered the National Phase of the Patent Cooperation Treaty, or PCT. This patent family includes an issued U.S. patent directed to specific methods of using octreotide capsules and is due to expire in 2036, absent any adjustments or extensions. There are corresponding pending applications in the United States and abroad all of which are expected to expire in 2036, absent any adjustments or extensions.

We also own a family of patent applications directed to oral octreotide combinations, which has entered the National Phase of the PCT. Patents issuing from any U.S. nonprovisional and foreign-filed applications claiming priority to this PCT application are expected to expire in 2035, absent any adjustments or extensions.

Additionally, we own two U.S. utility patents directed to proprietary packaging for distribution of octreotide capsules which are expected to expire in 2035, absent any adjustments or extensions. We also own two U.S. design patents, which have been granted in several other jurisdictions and are expected to expire in the U.S. in 2030 and 2033, absent any adjustments or extensions, and we have a pending US design patent application.

Finally, we own two families of patents application directed to further uses of our TPE technology which have entered the National Phase of the PCT. Patents issuing from any U.S. nonprovisional and foreign-filed applications claiming priority to this PCT application are expected to expire in 2037, absent any adjustments or extensions.

Patent Term

The base term of a U.S. utility patent is 20 years from the filing date of the earliest-filed non-provisional patent application from which the patent claims priority. The base term of a U.S. design patent is 14 years from issuance for designs filed before the Patent Law Treaties Implementation Act of 2012 which took effect on May 13, 2015 and 15 years from issuance for designs filed after May 13, 2015. The term of a U.S. patent can be lengthened by patent term adjustment, which compensates the owner of the patent for administrative delays at the USPTO. In some cases, the term of a U.S. patent is shortened by terminal disclaimer that reduces its term to that of an earlier-expiring patent.

Government Regulation

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

United States Drug Development

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

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

- completion of extensive nonclinical, or preclinical, laboratory tests, animal studies and formulation studies in accordance with applicable regulations, including the FDA's Good Laboratory Practice, or GLP, regulations;
- submission to the FDA of an IND, which must become effective before human clinical trials may begin;
- performance of adequate and well-controlled human clinical trials in accordance with applicable IND and other clinical study related regulations, sometimes referred to as good clinical practices, or GCPs, to establish the safety and efficacy of the proposed drug for its proposed indication;
- submission to the FDA of an NDA;
- a determination by the FDA within 60 days of its receipt of an NDA to file the NDA for review;
- satisfactory completion of an FDA pre-approval inspection of the manufacturing facility or facilities where the drug is produced to assess compliance with the FDA's current good manufacturing practice, or cGMP, requirements to assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity;
- potential FDA audit of the clinical trial sites that generated the data or the contract research organization that aggregated the data in support of the NDA; and
- FDA review and approval of the NDA prior to any commercial marketing or sale of the drug in the United States.

The data required to support an NDA are generated in two distinct development stages: nonclinical and clinical. For new chemical entities, the nonclinical development stage generally involves synthesizing the active component, developing the formulation and determining the manufacturing process, as well as carrying out non-human toxicology, pharmacology and drug metabolism studies in the laboratory, which support subsequent clinical testing. The conduct of the nonclinical tests must comply with federal regulations and requirements including GLPs. The sponsor must submit the results of the nonclinical tests, together with manufacturing information, analytical data, any available clinical data or published literature and a proposed clinical protocol, to the FDA as part of the IND. An IND is a request for authorization from the FDA to administer an investigational drug product to humans. The central focus of an IND submission is on the general investigational plan and the protocol(s) for human studies. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA raises concerns or questions regarding the proposed clinical trials and places the IND on clinical hold within that 30-day time period. In such a case, the IND sponsor and the FDA must resolve any outstanding

concerns before the clinical trial can begin. The FDA may also impose clinical holds on a drug candidate at any time before or during clinical trials due to safety concerns or non-compliance. Accordingly, we cannot be sure that submission of an IND will result in the FDA allowing clinical trials to begin, or that, once begun, issues will not arise that could cause the trial to be suspended or terminated.

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

Clinical trials are generally conducted in three sequential phases, known as Phase 1, Phase 2 and Phase 3 clinical trials, and may overlap. Phase 1 generally involves a small number of healthy volunteers who are initially exposed to a single dose and then multiple doses of the product candidate. The primary purpose of these studies is to assess the metabolism, pharmacological action, side effect tolerability and safety of the drug. Phase 2 trials typically involve studies in disease-affected patients to determine the dose required to produce the desired benefits. At the same time, safety and further pharmacokinetic and pharmacodynamic information is collected, as well as identification of possible adverse effects and safety risks and preliminary evaluation of efficacy. Phase 3 trials generally involve large numbers of patients at multiple sites and are designed to provide the data necessary to demonstrate the effectiveness of the product for its intended use, its safety in use, and to establish the overall benefit/risk relationship of the product and provide an adequate basis for product approval. Phase 3 trials may include comparisons with placebo and/or other comparator treatments. The duration of treatment is often extended to mimic the actual use of a product during marketing. Generally, two adequate and well-controlled Phase 3 clinical trials are required by the FDA for approval of an NDA.

Post-approval trials, sometimes referred to as Phase 4 clinical trials, may be conducted after initial marketing approval. These studies are used to gain additional experience from the treatment of patients in the intended therapeutic indication. In certain instances, FDA may mandate the performance of Phase 4 trials.

Progress reports detailing the results of the clinical trials, among other information, must be submitted at least annually to the FDA. Within 15 calendar days after the sponsor determines that the information qualifies for reporting, written IND safety reports must be submitted to the FDA and the investigators for serious and unexpected adverse events, findings from other studies or animal or *in vitro* testing that suggest a significant risk to humans exposed to the drug and any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. The sponsor also must notify the FDA of any unexpected fatal or life-threatening suspected adverse reaction within seven calendar days after the sponsor's initial receipt of the information. Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, if at all. The FDA or the clinical trial sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients. Additionally, some clinical trials are overseen by an independent group of qualified experts organized by the clinical trial sponsor, known as a data safety monitoring

board or committee. This group provides authorization for whether or not a trial may move forward at designated check points based on access to certain data from the study. The clinical trial sponsor may also suspend or terminate a clinical trial based on evolving business objectives and/or competitive climate.

Concurrent with clinical trials, companies usually complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the drug as well as finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the drug candidate and, among other things, must develop methods for testing the identity, strength, quality and purity of the final drug product. Additionally, appropriate packaging must be selected and tested, and stability studies must be conducted to demonstrate that the drug candidate does not undergo unacceptable deterioration over its shelf life.

A manufacturer of an investigational drug for a serious disease or condition is required to make available, such as by posting on its website, its policy on evaluating and responding to requests for individual patient access to such investigational drug. This requirement applies on the earlier of the first initiation of a Phase 2 or Phase 3 trial of the investigational drug or, as applicable, 15 days after the drug receives a designation as a breakthrough therapy, fast track product, or regenerative advanced therapy.

NDA and FDA Review Process

Following trial completion, trial data are analyzed to assess safety and efficacy. The results of nonclinical studies and clinical trials are then submitted to the FDA in an NDA along with proposed labeling for the product and information about the manufacturing process and facilities that will be used to ensure product quality, results of analytical testing conducted on the chemistry of the drug, and other relevant information. The NDA is a request for approval to market the drug and must contain proof of safety and efficacy, which is demonstrated by extensive nonclinical and clinical testing. The application includes both negative or ambiguous results of nonclinical studies and clinical trials as well as positive findings. Data may come from company-sponsored clinical trials intended to test the safety and effectiveness of a use of a product, or from a number of alternative sources, including studies initiated by investigators. To support marketing approval, the data submitted must be sufficient in quality and quantity to establish the safety and effectiveness of the investigational drug product to the satisfaction of the FDA. The submission of an NDA is subject to the payment of substantial user fees; a waiver of such fees may be obtained under certain limited circumstances. FDA approval of an NDA must be obtained before marketing a drug in the United States.

In addition, under the Pediatric Research Equity Act, or PREA, as amended, an NDA or supplement to an NDA must contain data to assess the safety and effectiveness of the drug for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA may grant deferrals for submission of data or full or partial waivers. An NDA applicant must submit to the FDA a pediatric study plan typically 60 days after an end-of-Phase 2 meeting with the FDA. Because octreotide capsules received orphan drug designation for the treatment of acromegaly, we do not need to comply with the requirements of PREA at this time. If, however, we seek other indications for octreotide capsules or pursue approval of any other product candidate that does not have orphan drug designation, we may need to comply with PREA or otherwise seek a waiver.

The FDA reviews all NDAs submitted before it accepts them for filing and may request additional information rather than accepting an NDA for filing. The FDA must make a decision on accepting an NDA for filing within 60 days of receipt and within 30 days of receipt for an NDA resubmission. Once the submission is accepted for filing, the FDA begins an in-depth review of the NDA. The decision to accept the NDA for filing means that the FDA has made a threshold determination that the application is sufficiently complete to permit a substantive review. Under the goals and policies agreed to by the FDA under the PDUFA, the FDA has ten months from the receipt of an NDA for a non-new molecular entity in which to complete its initial review of a standard NDA and respond to the applicant, and six months from the receipt of an NDA resubmission in response to a CRL where

new clinical data is required. The FDA does not always meet its PDUFA goal dates for standard NDAs or NDA resubmissions, and the review process is often significantly extended by FDA requests for additional information or clarification.

After the NDA submission is accepted for filing (or an NDA resubmission is accepted as a complete response), the FDA reviews the NDA to determine, among other things, whether the proposed product is safe and effective for its intended use, and whether the product is being manufactured in accordance with cGMPs to assure and preserve the product's identity, strength, quality and purity. The FDA may refer applications for novel drug products or drug products which present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions. The FDA will likely re-analyze the clinical trial data, which could result in extensive discussions between the FDA and us during the review process. The review and evaluation of an NDA by the FDA is extensive and time consuming and may take longer than originally planned to complete, and we may not receive a timely approval, if at all.

Before approving an NDA, the FDA will conduct a pre-approval inspection of the manufacturing facilities for the new product to determine whether they comply with cGMPs. The FDA will not approve the product unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. In addition, before approving an NDA, the FDA may also audit data from clinical trials to ensure compliance with GCP requirements. After the FDA evaluates the application, manufacturing process and manufacturing facilities, it may issue an approval letter or a Complete Response Letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications. A Complete Response Letter indicates that the review cycle of the application is complete and the application will not be approved in its present form. A Complete Response Letter usually describes all of the specific deficiencies in the NDA identified by the FDA. The Complete Response Letter may require additional clinical data and/or an additional pivotal Phase 3 clinical trial(s), and/or other significant and time-consuming requirements related to clinical trials, nonclinical studies or manufacturing. If a Complete Response Letter is issued, the applicant may either resubmit the NDA, addressing all of the deficiencies identified in the letter, withdraw the application or request a hearing. Even if such data and information are submitted, the FDA may ultimately decide that the NDA does not satisfy the criteria for approval. Data obtained from clinical trials are not always conclusive, and the FDA may interpret data differently than we interpret the same data.

There is no assurance that the FDA will ultimately approve a drug product for marketing in the United States, and we may encounter significant difficulties or costs during the review process. If a product receives marketing approval, the approval may be significantly limited to specific diseases and dosages or the indications for use may otherwise be limited, which could restrict the commercial value of the product. Further, the FDA may require that certain contraindications, warnings or precautions be included in the product labeling or may condition the approval of the NDA on other changes to the proposed labeling, development of adequate controls and specifications, or a commitment to conduct post-market testing or clinical trials and surveillance to monitor the effects of approved products. For example, the FDA may require Phase 4 testing which involves clinical trials designed to further assess drug safety and effectiveness and may require testing and surveillance programs to monitor the safety of approved products that have been commercialized. The FDA may also place other conditions on approvals including the requirement for a risk evaluation and mitigation strategy, or REMS, to assure the safe use of the drug. If the FDA concludes a REMS is needed, the sponsor of the NDA must submit a proposed REMS; the FDA will not approve the NDA without an approved REMS, if required. A REMS could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. Any of these limitations on approval or marketing could restrict the commercial promotion, distribution, prescription or dispensing of products. Product

approvals may be withdrawn for non-compliance with regulatory requirements or if problems occur following initial marketing.

FDA's NDA Resubmission Policy Following a Complete Response Letter

Under the FDA's policies and procedures, an NDA that is resubmitted following the issuance of a CRL will be evaluated by the FDA to determine whether the resubmission addresses all of the deficiencies raised in the CRL. If so, the FDA will classify the resubmission as either Class 1 or Class 2. The FDA will review and act on Class 1 resubmissions within two months of the NDA receipt date and on Class 2 resubmissions within six months of the NDA receipt date. Based on the positive results from the CHIASMA OPTIMAL trial, we resubmitted our NDA, seeking approval of MYCAPSSA capsules as a maintenance therapy for adult patients with acromegaly to the FDA. In January 2020, the FDA accepted for review the resubmission of the NDA as a complete response to deficiencies identified in the CRL to our original NDA and assigned an action date of June 26, 2020 under the PDUFA. If we obtain marketing approval of octreotide capsules from the FDA, we plan to submit two prior approval manufacturing supplements to qualify two large-scale API manufacturing sites from which we are currently procuring API for our planned commercial use. According to recent regulatory guidelines, prior approval manufacturing supplements are reviewed by FDA with four-month PDUFA review goals, which may be extended to six-months if FDA elects to inspect the manufacturing site. However, there can be no assurance that the FDA will review and approve these supplements in a timely manner or at all.

505(b)(2) Approval Process

Section 505(b)(2) of the FDCA provides an alternate regulatory pathway for the FDA to approve a new drug and permits reliance for such approval on published literature or an FDA finding of safety and effectiveness for a previously approved drug product. Specifically, section 505(b)(2) permits the filing of an NDA where one or more of the investigations relied upon by the applicant for approval were not conducted by or for the applicant and for which the applicant has not obtained a right of reference. The applicant may rely upon published literature and/or the FDA's findings of safety and effectiveness for a previously approved drug. Typically, 505(b)(2) applicants must perform additional trials to support the change from the previously approved drug and to further demonstrate the new drug's safety and effectiveness. The FDA may then approve the new product candidate for all or some of the labeled indications for which the referenced product has been approved, as well as for any new indication sought by the section 505(b)(2) applicant.

Our product candidate, octreotide capsules, is based upon an already approved version of the same drug in an immediate-release formulation for subcutaneous injection, rather than a new chemical entity product candidate. Accordingly, we expect to be able to rely on information from previously conducted studies involving the immediate-release subcutaneous octreotide product in our clinical development plans and our NDA resubmission.

Post-Marketing Requirements

Following approval of a new product, a pharmaceutical company and the approved product are subject to continuing regulation by the FDA, including, among other things, monitoring and recordkeeping activities, reporting to the applicable regulatory authorities of adverse events with the product, providing the regulatory authorities with updated safety and efficacy information, and product sampling and distribution requirements in accordance with the Prescription Drug Marketing Act, a part of the FDCA. Modifications or enhancements to the product or its labeling or changes of the site of manufacture are often subject to the approval of the FDA and other regulators, which may or may not be received or may result in a lengthy review process.

Prescription drug advertising is subject to federal, state and foreign regulations. In the United States, the FDA regulates prescription drug promotion and advertising, including direct-to-consumer advertising. Prescription drug promotional materials must be submitted to the FDA in conjunction with their first use. In addition, a

pharmaceutical company must comply with restrictions on promoting drugs for uses or in patient populations that are not described in the drug's approved labeling (known as "off-label use"), limitations on industry-sponsored scientific and educational activities, and requirements for promotional activities involving the internet. Although physicians may prescribe legally available drugs for off-label uses, manufacturers may not market or promote such off-label uses.

In the United States, once a product is approved, its manufacture is subject to comprehensive and continuing regulation by the FDA. The FDA regulations require that products be manufactured in specific approved facilities and in accordance with cGMPs. We rely on third parties for the production of clinical quantities of octreotide capsules and expect to rely on third parties for the production of commercial quantities of our octreotide capsules, in both cases in accordance with cGMP regulations. cGMP regulations require among other things, quality control and quality assurance as well as the corresponding maintenance of records and documentation and the obligation to investigate and correct any deviations from cGMP. Drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMPs and other laws. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance. These regulations also impose certain organizational, procedural and documentation requirements with respect to manufacturing and quality assurance activities. NDA holders using contract manufacturers, laboratories or packagers are responsible for the selection and monitoring of qualified firms, and, in certain circumstances, qualified suppliers to these firms. These firms and, where applicable, their suppliers are subject to inspections by the FDA at any time, and the discovery of violative conditions, including failure to conform to cGMPs, could result in enforcement actions that interrupt the operation of any such facilities or the ability to distribute products manufactured, processed or tested by them. Discovery of problems with a product after approval may result in restrictions on a product, manufacturer, or holder of an approved NDA, including, among other things, recall or withdrawal of the product from the market. In addition, changes in some of the conditions established in an approved NDA, including changes in manufacturers, manufacturing processes or manufacturing facilities, require submission and FDA review and approval of a supplement to the approved NDA before the changes can be implemented. For example, if we obtain marketing approval of octreotide capsules from the FDA, we plan to submit two prior approval manufacturing supplements to qualify two large-scale API manufacturing sites from which we are currently procuring API for our planned commercial use. The FDA review process of supplements for proposed changes in manufacturers, manufacturing processes or manufacturing facilities may require four to six months or longer to complete and may involve cGMP compliance inspections of manufacturing facilities. There can be no assurance that our two planned prior approval manufacturing supplements will be reviewed and approved in a timely manner or at all.

The FDA also may require post-marketing testing, known as Phase 4 testing, REMS and surveillance to monitor the effects of an approved product or place conditions on an approval that could restrict the distribution or use of the product. Discovery of previously unknown problems with a product or the failure to comply with applicable FDA requirements can have negative consequences, including adverse publicity, judicial or administrative enforcement, untitled or warning letters from the FDA, mandated corrective advertising or communications with doctors, and civil or criminal penalties, among others. Newly discovered or developed safety or effectiveness data may require changes to a product's approved labeling, including the addition of new warnings and contraindications, and also may require the implementation of other risk management measures. Also, new government requirements, including those resulting from new legislation, may be established, or the FDA's policies may change, which could delay or prevent regulatory approval of our products under development and impact approved products already on the market.

Other Regulatory Matters

The distribution of pharmaceutical products is subject to additional requirements and regulations, including extensive record-keeping, licensing, storage and security requirements intended to prevent the unauthorized sale

of pharmaceutical products. For example, the Drug Supply Chain Security Act, or DSCSA, was enacted in 2013 with the aim of building an electronic system to identify and trace certain prescription drugs distributed in the United States. The DSCSA mandates phased-in and resource-intensive obligations for pharmaceutical manufacturers, wholesale distributors, and dispensers over a 10-year period that is expected to culminate in November 2023. The law's requirements include the quarantine and prompt investigation of a suspect product, to determine if it is illegitimate, and notifying trading partners and FDA of any illegitimate product. Drug manufacturers and their collaborators are also required to place a unique product identifier on prescription drug packages. This identifier consists of the National Drug Code, serial number, lot number and expiration date, in the form of a two-dimensional data matrix barcode that can be read by humans and machines.

The failure to comply with regulatory requirements subjects firms to possible legal or regulatory action. Depending on the circumstances, failure to meet applicable regulatory requirements can result in criminal prosecution, fines or other penalties, injunctions, voluntary recall, seizure of products, total or partial suspension of production, denial or withdrawal of product approvals, exclusion from federal healthcare programs, or refusal to allow a firm to enter into supply contracts, including government contracts. In addition, even if a firm complies with FDA and other requirements, new information regarding the safety or effectiveness of a product could lead the FDA to modify or withdraw product approval. Prohibitions or restrictions on sales or withdrawal of future products marketed by us could materially affect our business in an adverse way.

Changes in regulations, statutes or the interpretation of existing regulations could impact our business in the future by requiring, for example: (i) changes to our manufacturing arrangements; (ii) additions or modifications to product labeling; (iii) the voluntary recall or discontinuation of our products; or (iv) additional record-keeping requirements. If any such changes were to be imposed, they could adversely affect the operation of our business.

Orphan Designation and Exclusivity

The FDA may grant orphan drug designation to drugs intended to treat a rare disease or condition that affects fewer than 200,000 individuals in the United States. Alternatively, orphan drug designation may be available if the disease or the condition affects more than 200,000 individuals in the United States and there is no reasonable expectation that the cost of developing and making the drug for this type of disease or condition will be recovered from sales in the United States. A company must request orphan product designation before submitting an NDA. If the request is granted, the FDA will disclose the identity of the therapeutic agent and its potential use. Orphan product designation does not convey any advantage in or shorten the duration of the regulatory review and approval process. Octreotide capsules have been granted orphan designation in the United States for the treatment of acromegaly.

Orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages, and user-fee waivers. In addition, if a product is the first to receive FDA approval of the indication for which it has orphan designation, the product is entitled to orphan drug exclusivity, which means the FDA may not approve any other application to market the same drug for the same indication for a period of seven years, except in limited circumstances. Competitors may receive approval of different products for the indication for which the orphan product has exclusivity and may obtain approval for the same product but for a different indication. If a drug or drug product designated as an orphan product ultimately receives marketing approval for an indication broader than what was designated in its orphan product application, it may not be entitled to exclusivity.

Orphan drug exclusivity will not bar approval of another orphan drug under certain circumstances, including if a subsequent product with the same drug for the same indication is shown to be clinically superior over the approved product with orphan exclusivity on the basis of greater efficacy or safety, or providing a major contribution to patient care, or if the company with orphan drug exclusivity is not able to meet market demand.

U.S. Marketing Exclusivity

Market exclusivity provisions under the FDCA can also delay the submission or the approval of certain marketing applications. The FDA provides three years of marketing exclusivity for an NDA, or supplement to an existing NDA, if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, for example new indications, dosages or strengths of an existing drug. This three-year exclusivity covers only the modification for which the drug received approval on the basis of the new clinical investigations and does not prohibit the FDA from approving ANDAs for drugs containing the active agent for the original indication or condition of use. Three-year exclusivity will not delay the submission or approval of a full NDA. However, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the nonclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness. Orphan drug exclusivity, as described above, may offer a seven-year period of marketing exclusivity, except in certain circumstances. Pediatric exclusivity is another type of regulatory market exclusivity in the United States. Pediatric exclusivity adds six months of exclusivity, which runs from the end of other exclusivity protection and patent term, and may be granted based on the voluntary completion of a pediatric trial in accordance with an FDA-issued "Written Request" for such a trial.

Other Regulations

We are also subject to numerous federal, state and local laws relating to such matters as safe working conditions, manufacturing practices, environmental protection and fire hazard control. We may incur significant costs to comply with such laws and regulations now or in the future.

European Orphan Designation and Exclusivity

In the European Union, the European Commission, after reviewing the opinion of the EMA's Committee for Orphan Medicinal Products, grants orphan drug designation to promote the development of products that are intended for the diagnosis, prevention or treatment of life-threatening or chronically debilitating conditions that affect not more than five in 10,000 persons in the European Union Community, or when, without incentives, it is unlikely that sales of such products in the European Union would be sufficient to justify the necessary investment in developing the products. Additionally, orphan drug designation is only available where no satisfactory method of diagnosis, prevention, or treatment of the condition has been authorized (or the product would be a significant benefit to those affected).

In the European Union, orphan drug designation entitles a party to financial incentives such as reduction of fees or fee waivers and 10 years of market exclusivity is granted following medicinal product approval. This period may be reduced to six years if the orphan drug designation criteria are no longer met, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity. Market exclusivity would not prevent the approval of a similar drug that is shown to be safer, more effective or otherwise clinically superior.

Orphan drug designation must be requested before submitting an application for marketing approval. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

Coverage and Reimbursement

Sales of any products for which we receive regulatory approval for commercial sale will depend in part on the availability of coverage and adequate reimbursement from third-party payors, including government healthcare program administrative authorities, managed care organizations, private health insurers, and other entities. Patients who are prescribed medications for the treatment of their conditions, and their prescribing physicians,

generally rely on third-party payors to reimburse all or part of the costs associated with their prescription drugs. Patients are unlikely to use our products unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of our products. Therefore, our products, if approved, may not obtain market acceptance unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of our products.

The process for determining whether a third-party payor will provide coverage for a drug product typically is separate from the process for setting the price of a drug product or for establishing the reimbursement rate that the payor will pay for the drug product once coverage is approved. Third-party payors may limit coverage to specific drug products on an approved list, also known as a formulary, which might not include all of the FDA-approved drugs for a particular indication. A decision by a third-party payor not to cover our product candidates could reduce physician utilization of our products once approved. Moreover, a third-party payor's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved or that any required patient cost-sharing amount will be acceptable to the patient. Adequate third-party reimbursement may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development. Additionally, coverage and reimbursement for drug products can differ significantly from payor to payor and among the insured lives of an individual payor depending upon the benefits applicable to the insured person. One third-party payor's decision to cover a particular drug product or service does not ensure that other payors will also provide coverage for the medical product or service, or will provide coverage at an adequate reimbursement rate. As a result, the coverage determination process will require us to provide scientific and clinical support for the use of our products to each payor separately and will be a time-consuming process.

The containment of healthcare costs has become a priority of federal, state and foreign governments, and the prices of drugs have been a focus in this effort. Third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular drug products and are increasingly challenging the prices charged for drug products and medical services, examining the medical necessity and reviewing the cost effectiveness of drug products and medical services, in addition to questioning safety and efficacy. If these third-party payors do not consider our products to be cost-effective compared to other available therapies, they may not cover our products after FDA approval or, if they do, the level of payment may not be sufficient to allow us to sell our products at a profit. In the United States, the principal decisions about reimbursement for new drug products are typically made by CMS, an agency within the HHS. CMS decides whether and to what extent a new drug product will be covered and reimbursed under Medicare, and private payors tend to follow CMS to a substantial degree. However, no uniform policy of coverage and reimbursement for drug products exists among third-party payors and coverage and reimbursement levels for drug products can differ significantly from payor to payor. In many countries, the prices of drug products are subject to varying price control mechanisms as part of national health systems. In general, the prices of drug products under such systems are substantially lower than in the United States. Other countries allow companies to fix their own prices for drug products, but monitor and control company profits. Accordingly, in markets outside the United States, the reimbursement for drug products may be reduced compared with the United States.

The U.S. government, state legislatures and foreign governments have also shown significant interest in implementing cost containment programs to limit the growth of government-paid health care costs, including price controls, restrictions on reimbursement and requirements for substitution of generic products for branded prescription drugs. By way of example, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, collectively, the Affordable Care Act, contains provisions that may reduce the profitability of drug products, including, for example, increased rebates for drugs sold to Medicaid programs, extension of Medicaid rebates to Medicaid managed care plans, mandatory discounts for certain Medicare Part D beneficiaries and annual fees based on pharmaceutical companies' share of sales to federal health care programs. Some of the provisions of the Affordable Care Act have yet to be fully implemented, while certain provisions have been subject to judicial and Congressional challenges. For example, on January 20, 2017, President Trump signed an Executive Order directing federal agencies with authorities and

responsibilities under the Affordable Care Act to waive, defer, grant exemptions from, or delay the implementation of any provision of the Affordable Care Act 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.

Other legislative changes have been proposed and adopted since the ACA was enacted. While Congress has not passed comprehensive repeal legislation, it has enacted laws that modify certain provisions of the ACA, including eliminating a tax-based shared responsibility payment imposed on certain individuals who fail to maintain qualifying health coverage for all or part of a year, which is commonly referred to as the "individual mandate". Various portions of the ACA are currently undergoing legal and constitutional challenges in the Fifth Circuit Court and the United States Supreme Court. Thus, the full impact of the Affordable Care Act, or any law replacing elements of it, on our business remains unclear. Adoption of government controls and measures, and tightening of restrictive policies in jurisdictions with existing controls and measures, could limit payments for pharmaceuticals.

In addition, in some foreign countries, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing vary widely from country to country. For example, the European Union provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. A member state may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our products, if approved. Historically, products launched in the European Union do not follow price structures of the United States and generally tend to be significantly lower.

Anti-Kickback and False Claims Laws and Other Regulatory Matters

In the United States, among other things, the research, manufacturing, distribution, sale and promotion of drug products are potentially subject to regulation and enforcement by various federal, state and local authorities in addition to the FDA, including the Centers for Medicare & Medicaid Services, other divisions of the United States Department of Health and Human Services (e.g., the Office of Inspector General), the Drug Enforcement Administration, the Consumer Product Safety Commission, the Federal Trade Commission, the Occupational Safety & Health Administration, the Environmental Protection Agency, state attorneys general and other state and local government agencies. Our current and future business activities, including for example, sales, marketing and scientific/educational grant programs must comply with healthcare regulatory laws, including the Federal Anti-Kickback Statute, the Federal False Claims Act, as amended, the privacy regulations promulgated under the Health Insurance Portability and Accountability Act, or HIPAA, as amended, physician payment transparency laws, and similar state laws. Pricing and rebate programs must comply with the Medicaid Drug Rebate Program requirements of the Omnibus Budget Reconciliation Act of 1990, as amended, and the Veterans Health Care Act of 1992, as amended. If products are made available to authorized users of the Federal Supply Schedule of the General Services Administration, additional laws and requirements apply. The handling of any controlled substances must comply with the U.S. Controlled Substances Act and Controlled Substances Import and Export Act. Products must meet applicable child-resistant packaging requirements under the U.S. Poison Prevention Packaging Act. All of these activities are also potentially subject to federal and state consumer protection and unfair competition laws.

The Federal Anti-Kickback Statute makes it illegal for any person, including a prescription drug manufacturer (or a party acting on its behalf) to knowingly and willfully solicit, receive, offer, or pay any remuneration that is intended to induce the referral of business, including the purchasing, leasing, ordering or arranging for or recommending the purchase, lease or order of, any good, facility, item or service for which payment may be made, in whole or in part, under a federal healthcare program, such as Medicare or Medicaid. The term

"remuneration" has been broadly interpreted to include anything of value. The Federal Anti-Kickback Statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on one hand and prescribers, purchasers and formulary managers on the other. Although there are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution, the exceptions and safe harbors are drawn narrowly. Practices that involve remuneration that may be alleged to be intended to induce prescribing, purchases or recommendations may be subject to scrutiny if they do not qualify for an exception or safe harbor. Failure to meet all of the requirements of a particular applicable statutory exception or regulatory safe harbor does not make the conduct per se illegal under the Federal Anti-Kickback Statute. Instead, the legality of the arrangement will be evaluated on a case-by-case basis based on a cumulative review of all of its facts and circumstances. Additionally, the intent standard under the Federal Anti-Kickback Statute was amended by the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively the ACA, to a stricter standard such that a person or entity no longer needs to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. In addition, the ACA codified case law that a claim including items or services resulting from a violation of the Federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the Federal False Claims Act. Violations of this law are punishable by up to five years in prison, criminal fines, administrative civil money penalties, and exclusion from participation in federal healthcare programs. In addition, many states have adopted laws similar to the Federal Anti-Kickback Statute. Some of these state prohibitions apply to the referral of patients for healthcare services reimbursed by any insurer, not just federal healthcare programs such as Medicare and Medicaid. Due to the breadth of these federal and state anti-kickback laws, and the potential for additional legal or regulatory change in this area, it is possible that our future business activities, including our sales and marketing practices and/or our future relationships with endocrinologists and other healthcare providers might be challenged under anti-kickback laws, which could harm us.

The Federal False Claims Act prohibits anyone from, among other things, knowingly presenting, or causing to be presented, for payment to federal programs (including Medicare and Medicaid) claims for items or services, including drugs, that are false or fraudulent. This statute has been interpreted to prohibit presenting claims for items or services not provided as claimed, or claims for medically unnecessary items or services. Although we would not submit claims directly to payors, manufacturers can be held liable under these laws if they are deemed to "cause" the submission of false or fraudulent claims by, for example, providing inaccurate billing or coding information to customers or promoting a product off-label. In addition, our future activities relating to the reporting of wholesaler or estimated retail prices for our products, the reporting of prices used to calculate Medicaid rebate information and other information affecting federal, state and third-party reimbursement for our products, and the sale and marketing of our products, are subject to scrutiny under this law. For example, pharmaceutical companies have been found liable under the Federal False Claims Act in connection with their off-label promotion of drugs. Penalties for a False Claims Act violation include three times the actual damages sustained by the government, plus mandatory civil penalties for each separate false claim, the potential for exclusion from participation in federal healthcare programs, and, although the Federal False Claims Act is a civil statute, conduct that results in a False Claims Act violation may also implicate various federal criminal statutes. If the government were to allege that we were, or convict us of, violating these false claims laws, we could be subject to a substantial fine and may suffer a decline in our stock price. In addition, private individuals have the ability to bring actions under the Federal False Claims Act and certain states have enacted laws modeled after the Federal False Claims Act.

Similarly, the civil monetary penalties statute imposes penalties against any person or entity who, among other things, is determined to have presented or caused to be presented a claim to a federal health program that the person knows or should know is for an item or service that was not provided as claimed or is false or fraudulent.

Additionally, HIPAA created federal criminal statutes that prohibit, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, including private third-party payors and knowingly and willfully falsifying, concealing or covering up a material fact or making any

materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services.

The ACA included a provision commonly referred to as the Sunshine Act, which requires certain pharmaceutical manufacturers to track and report annually certain financial arrangements with physicians (currently defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals, including any "transfer of value" provided, as well as any ownership or investment interests held by physicians and their immediate family members. Covered manufacturers are required to submit reports to CMS by the 90th day of each subsequent calendar year. The information reported is publicly available and searchable on the CMS website. Effective January 1, 2022, these reporting obligations will extend to include transfers of value made to certain non-physician providers such as physician assistants and nurse practitioners. There are also an increasing number of state and foreign laws that require manufacturers to make reports to states or foreign governments on pricing and marketing information. Many of these laws contain ambiguities as to what is required to comply with the laws. In addition, given the lack of clarity with respect to these laws and their implementation, our reporting actions could be subject to the penalty provisions of the pertinent state, federal or foreign authorities. These laws may affect our sales, marketing and other promotional activities by imposing administrative and compliance burdens on us. We are engaging in significant efforts to establish systems and processes in order to comply with these laws and regulations. Failure to comply with the reporting requirements would result in significant civil monetary penalties.

In addition, we may be subject to data privacy and security regulation by both the federal government and the states in which we conduct our business. HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and their respective implementing regulations, including the final omnibus rule published on January 25, 2013, imposes specified requirements relating to the privacy, security and transmission of individually identifiable health information. Among other things, HITECH makes certain of HIPAA's privacy and security standards directly applicable to business associates, defined as an entity that performs certain functions that create, receive, maintain or transmit protected health information in connection with providing a service for or on behalf of a covered entity. HITECH also created four new tiers of civil monetary penalties and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorneys' fees and costs associated with pursuing federal civil actions.

In addition to HIPAA and HITECH, other federal and state laws, including state security breach notification laws, state health information privacy laws and federal and state consumer protection laws, govern the collection, use and disclosure of personal information. For example, in June 2018 California enacted the California Consumer Privacy Act which took effect on January 1, 2020 and broadly defines personal information, gives California residents expanded privacy rights and protections, provides civil penalties for violations, and creates a private right of action and statutory damages for victims of data breaches. Other states, including the state of Washington, are considering similar laws or other laws that regulate specific types of personal information, including biometric data. Many state laws that govern the privacy and security of health information in certain circumstances differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts. Various foreign countries also have, or are developing, laws governing the collection, use and transmission of personal information. The legislative and regulatory landscape for privacy and data protection continues to evolve, and there has been an increasing amount of focus on privacy and data protection issues with the potential to affect our business.

The failure to comply with applicable regulatory requirements subjects us to possible legal or regulatory action. Depending on the circumstances, failure to meet applicable regulatory requirements can result in significant criminal, civil and/or administrative penalties, damages, fines, disgorgement, exclusion from participation in federal healthcare programs, such as Medicare and Medicaid, injunctions, recall or seizure of products, total or partial suspension of production, denial or withdrawal of product approvals, refusal to allow us to enter into supply contracts, including government contracts, contractual damages, reputational harm, administrative

burdens, diminished profits and future earnings, and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations. Even if we are not determined to have violated applicable regulatory or legal requirements, government investigations into alleged violations typically requires the expenditure of significant resources and could generate negative publicity, which could harm our business.

Affordable Care Act and Other Reform Initiatives

In the United States and some foreign jurisdictions, there have been, and likely will continue to be, a number of legislative and regulatory changes and proposed changes regarding the healthcare system directed at broadening the availability of healthcare and containing or lowering the cost of healthcare.

In March 2010, the ACA was enacted. The ACA includes measures that have significantly changed, and are expected to continue to significantly change, the way healthcare is financed by both governmental and private insurers. Among the provisions of the ACA of greatest importance to the pharmaceutical industry are the following:

- The Medicaid Drug Rebate Program requires pharmaceutical manufacturers to enter into and have in effect a national rebate agreement with the Secretary of the Department of Health and Human Services in exchange for state Medicaid coverage of most of the manufacturer's drugs. ACA made several changes to the Medicaid Drug Rebate Program, including increasing pharmaceutical manufacturers' rebate liability by raising the minimum basic Medicaid rebate on most branded prescription drugs and biologic products to 23.1% of average manufacturer price, or AMP, and adding a new rebate calculation for "line extensions" (i.e., new formulations, such as extended release formulations) of solid oral dosage forms of branded products, as well as potentially impacting their rebate liability by modifying the statutory definition of AMP.
- The ACA expanded the types of entities eligible to receive discounted 340B pricing, although, with the exception of children's hospitals, these newly eligible entities will not be eligible to receive discounted 340B pricing on orphan drugs used in orphan indications. In addition, because 340B pricing is determined based on AMP and Medicaid drug rebate data, the revisions to the Medicaid rebate formula and AMP definition described above could cause the required 340B discounts to increase. The ACA imposed a requirement on manufacturers of branded drugs and biologic agents to provide a 50% discount off the negotiated price of branded drugs dispensed to Medicare Part D beneficiaries in the coverage gap (i.e., "donut hole"). The required discount was increased to 70% on January 1, 2019 pursuant to the Bipartisan Budget Act of 2018.
- The ACA imposed an annual, nondeductible fee on any entity that manufactures or imports certain branded prescription drugs and biologic products, apportioned among these entities according to their market share in certain government healthcare programs, although this fee would not apply to sales of certain products approved exclusively for orphan indications.
- The ACA included the Sunshine Act, which required certain pharmaceutical manufacturers to track and annually report to CMS certain financial arrangements with physicians and teaching hospitals, including any "transfer of value" provided, as well as any ownership or investment interests held by physicians and their immediate family members.
- The ACA established a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research. The research conducted by the Patient-Centered Outcomes Research Institute may affect the market for certain pharmaceutical products.
- The ACA established the Center for Medicare and Medicaid Innovation within CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending. Funding has been allocated to support the mission of the Center for Medicare and Medicaid Innovation through 2019.

Some of the provisions of the ACA have yet to be fully implemented, while certain provisions have been subject to judicial and Congressional challenges. For example, the Tax Cuts and Jobs Act of 2017, or TCJA, includes a provision repealing, effective January 1, 2019, the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate." Further, the Bipartisan Budget Act of 2018, or the BBA, among other things, amends the ACA, effective January 1, 2019, to reduce the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole." Congress may consider other legislation to modify, repeal, or replace elements of the ACA. Thus, the full impact of the ACA, or any law replacing elements of it, on our business remains unclear.

Other legislative changes have been proposed and adopted in the United States since the ACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions of Medicare payments to providers up to 2% per fiscal year, which went into effect in April 2013 and will remain in effect through 2029 unless additional congressional action is taken. In January 2013, former President Barack Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, further reduced Medicare payments to several providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors, which may adversely affect our future profitability.

European Union Drug Development

In the European Union, octreotide capsules and any future product candidates we may develop will also be subject to extensive regulatory requirements. As in the United States, medicinal products can only be marketed if marketing authorizations from the competent regulatory agencies have been obtained.

Similar to the United States, the various phases of nonclinical and clinical research in the European Union are subject to significant regulatory controls. Although the European Union Clinical Trials Directive 2001/20/EC has sought to harmonize the EU clinical trials regulatory framework, setting out common rules for the control and authorization of clinical trials in the EU, the EU Member States have transposed and applied the provisions of the Directive differently. This has led to significant variations in the member state regimes. Under the current regime, before a clinical trial can be initiated it must be approved in each of the EU countries where the trial is to be conducted by two distinct bodies: the National Competent Authority, or NCA, and one or more Ethics Committees, or ECs. Under the current regime all suspected unexpected serious adverse reactions to the investigated drug that occur during the clinical trial have to be reported to the NCA and ECs of the Member State where they occurred.

On April 16, 2014, the European Commission adopted Clinical Trial Regulation EU No. 536/2014 in an effort to ensure that the rules for conducting clinical trials in the EU will be identical. The new regulation, among other things, will implement a streamlined application procedure with a single entry point for review, harmonize the process for assessing applications for clinical trials, simplify reporting procedures, and increase transparency regarding clinical trials and their outcomes. It is expected that the new Clinical Trials Regulation (EU) No 536/2014 will come into effect in 2020 with a three-year transition period. Until then, the current law, Clinical Trials Directive 2001/20/EC, continues to govern all clinical trials performed in the EU.

European Union Drug Review and Approval

In the European Economic Area, or EEA, which is comprised of the 28 Member States of the European Union plus Norway, Iceland and Liechtenstein, medicinal products can only be commercialized after obtaining a Marketing Authorization, or MA. There are two types of marketing authorizations:

The *Community MA* is issued by the European Commission through the Centralized Procedure, based on the opinion of the Committee for Medicinal Products for Human Use, or the CHMP, of the EMA, and is valid throughout the entire territory of the EEA. The Centralized Procedure is mandatory for certain types of products, such as biotechnology medicinal products, orphan medicinal products, such as octreotide capsules, and medicinal products containing a new active substance indicated for the treatment of AIDS, cancer, neurodegenerative disorders, diabetes, auto-immune and viral diseases. The Centralized Procedure is optional for products containing a new active substance not yet authorized in the EEA, or for products that constitute a significant therapeutic, scientific or technical innovation or which are in the interest of public health in the EU.

National MAs, which are issued by the competent authorities of the Member States of the EEA and only cover their respective territory, are available for products not falling within the mandatory scope of the Centralized Procedure. Where a product has already been authorized for marketing in a Member State of the EEA, this National MA can be recognized in another Member States through the Mutual Recognition Procedure. If the product has not received a National MA in any Member State at the time of application, it can be approved simultaneously in various Member States through the Decentralized Procedure. Under the Decentralized Procedure an identical dossier is submitted to the competent authorities of each of the Member States in which the MA is sought, one of which is selected by the applicant as the Reference Member State, or RMS. The competent authority of the RMS prepares a draft assessment report, a draft summary of the product characteristics, or SPC, and a draft of the labeling and package leaflet, which are sent to the other Member States (referred to as the Member States Concerned) for their approval. If the Member States Concerned raise no objections, based on a potential serious risk to public health, to the assessment, SPC, labeling, or packaging proposed by the RMS, the product is subsequently granted a national MA in all the Member States (i.e. in the RMS and the Member States Concerned).

Under the above described procedures, before granting the MA, the EMA or the competent authorities of the Member States of the EEA make an assessment of the risk-benefit balance of the product on the basis of scientific criteria concerning its quality, safety and efficacy and whether the product has a positive benefit to risk profile.

The approval process and requirements governing the conduct of clinical trials, drug review and approval, product licensing, pricing and reimbursement vary greatly from place to place. FDA approval is no guarantee of approval of the same product in the EEA and other foreign territories, either at all or within the same timescale as approval may be granted within the United States.

Brexit and the Regulatory Framework in the United Kingdom

On June 23, 2016, the electorate in the United Kingdom voted in favor of leaving the European Union (commonly referred to as “Brexit”). Thereafter, on March 29, 2017, the country formally notified the European Union of its intention to withdraw pursuant to Article 50 of the Lisbon Treaty. The United Kingdom formally left the European Union on January 31, 2020. A transition period began on February 1, 2020, during which European Union pharmaceutical law remains applicable to the United Kingdom. This transition period is due to end on December 31, 2020. Since the regulatory framework for pharmaceutical products in the United Kingdom covering quality, safety and efficacy of pharmaceutical products, clinical trials, marketing authorization, commercial sales and distribution of pharmaceutical products is derived from European Union directives and regulations, Brexit could materially impact the future regulatory regime which applies to products and the approval of product candidates in the United Kingdom. It remains to be seen how Brexit will impact regulatory requirements for product candidates and products in the United Kingdom.

Employees

As of March 9, 2020, we had 48 full-time employees located in the United States and in Israel. While none of our employees are represented by a labor union or party to any collective bargaining agreement, certain provisions of the collective bargaining agreements between the Histadrut (General Federation of Labor in Israel) and the Coordination Bureau of Economic Organizations (including the Industrialists' Associations) are applicable to our employees in Israel by extension orders issued by the Israel Ministry of Economy (previously the Israeli Ministry of Trade, Industry and Labor).

Israeli labor laws principally govern the length of the workday, minimum wages for employees, procedures for hiring and dismissing employees, determination of severance pay, annual leave, sick days, advance notice of termination of employment, equal opportunity and anti-discrimination laws and other conditions of employment. Subject to certain exceptions, Israeli law generally requires severance pay upon the retirement, death or dismissal of an employee, and requires us and our employees to make payments to the National Insurance Institute, which is similar to the U.S. Social Security Administration. Our Israeli employees have defined-benefit pension plans that comply with applicable Israeli legal requirements, which also include the mandatory pension payments required by applicable law and allocations for severance pay.

Although we experienced two separate reductions in force in 2016 aggregating greater than 60% of our workforce following our receipt of the CRL, we have never experienced any employment-related work stoppages and believe our relationship with our current employees is good.

Research and Development

During the year ended December 31, 2019, our total research and development expense was $22.5 million compared to $22.4 million and $17.9 million in the years ended December 31, 2018 and 2017, respectively. The increase in 2019 was primarily due to an increase in manufacturing, and regulatory costs offset by a decrease in clinical trial costs. The increase in 2018 was primarily due to increased costs related to the CHIASMA OPTIMAL clinical trial which we initiated in September 2017, and the MPOWERED trial and were partially offset by reduced personnel costs associated with the transition of our former Chief Development Officer from a full-time employee to a member of the board of directors of both our company and our Israeli subsidiary.

Corporate Information

We were incorporated under the laws of the State of Delaware and commenced business operations in 2001. Our principal executive offices are located at 140 Kendrick Street, Building C East, Needham, MA 02494 and our telephone number is (617) 928-5300. Our website address is www.chiasmapharma.com. Through our website, we make available, free of charge, our annual report on Form 10-K, quarterly reports on Form 10-Q, proxy statement, current reports on Form 8-K, and any amendments to these reports, as soon as reasonably practicable after we electronically file such material or furnish them to the Securities and Exchange Commission, or the SEC. The SEC also maintains a website containing reports, proxy materials and information statements, among other information, at *http://www.sec.gov*. The information contained on our website, or that can be accessed through our website, is not a part of this annual report on Form 10-K and is not incorporated by reference into this Form 10-K.

We own various U.S. federal and foreign trademark registrations and applications, as well as pending and unregistered trademarks and service marks, including "CHIASMA", "TPE", "MYCAPSSA", "MYCAPSSA logo", "ACROMEGALY.CARE plus logo", "TPE logo", "CAPS plus logo" and "CHIASMA logo" for our corporate logo. "CHIASMA", "MYCAPSSA", "TPE", CHIASMA logo, ACROMEGALY.CARE plus logo and CAPS plus logo are U.S. federal trademarks registered to Chiasma, Inc. All trademarks or trade names referred to in this Form 10-K including those of third parties are the property of their respective owners. Solely for convenience, the trademarks and trade names in this Form 10-K may be referred to without the ® and ™ symbols,

but such references should not be construed as any indicator that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto. We do not intend our use or display of other companies' trademarks and trade names to imply a relationship with, or endorsement or sponsorship of us by, any other companies. During 2018 we obtained a copyright registration in the United States for our Acro-TSQ.

Item 1A. Risk Factors

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

Risks Related to 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 United States Food and Drug Administration, or the FDA, in April 2016 regarding our original New Drug Application, or NDA, for octreotide capsules for the maintenance treatment of U.S. adult patients with acromegaly, despite our receipt of a Special Protocol Assessment, or SPA, for our CHIASMA OPTIMAL Phase 3 clinical trial, positive results from the CHIASMA OPTIMAL trial and acceptance by the FDA of the resubmission of our NDA for review, the approvability of octreotide capsules is uncertain and we may never obtain regulatory approval in the United States, which would jeopardize our viability as a business.

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. 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 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. In August 2017, we reached agreement with the FDA under its SPA procedures of a new Phase 3 clinical trial of octreotide capsules in adult acromegaly patients, which includes a placebo control. This clinical trial was designed to address the concerns previously raised in the CRL and support a potential resubmission of our NDA for octreotide capsules as a treatment for acromegaly. In May 2018, we received a SPA Agreement Modification Letter from the FDA agreeing to our proposed modification to the hierarchical set of secondary endpoints. We refer to this Phase 3 trial, which we initiated in September 2017, using the acronym CHIASMA OPTIMAL.

In July 2019, we reported statistically significant top-line data from the CHIASMA OPTIMAL trial. Based on the positive results from the CHIASMA OPTIMAL trial, we resubmitted our NDA seeking approval of octreotide capsules as a maintenance therapy for adult patients with acromegaly to the FDA. In January 2020, the FDA accepted for review the resubmission of the NDA as a complete response to deficiencies identified in the CRL and assigned a target action date of June 26, 2020 under the PDUFA. The time provided for the NDA review could take longer than we expect, including if the FDA requires us to submit additional data, such as efficacy data from our MPOWERED clinical trial. Although we currently estimate that our existing cash, cash equivalents and marketable securities will be sufficient to fund our operations through the target PDUFA date, regulatory outcomes are inherently uncertain and, in the event of a delay, we may not have the sufficient capital resources necessary to fund our operations. Further, we may not have sufficient capital resources to fund any additional trials that the FDA may require as a condition to approval.

We also cannot provide any assurance that the data from the CHIASMA OPTIMAL trial are sufficiently positive to support U.S. regulatory approval of octreotide capsules for the maintenance therapy of adult patients with 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. 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 FDA evaluated our NDA. In April 2016, the FDA issued a CRL.

If CHIASMA OPTIMAL fails to address the concerns raised by the FDA in the CRL or if the FDA determines that the data from the trial are insufficient to support marketing approval, 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. Furthermore, if the CHIASMA OPTIMAL trial data is not sufficient to support U.S. regulatory approval, our ability to pursue regulatory approval in the European Union, if the MPOWERED Phase 3 clinical trial is positive, will require significant additional time and capital, which we may not be able to secure on favorable terms, if at all. The prospects for our business under these circumstances will be significantly diminished, our ability to continue as a standalone business could be materially impaired and we may need to cease operations.

Even though our Phase 3 CHIASMA OPTIMAL trial was 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 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 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, as our SPA was in May 2018, with the written agreement of the FDA and the trial sponsor and, according to 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, and the data and results from the applicable clinical trial.

Further, the results from the CHIASMA OPTIMAL trial, a double-blind, placebo controlled clinical trial, may not be sufficiently robust to support the approval of our NDA resubmission. In particular, the CHIASMA OPTIMAL trial had a relatively small sample size, 56 patients enrolled, and therefore the FDA has indicated that missing data, which might be only a few measurements, may raise questions about data quality and may, ultimately, invalidate the trial results.

We anticipate that the FDA will review the totality of the data collected from the CHIASMA OPTIMAL trial, including both primary and secondary endpoints, including but not limited to data related to the loss of biochemical response when switching from injectable somatostatin analogs to octreotide capsules, together with certain data from our other clinical trials of octreotide capsules, in evaluating octreotide capsules treatment effect in our NDA resubmission and determining whether to grant approval. Therefore, our achievement of the primary endpoint and all secondary endpoints in the CHIASMA OPTIMAL trial alone may not be sufficient to support approval. Not all endpoints measured in our clinical trials may be supportive of octreotide capsules' efficacy or safety.

We also anticipate that the FDA will review whether the data collected from CHIASMA OPTIMAL and our other clinical trials are sufficiently robust to support the interpretability of these analyses, in determining whether to approve our NDA resubmission. Consequently, there can be no assurance that the data collected from the CHIASMA OPTIMAL trial will be sufficient to support approval of our NDA for the marketing and sale of octreotide capsules. If the data from CHIASMA OPTIMAL are insufficient to support approval of our NDA, our ability to continue as a standalone business could be materially impaired and we may need to cease operations.

We are substantially dependent on the regulatory approvals and subsequent commercial success of octreotide capsules for the treatment of acromegaly in the United States and European Union, both of which may never occur or may be substantially delayed.

We are a clinical, late-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 and European Union. 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 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.

Our NDA resubmission that was accepted by the FDA for review in January 2020 references one small-scale manufacturing site for the active pharmaceutical ingredient, or API, in octreotide owned by our planned secondary commercial API manufacturer. This site was also included in our original NDA. However, we do not expect to procure commercial API from this manufacturing site for our planned commercial launch. Accordingly, even if we obtain FDA approval of our NDA, in order to commercially launch octreotide capsules, following the

June 26, 2020 PDUFA date, we plan to submit to the FDA a prior approval manufacturing supplement to the NDA to provide for the approval of our primary API manufacturer and one of its large-scale manufacturing sites that was included in our original NDA. We also plan to concurrently file a second prior approval manufacturing supplement to the NDA to provide for a large-scale manufacturing site affiliated with the small-scale manufacturing site currently referenced in the NDA resubmission. These two manufacturing sources were not referenced in our December 2019 NDA resubmission in order to allow for further time for the additional API manufacturer not referenced in the NDA resubmission to resolve observations from a recent regulatory inspection and to allow us to seek the FDA's designation of the resubmission of the NDA as a Class 2 resubmission entailing a six-month review period, which designation we obtained from the FDA in January 2020. Assuming we obtain the FDA's approval of our NDA, in order to have oral octreotide capsules available for our planned commercial launch in the fourth quarter of 2020, we must also obtain the FDA's approval of either one of our two planned prior approval manufacturing supplements in a timely manner or our planned commercial launch could be prevented or substantially delayed. The review of any prior approval manufacturing supplement to the NDA will require FDA review and approval of the manufacturing process, facility, equipment and procedures in place at each manufacturing site in accordance with the FDA's cGMP requirements and may require regulatory inspections of each manufacturing site, which could prevent or delay approval of any such prior approval manufacturing supplement and prevent or delay our planned commercial launch. The timing of the FDA's review process related to our planned prior approval manufacturing supplements and the outcome of such reviews are inherently uncertain, and we can provide no assurances that either planned prior approval manufacturing supplement will be approved in a timely manner or at all.

Even if we receive regulatory approval of our NDA resubmission and one or both of our planned prior approval manufacturing supplements, the timing and success 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, marketing and other commercial personnel, implementing internal systems and infrastructure in order to support a commercial sales organization and establish patient-focused programs, obtain pricing and reimbursement, the timely production and delivery of sufficient quantities of commercial drug product (especially since we have only recently provided our commercial suppliers with purchase orders and initial forecasts regarding anticipated commercial supply requirements) implementation of a distribution infrastructure, the efficacy and safety data from our clinical trials, particularly our MPOWERED Phase 3 clinical trial from which we expect to report topline data in the fourth quarter of 2020 comparing the safety and efficacy of octreotide capsules to the current standard of care somatostatin analog injections, and the competitive landscape. 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 CHIASMA OPTIMAL trial or the MPOWERED clinical 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 the event that the CHIASMA OPTIMAL trial is not interpreted to be successful by the FDA, or we are otherwise unable to obtain U.S. regulatory approval for the marketing and sale of octreotide capsules, we may not be able to ever reach or achieve profitability, or even commercial viability, based solely on the prospects of marketing authorization approval of octreotide capsules in the European Union. Further, the MPOWERED trial, even if successful, may no longer be sufficient evidence to warrant EMA approval of octreotide capsules as we expect that any failure to achieve U.S. regulatory approval to commercialize octreotide capsules may reduce the likelihood of approval of octreotide capsules by the EMA. Our potential for financial success in the European Union as a standalone market will largely be dependent upon our ability to raise significant additional capital at least through the MAA approval date, which is uncertain, to obtain timely and adequate pricing and reimbursement approval for octreotide capsules from countries comprising the European Union, if approved, to achieve market acceptance of octreotide capsules in the European Union, to build our commercial infrastructure and distribution capabilities in the European Union, and to grow the octreotide capsules business in the European Union and other ex-U.S. markets to a certain scale. As such, there can be no assurance that the commercialization of octreotide capsules or our business plans are at all viable in the absence of FDA approval of octreotide capsules.

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 European Union, and subsequent commercialization of octreotide capsules, if approvals are obtained. The success of octreotide capsules, if our NDA and one or both of our planned prior approval manufacturing supplements are approved, will depend on several factors, including:

- the efficacy and safety data from our clinical trials;
- execution of an effective sales and marketing strategy for the commercialization of octreotide capsules;
- acceptance by patients, the medical community and third-party and government payors;
- the incidence and prevalence of acromegaly in those markets in which octreotide capsules are 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 quantities of commercial drug product;
- our ability, and the ability of our third-party manufacturers and other vendors, to maintain compliance with regulatory requirements, including 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.

Other than octreotide capsules, we have no other product candidates in clinical development. As a result, we continue to be highly dependent on the regulatory approval and successful commercialization of octreotide capsules, the failure or delay of which could raise substantial doubt of our ability to continue as a viable business.

If we are not able to obtain required regulatory approvals for octreotide capsules, particularly in the U.S., including our planned prior approval manufacturing supplements to our NDA, 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 April 2015, the FDA issued a CRL regarding our NDA for octreotide capsules for the maintenance therapy of acromegaly, 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 a global, randomized, open-label and active-controlled 15-month trial initially designed to enroll up to 150 patients in Europe, 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 an MAA and potential approval. The FDA advised us that positive data from the ongoing MPOWERED clinical trial, if obtained, would not be sufficient to address the concerns identified by the FDA in the CRL. Shortly following the receipt of this information, we commenced the SPA process with FDA for the Phase 3 CHIASMA OPTIMAL clinical trial. Even though we believe the CHIASMA OPTIMAL trial was successful and the FDA accepted the resubmission of our NDA for octreotide capsule for review, the FDA may

never approve our NDA. Our ongoing MPOWERED Phase 3 clinical trial may not be successful, or acceptable to the EMA to support regulatory approval in the European Union. The CRL, a decision by FDA not to approve our resubmitted NDA or data produced from the CHIASMA OPTIMAL trial could adversely impact the EMA's review of our regulatory submission, if submitted, and therefore we may never receive approval to market octreotide capsules in the United States, European Union or elsewhere.

Importantly, the safety data generated in our completed clinical trials of octreotide capsules, including our first Phase 3 clinical trial and the CHIASMA OPTIMAL clinical trial as well as certain safety data from the MPOWERED clinical trial, as well as the efficacy data from our completed first Phase 3 clinical trial and the CHIASMA OPTIMAL trial, are integrated into the NDA resubmission. We further expect the safety and efficacy data from all three of our Phase 3 clinical trials to be submitted in our planned MAA filing. While CHIASMA OPTIMAL was designed to address the FDA's concerns in the CRL and the MPOWERED trial design has been accepted by the EMA, our ultimate success in the regulatory review process of the NDA we resubmitted to the FDA or planned application for marketing approval in the European Union could be negatively impacted by the results from any of our clinical trials.

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.

Our NDA resubmission that was accepted by the FDA in January 2020 for review references one small-scale API manufacturer that was included in our original NDA and is owned by our planned secondary commercial API manufacturer. However, we do not expect to procure commercial API from this small-scale manufacturing site. Accordingly, even if we obtain FDA approval of our NDA, in order to commercially launch octreotide capsules, following the June 26, 2020 PDUFA date, we plan to submit to the FDA a prior approval manufacturing supplement to the NDA seeking approval of our primary API manufacturer and one of its large-scale manufacturing sites that was included in our original NDA. We also plan to concurrently file a second prior approval manufacturing supplement to the NDA to provide for a large-scale manufacturing site affiliated with the small-scale manufacturing site currently referenced in the NDA resubmission. If we are unable to obtain or are delayed in obtaining regulatory approval of our NDA or both of our two planned prior approval manufacturing supplements, we could be prevented from commercializing the product candidate in a timely manner or at all.

Other than the June 2015 submission of our NDA for octreotide capsules as a treatment for acromegaly to the FDA and the recent resubmission of our NDA, we have not yet submitted comparable applications to other regulatory authorities, nor have we submitted prior approval manufacturing supplements to any regulatory authority. If our development efforts for octreotide capsules, including our ability to obtain regulatory approval, are not successful for the acromegaly indication or are delayed, if we are unsuccessful or delayed in obtaining regulatory approval of the planned prior approval manufacturing supplements to our NDA or if adequate demand for octreotide capsules are not generated, our business and ability to generate revenues will be materially harmed. Failure to obtain regulatory approval for marketing octreotide capsules as a treatment for acromegaly or for our planned prior approval manufacturing supplements will prevent us from commercializing the product candidate in a timely manner or at all, which could raise significant concerns about our continued viability as a business.

The success of octreotide capsules will depend on the receipt of regulatory approvals, including the planned prior approval manufacturing supplements, 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;
- the results of our clinical trials may not provide acceptable evidence of octreotide capsules' safety and efficacy;
- the results of our clinical trials may not be sufficiently robust or meet the level of statistical or clinical significance required by the FDA, the EMA or other regulatory agencies for marketing approval;
- the dosing of octreotide capsules in a particular clinical trial may not be at an optimal level;
- patients in our clinical trials may suffer adverse effects for reasons that may or may not be related to octreotide capsules;
- the data collected from our clinical trials may not be sufficient to obtain regulatory approval in the United States or elsewhere;
- the FDA or comparable foreign regulatory authorities may identify deficiencies with the manufacturing processes or facilities of third-party manufacturers with which we contract for clinical and commercial supplies, one of which was identified by the FDA in its CRL and a second of which had unresolved observations from a recent regulatory inspection at the time of our NDA resubmission, 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 first Phase 3 clinical trial contained in the original 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 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 in the European Union. As such, our original NDA relied, and the NDA we resubmitted that was accepted for review by the FDA in January 2020 continues to rely, and we intend that our MAA 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 the European Union, the relevant regulatory authorities may require us to perform additional clinical trials or measurements to support approval over and above the clinical trials that we have already completed or initiated. The relevant regulatory authorities also may determine that we have not provided sufficient data to justify reliance on prior investigations involving the approved immediate-release injectable octreotide product.

In addition, notwithstanding the approval of many products by the FDA pursuant to Section 505(b)(2), in the past some pharmaceutical companies and others have objected to the FDA's interpretation of Section 505(b)(2). For example, parties have filed citizen petitions objecting to the FDA approving a Section 505(b)(2) NDA on scientific, legal and regulatory grounds. Scientific arguments have included the assertions that for the FDA to determine the similarity of the drug in the 505(b)(2) NDA to the listed drug, the FDA 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 FDA, 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 called MPOWERED to support potential regulatory approval in the European Union. 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 conducted a third Phase 3 clinical trial, called the CHIASMA OPTIMAL trial under the FDA's SPA procedures. This trial was initiated in September 2017, and we announced positive top-line data in July 2019. Based on the positive results from the CHIASMA OPTIMAL trial, we resubmitted our NDA seeking approval of octreotide capsules as a maintenance therapy for adult patients with acromegaly to the FDA. In January 2020, the FDA accepted for review the resubmission of the NDA as a complete response to deficiencies identified in the CRL to our original NDA and assigned a target action date of June 26, 2020 under the PDUFA. However, there can be no assurance that the FDA will approve our NDA in a timely manner or at all. If we successfully secure regulatory approval in acromegaly, we may also consider clinical trials of octreotide capsules in indications other than acromegaly, assuming financing is available to us. 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 past, current or future trials, such as the MPOWERED trial, can adversely affect prospects of securing regulatory approval or 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, including the CHIASMA OPTIMAL Phase 3 trial, do not ensure that future clinical trials, including the MPOWERED Phase 3 trial designed to support EMA approval, 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. While 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, the FDA agreed that we use IGF-1 £ 1.0 times the upper limit of normal in the CHIASMA 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 CHIASMA OPTIMAL Phase 3 clinical trials, and the ability for the data from each trial to support regulatory approval. We cannot provide assurance that the FDA or EMA will view the results as we do or that any of our ongoing or future trials of octreotide capsules, including our MPOWERED Phase 3 clinical trial in acromegaly, or any clinical trials we may conduct 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 current or 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, differences in evaluation period, and varying patient characteristics, including demographic factors and health status. If later-stage clinical trials, such as MPOWERED, do not produce favorable results, it will raise substantial doubt about our ability to achieve regulatory approval of octreotide capsules for the treatment of acromegaly or other indications.

Further, our resubmitted NDA relies 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 the European Union. 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 as a treatment for acromegaly in the European Union, the clinical trials of octreotide capsules for other indications we may pursue, 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 increase our product development costs and jeopardize our ability to commercialize octreotide capsules. For example, if the topline data from the Phase 3 MPOWERED clinical trial, which we expect to report in the fourth quarter of 2020, are negative, those data could negatively impact the commercial prospects for octreotide capsules in the U.S., if FDA approval is obtained.

Furthermore, 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 enrollment and randomization are complete, we do not know whether the MPOWERED Phase 3 trial will be completed on schedule or will be successful. In light of the FDA's position that the MPOWERED clinical trial would 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 that were necessary to conduct the CHIASMA OPTIMAL Phase 3 trial. The modifications to the MPOWERED trial, together with our decision in October 2018 to enroll 15 additional patients, delayed the expected timing of an MAA submission with the EMA. We now expect top-line data from the MPOWERED study in the fourth quarter of 2020. The completion of the MPOWERED Phase 3 trial or other clinical trials we may conduct could 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, as well as other ongoing clinical trials in adult acromegaly patients;
- 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 and as was observed in a recent regulatory inspection at the time of our NDA resubmission, 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 or a failure to successfully manufacture qualifying clinical trial supplies of oral octreotide capsules or placebo;
- 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;
- 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 trials 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 original 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.

Changes in funding for, or leadership at, or disruptions at the FDA, the SEC and other government agencies could hinder their ability to hire and retain key personnel, prevent new products and services from being developed, approved or commercialized in a timely manner or otherwise prevent those agencies from performing normal functions on which the operation of our business may rely, which could negatively impact our business.

The ability of the FDA to review and approve new products or take action with respect to other regulatory matters can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept payment of user fees, and statutory, regulatory and policy changes. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of the SEC, the FDA and other government agencies on which our business relies is subject to the political process, which is inherently fluid and unpredictable.

Disruptions at the FDA and other agencies may also slow the time necessary for new drugs to be reviewed and/or approved, or for other actions to be taken, by relevant government agencies, which would adversely affect our business. For example, over the last several years, including for 35 days beginning on December 22, 2018, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA and the SEC, have had to furlough critical FDA, SEC and other government employees and stop critical activities. In addition, the FDA recently announced that it has postponed most foreign inspections through April 2020 in response to the

recent outbreak of the novel coronavirus COVID-19. If a prolonged government shutdown or other disruption occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, including our NDA resubmission for octreotide capsules as a treatment for acromegaly currently under review by the FDA, which could have a material adverse effect on our business. Moreover, changes in leadership at the FDA could have an adverse impact on our ability to receive regulatory approval for octreotide capsules in the United States. Similarly, a prolonged government shutdown or other disruption could prevent the timely review of patent applications by the United States Patent and Trademark Office, or USPTO, which could delay the issuance of any U.S. patents to which we might otherwise be entitled. Further, in our operations as a public company, future government shutdowns could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations.

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 or they are unwilling to enroll and stay in a clinical trial with a placebo-controlled design, 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 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 the United States, 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 the European Union. The same limitation was true for our CHIASMA OPTIMAL trial. Further, in light of the FDA's position that the MPOWERED clinical trial would not be sufficient to address the concerns in the CRL, we modified certain elements of the MPOWERED trial in an effort to preserve patients, sites and other resources necessary to conduct the CHIASMA OPTIMAL Phase 3 trial.

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;
- perceived risks and benefits of the product candidate under trial;
- possibility of receiving placebo rather than active drug in certain controlled trials, such as was the case in the CHIASMA OPTIMAL trial;
- eligibility criteria for the trial in question;
- possibility of being randomized back to current injectable therapies, such as in the MPOWERED trial, or rescued back to current injectable therapies following a loss of biochemical and symptom control, such as was the case in the CHIASMA 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 that we may develop in lieu of prescribing existing treatments that have established safety and efficacy profiles. We may not be able to initiate or continue clinical trials if we cannot enroll a sufficient number of eligible patients to participate in the clinical trials required by the FDA, the EMA or other regulatory authorities. Our ability to successfully initiate, enroll and complete a clinical trial in any foreign country is subject to numerous risks unique to conducting business in foreign countries, including the:

- difficulty in establishing or managing relationships with CROs and physicians;
- different requirements and standards for conducting clinical trials;
- inability to locate qualified local consultants, physicians and partners; and
- potential burden of complying with a variety of foreign laws, medical standards and regulatory requirements, including the regulation of pharmaceutical and biotechnology products and treatments.

Even if we receive regulatory approval of our NDA resubmission for octreotide capsules as a treatment for acromegaly, we must obtain regulatory approval of at least one of our two planned prior approval manufacturing supplements and may still face additional future development and regulatory challenges, each of which could inhibit or preclude our ability to commercialize octreotide capsules for any indication.

Assuming we obtain the FDA's approval of our NDA, in order to have octreotide capsules available for our planned commercial launch in the fourth quarter of 2020, we must also obtain the FDA's approval of either one of our two planned prior approval manufacturing supplements for our sources of commercial API. If we are unable to obtain or are delayed in obtaining regulatory approval of our NDA and either one of our two planned prior approval manufacturing supplements, we could be prevented from commercializing the product candidate in a timely manner or at all. Further, even if we obtain regulatory approval of our NDA resubmission for octreotide capsules as a 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 or exclude the symptom improvement data observed in our first completed Phase 3 clinical trial, 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. The third-party contract manufacturers that we utilize or plan to utilize for commercial supply have been subject to ongoing regulatory inspections from time to time that resulted in inspectional observations. For example, in the CRL, the FDA advised that, during a site inspection, certain deficiencies were conveyed to the representative of one of our suppliers. In addition, in connection with the resubmission of our NDA, we did not reference in the NDA resubmission our planned primary commercial API manufacturer due to unresolved observations from a recent regulatory inspection. If we or a regulatory authority discover any new or previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or with any 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.

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, similar data was produced in the CHIASMA OPTIMAL trial, or may also occur in the MPOWERED clinical trial. Competition could also force us to lower prices or could result in reduced sales.

The standards of care for patients suffering from acromegaly all involve injectable therapies, other than cabergoline, an oral agent used for the treatment of mild acromegaly. Novartis markets octreotide LAR, which is administered monthly and intramuscularly using a large gauge needle. Ipsen markets lanreotide, another long-acting analog of somatostatin, like octreotide, which is administered monthly using a deep subcutaneous injection. Pfizer markets pegvisomant daily injections and Recordati also markets pasireotide LAR, which is another somatostatin analog administered via intramuscular injection. Generic versions of these drugs may also bring additional competition to the treatment landscape. For example, while octreotide LAR and lanreotide currently have no generic competitors in the United States, generic versions are available in some markets in the European Union. In addition, we are aware of other companies involved in early-stage nonclinical and clinical studies of similar somatostatin analogs. Most notably, Camurus AB is developing CAM2029, a subcutaneous octreotide depot for the potential treatment of neuroendocrine tumors and acromegaly. Camurus AB received FDA approval of its IND in June 2019 to initiate a Phase 3 acromegaly trial. MidaTech Pharma PLC also conducted its first in human study and also recently initiated a Phase 1 study of Q-Octreotide (MTD201), Midatech's injectable treatment for acromegaly built on its Q-Sphera sustained release platform technology. In 2019, Crinetics Pharmaceuticals, Inc. announced the initiation of two Phase 2 clinical trials to evaluate the safety and efficacy of CRN00808 in acromegaly patients. CRN00808 is a nonpeptide somatostatin agonist designed to be taken orally once per day. In May 2017, Dauntless Pharmaceuticals, Inc., a privately held biopharmaceutical company, announced positive results from its two-part, Phase 1 pharmacokinetic/pharmacodynamic study evaluating DP1038, a novel formulation of octreotide acetate for intranasal administration. In 2018, Ionis Pharmaceuticals initiated a Phase 2 trial of IONIS-GHR-$_{RX}$, its growth hormone receptor antagonist to control growth hormone production in acromegaly patients. In January 2020, Rani Therapeutics (RaniPill™ capsule containing octreotide) announced the completion of a Phase 1 study in 58 healthy volunteers, indicating that the RaniPill performed as designed. Per published reports, Rani Therapeutics plans to conduct a head-to-head study in acromegaly patients and demonstrate equivalence or non-inferiority to the injectable version of octreotide sc. We are also aware that Strongbridge Biopharm (valdoreotide or COR-005) may also be actively developing products for the maintenance treatment of acromegaly. If any or a combination of CAM2029, MTD201, CRN00808, DP1038, IONIS-GHR-$_{RX}$, RaniPill or the other products in development for acromegaly receive regulatory approval before, or in a similar timeframe as, our octreotide capsules, or demonstrate superior clinical results to octreotide capsules, we may encounter significant difficulties with our commercial launch of octreotide capsules.

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 either a somatostatin analog or non-somatostatin analog or other technology that could make administration of peptide-based therapies more convenient. If we are unable to compete effectively, our opportunity to generate revenue from the sale of octreotide capsules or any future product candidates we may develop, if approved, could be impaired.

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

We estimate that there are an estimated 69,000 individuals with acromegaly in the developed world. 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, 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. Data from a 2017 study by Lavrentaki et. al. suggest that the global prevalence of acromegaly may be between 28 and 137 cases per million people. Based upon our own market research, 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 the regulatory approvals necessary to commercialize octreotide capsules, it may not achieve or maintain 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 we obtain the necessary regulatory approvals, will depend in large part on the willingness of physicians to prescribe them to their patients. If we obtain the necessary regulatory approvals to commercialize octreotide capsules, the product will compete against products that have achieved broad recognition and acceptance among medical professionals. In order to achieve and maintain an acceptable level of prescriptions for octreotide capsules, if we obtain the necessary regulatory approvals, 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 we obtain the necessary regulatory approvals, will depend on a number of factors, including:

- the clinical safety, efficacy, tolerability and other factors regarding octreotide capsules observed in our completed ongoing and potential future clinical trials, including relative to injectable somatostatin analogs such as the relative topline data from our MPOWERED trial expected in the fourth quarter of 2020, and any other treatments available at the time;
- 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 and adhere to them;
- 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, particularly compared to alternative treatments;
- the effectiveness of our or any future collaborators' sales and marketing, as well as disease education and awareness programs;
- limitations or warnings contained in labeling approved by the FDA or comparable foreign regulatory authorities;
- our ability to obtain and maintain sufficient third-party coverage and adequate reimbursement from government health care programs, including Medicare and Medicaid, private health insurers and other third-party payors;
- the willingness of patients to pay out-of-pocket in the absence of third-party coverage or reimbursement;
- competitor activities; and
- our ability to reliably manufacture and supply octreotide capsules.

In addition, even if we obtain the necessary 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 our plan to submit prior approval manufacturing supplements for the approval of the sources of commercial API required in order to have octreotide capsules available for our planned commercial launch, 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. While we believe that our completed first Phase 3 clinical trial demonstrated acromegaly symptom improvements in patients who completed the trial, we believe there is a substantial likelihood that the FDA may not include this data in an approved label, if any, for oral octreotide due to the CRL, and the CHIASMA OPTIMAL trial was not designed to, and did not, demonstrate validated symptom improvement data. While the MPOWERED trial employs a validated treatment satisfaction

questionnaire for patient completion, the final symptom and treatment satisfaction data may be negative when comparing oral octreotide capsules to standard of care somatostatin analog injectables. The symptom data from our Phase 3 trials, even if deemed positive, may not be contained in our octreotide capsules product label, if approved. Any of the foregoing scenarios could harm the commercial prospects for octreotide capsules.

Even if octreotide capsules are approved and commercialized in one or more geographies, they may not achieve and maintain 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. Any concerns about or negative perception of octreotide capsules or the clinical data of octreotide capsules within the patient or medical communities 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 or European Union in the future. The perception of octreotide capsules within the patient and medical communities could be negatively impacted by clinical data from ongoing or future clinical studies, including comparative safety and efficacy data from the MPOWERED trial from which topline data is expected in the fourth quarter of 2020, as well as by real-world data on acromegaly treatments that we expect will be generated from our disease state registry for acromegaly. Our revenue and profitability may also be delayed during the potential 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 capsules decreases, we may not generate sufficient revenue.

We do not have a sales organization and only recently established marketing and market access organizations and, as a company, have not commercialized any products. If we are able to secure regulatory approvals for commercializing octreotide capsules as a treatment for acromegaly but are unable to establish effective sales and marketing capabilities in the United States and access them in the European Union and other international markets, we may not succeed in commercializing octreotide capsules.

We essentially do not have sales personnel and have only recently hired marketing and market access personnel.
We have not engaged a partner to commercialize octreotide capsules in the United States, if we obtain the necessary regulatory approvals and, therefore, we currently intend to build our sales and marketing infrastructure to support commercial launch in the United States, assuming our NDA is approved. If we obtain the necessary regulatory approvals to commercialize octreotide capsules when we expect, our sales, market access and marketing teams will have worked together for only a limited period prior to our anticipated commercial launch of octreotide capsules. We cannot guarantee that we will be successful in marketing octreotide capsules in the United States. We may not be able to establish a direct sales force in a cost-effective manner or realize a positive return on this investment. In addition, we will have to compete with other pharmaceutical and biotechnology companies to recruit, hire, train and retain sales, market access and marketing personnel. Factors that may inhibit our efforts to successfully commercialize octreotide capsules in the United States ourselves include:

- our inability to recruit and retain adequate numbers of effective sales, market access and marketing personnel;
- the inability of our relatively small planned sales force to obtain access to or inform adequate numbers of physicians, particularly the pituitary centers and the significantly larger number of community endocrinologists, about the potential benefits of octreotide capsules;
- the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines;
- the inability to compete with larger, more established pharmaceutical sales and marketing organizations;

- the inability of market access personnel to obtain sufficient levels of pricing and reimbursement in each jurisdiction; and
- unforeseen costs, expenses and delays associated with creating a commercial organization.

Even if we are able to obtain the regulatory approvals for commercializing octreotide capsules, 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 other commercial personnel on a timely basis or rebuilding a sales, market access and marketing infrastructure, or if we do not successfully enter into appropriate collaboration arrangements, we will have difficulty commercializing octreotide capsules, if we obtain the necessary regulatory approvals, 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 the European Union 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 commercialize octreotide capsules in the United States;
- 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, including significantly lower prices for existing somatostatin analog injectables in European and other markets as well as the recent entry of generic somatostatin analog injectables into European markets, which could adversely affect our pricing in the European Union and 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;
- foreign currency exchange rate fluctuations;
- our 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.

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, European Union or elsewhere.

We have only recently established a medical affairs organization and, as a company, have limited experience in operating a medical affairs organization. If we are unable to establish effective medical affairs capabilities in the United States and build or access them in the European Union and other international markets, our business may suffer.

We have only recently established our 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 us, our product candidates, our disease areas of interest, or our 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 us execute plans for expansion into Europe or other international markets.

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

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

significant undertaking that requires substantial financial and managerial resources. As of March 9, 2020, we had 48 full-time employees. As our development and commercialization plans and strategies evolve, we will need to expand the size of our employee base for managerial, operational, sales, marketing, financial and other resources. The recruitment and hiring of these personnel will take time and could delay the commercialization of octreotide capsules. Future growth would impose significant added responsibilities on members of management, including the need to identify, recruit, maintain, motivate and integrate additional employees. Also, our management may have to divert a disproportionate amount of its attention away from our day-to-day activities and devote a substantial amount of time to managing these growth activities. Our future financial performance and our ability to commercialize octreotide capsules and other product candidates we may develop and to compete effectively will depend, in part, on our ability to effectively manage any future growth and related costs. We may not be able to effectively manage a rapid pace of growth and timely implement improvements to our management infrastructure and control systems.

We will need to build an effective healthcare compliance program to support the sales and marketing of an approved drug in a manner that is compliant with applicable laws and regulations.

Our marketing of pharmaceutical products is subject to extensive and complex laws and regulations. We are building a corporate compliance program designed to actively identify, prevent and mitigate risk through the implementation of compliance policies and systems, and through the establishment and communication of a culture of compliance. Among other laws, regulations and standards, we are subject to various U.S. federal and state laws, and comparable foreign laws pertaining to health care fraud and abuse, including anti-kickback and false claims statutes, laws prohibiting the promotion of drugs for unapproved or off-label uses, and laws requiring transparency regarding transfers of value to health care professionals and entities. Anti-kickback laws make it illegal for a prescription drug manufacturer to solicit, offer, receive or pay any remuneration to induce the referral of business, including the purchase or prescription of a particular drug; false claims laws prohibit anyone from presenting for payment to third-party payors, including Medicare and Medicaid, claims for reimbursed drugs or services that are false or fraudulent, claims for items or services not provided as claimed, or claims for medically unnecessary items or services; and the Sunshine Act and other state and federal transparency laws require certain pharmaceutical manufacturers to track and report certain financial arrangements with physicians and teaching hospitals, including certain “transfers of value” provided to them, as well as certain ownership or investment interests held by physicians and their immediate family members. Although effective compliance programs can mitigate the risk of investigation and prosecution for violations of these laws, these risks cannot be entirely eliminated. We expect to devote substantial resources to develop, administer and grow this compliance program, but we may not be able to develop and implement it rapidly enough to keep pace with the rapid growth and activity of the commercial organization.

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, including 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. In addition, any action against us for an alleged or suspected violation could cause us to incur significant legal expenses and could divert our management's attention from the operation of our business, even if our defense is successful. For example, the marketing and promotion of authorized products, including industry-sponsored continuing medical education and advertising directed toward the prescribers of drugs, are strictly regulated in the European Union under Directive 2001/83EC, as amended. The advertising of prescription-only medicines to the general public is not permitted in the European Union.

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 API, for octreotide capsules. The third-party contract manufacturers that we utilize or plan to utilize for commercial supply have been subject to regulatory inspections from time to time that resulted in inspectional observations. For example, in the CRL, the FDA advised that, during a site inspection, certain deficiencies were conveyed to the representative of one of our suppliers. In addition, we did not reference in the NDA resubmission our planned primary commercial API manufacturer due to unresolved observations from a recent regulatory inspection. We expect that our suppliers will be subject to additional regulatory inspections in the future, including in connection with the FDA's review of the NDA we resubmitted seeking approval of octreotide capsules as a treatment for acromegaly and in connection with its review of our planned prior approval manufacturing supplements. 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 such as those we expect to propose by submitting our planned prior approval manufacturing supplements to the FDA, may require prior FDA review and approval of the manufacturing process and procedures in accordance with the FDA's cGMP requirements. 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 planned commercial launch of our product.

Furthermore, in order to obtain approval of our current or future 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. Even if we obtain approval of our NDA from the FDA, in order to secure sources of commercial quantities of API to support our planned commercial launch of octreotide capsules, following the June 26, 2020 PDUFA date, we plan to submit to the FDA two prior approval manufacturing supplements for sources of commercial API. The review of any prior approval manufacturing supplement to the NDA will require FDA review and approval of the manufacturing process, facility, equipment and procedures in place at each manufacturing site in accordance with the FDA's cGMP requirements and may require regulatory inspections of each manufacturing site, which could prevent or delay approval of any such prior approval manufacturing supplement. If we are unable to obtain approval of our NDA and one of the two prior approval manufacturing supplements, we may be unable to secure API and the finished oral octreotide product in commercial quantities and our commercialization efforts may be harmed. The timing of the FDA's review process related to our planned prior approval manufacturing supplements and the outcome of such review are inherently uncertain, and we can provide no assurances that either planned prior approval manufacturing supplement will be approved in a timely manner or at all.

In addition, we expect our primary supplier for commercial API will require additional qualified capacity to meet future demand and each of our planned API suppliers may use a different method to manufacture API, which has the potential to increase the risk to us that our manufacturers will fail to meet our commercial demand for API or applicable regulatory requirements. If we obtain the necessary regulatory approvals to commercialize octreotide capsules, 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, product development and commercialization objectives. These milestones may include our expectations regarding the commencement or completion of clinical trials, the submission of regulatory filings, or initiation of commercialization. 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, submission of a marketing application for approval, 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 the design and conduct of our clinical trials;

- 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, including regulatory approvals, in the timeframes we announce and expect, the commercialization of octreotide capsules and any future product candidates we may develop may be prevented or 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.

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 in the future. 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, as well as the relative pricing of competing injectable somatostatin analogs 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 about the product candidate, including those raised in the CRL, End of Review meeting or by the FDA's review of data from the CHIASMA OPTIMAL trial or the MPOWERED trial. For example, we expect to report top-line data from the MPOWERED clinical trial in the fourth quarter of 2020, which will provide biochemical control data (GH and IGF-1) of octreotide capsules as compared to the standard of care injectable somatostatin analogs, octreotide LAR and lanreotide depot, as well as patient treatment satisfaction and symptom control data. If octreotide capsules are approved in the United States, and reported MPOWERED data is unfavorable, the reimbursement rates and market potential for octreotide capsules could be severely limited. Conversely, if octreotide capsules are not approved in the United States because, among other things, the FDA determines that the CHIASMA OPTIMAL trial results do not support approval, but we nevertheless receive regulatory approval in the European Union based upon data from the MPOWERED trial, the failure to obtain regulatory approval in the Unites States could impact reimbursement rates or reduce the willingness of physicians to prescribe octreotide capsules. Any such restrictions or potential reservations about efficacy expressed by the FDA, the EMA, 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, competitive pricing pressures, including potential generic entrants, 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 and will often consider the reimbursement levels of competing marketed standards of care. For example, injectable somatostatin analogs currently marketed in the European Union are reimbursed at levels that are far less than in the United States on a per patient, per year basis. The pricing of octreotide capsules in the European Union, if approved, will likely be determined by government payors following an assessment of the relative efficacy, safety and benefits of octreotide capsules versus standard of care somatostatin analog injections. We believe the MPOWERED trial will provide the information required to make these assessments, and if octreotide capsules are deemed inferior to standard of care injectable somatostatin analogs, octreotide capsules may lose its orphan designation in the European Union and receive pricing determination decisions at levels that are less than standard of care injectables, which would severely impact our ability to profitably market octreotide capsules in the European Union. 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. Future U.S. pharmaceutical pricing regulations may require that the U.S. price for octreotide capsules, if approved, be referenced to the lower or lowest price levels of the product as set in other ex-U.S. countries, which reference pricing impact could significantly harm our business.

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 potentially 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 as a treatment for 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 now have only limited 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 materially 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 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 acquisition, license or similar 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 acquiring or licensing product candidates, discovery programs or other technologies from third parties or licensing our TPE technology to third parties.

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 or endocrinology 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, business development or commercial sales 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 or if we are unable to obtain the necessary regulatory approvals to commercialize octreotide capsules in the United States or unable to successfully commercialize octreotide capsules in the United States, in each case, in a timely manner or at all third-party confidence in our TPE platform could be reduced and potentially make us a less attractive partner.

In addition, even if we are able to successfully license or acquire suitable technology from third parties, there can be no assurance that we will be able to successfully develop product candidates from such technology or receive necessary approvals to commercialize any such product candidates.

We only have limited human and financial resources to develop suitable potential product candidates through internal research programs, we may not have the resources to obtain rights to technologies or product candidates 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, as amended, the FDA may designate a product candidate as an orphan drug if it is intended to treat a rare disease or condition, which is generally defined as having a patient population of fewer than 200,000 individuals diagnosed annually in the United States, or a patient population greater than 200,000 in the United States where there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the United States. In the European Union, the European Commission, after reviewing the opinion of the EMA's Committee for Orphan Medicinal Products, or COMP, grants orphan drug designation to promote the development of products that are intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition affecting not more than five in 10,000 persons in the European Union. Additionally, designation is granted for products intended for the diagnosis, prevention or treatment of a life-threatening, seriously debilitating or serious and chronic condition when, without incentives, it is unlikely that sales of the drug in the European Union would be sufficient to justify the necessary investment in developing the product candidate. Even if we request orphan drug designation for any future product candidates we may develop, there can be no assurances that the FDA or the European Commission will grant any of these product candidates such designation. Additionally, the designation by the FDA or the European Commission 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 the European Union. 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 as a potential treatment for 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 such 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. Similarly, the European Commission may grant a marketing authorization for a similar medicinal product in the same therapeutic indication if the second applicant can establish that although their product is similar to the orphan medicinal product already authorized, the second product is safer, more effective or otherwise clinically superior.

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;
- 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;
- the federal Physician Payments Sunshine Act requires certain manufacturers of drugs, devices, biologics, and medical supplies for which payment is available under Medicare, Medicaid, or the Children's Health Insurance Program, with specific exceptions, to report annually to the CMS information related to payments or transfers of value made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals, as well as information regarding ownership and investment interests held by the physicians described above 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.

Some of the provisions of the ACA have yet to be fully implemented, while certain provisions have been subject to judicial and Congressional challenges. As a result of tax reform legislation passed in December 2017, the individual mandate has been eliminated effective January 1, 2019. Various portions of the ACA are currently undergoing legal and constitutional challenges in the Fifth Circuit Court and the United States Supreme Court; the Trump Administration has issued various Executive Orders which eliminated cost sharing subsidies and various provisions 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; and Congress has introduced several pieces of legislation aimed at significantly revising or repealing the ACA. It is unclear whether the ACA will be overturned, repealed, replaced, or further amended. We cannot predict what affect further changes to the ACA would have on our business.

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 2029 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.

Product liability lawsuits could cause us to incur substantial liabilities and limit potential commercialization of our product candidates, and 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 face an inherent risk of product liability exposure related to the testing of product candidates in human clinical trials and will face an even greater risk if we commercially sell any drugs that we may develop. For example, we may be sued if any drug we develop allegedly causes injury or is found to be otherwise unsuitable during clinical testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability or a breach of warranties. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against claims that our product candidates or drugs caused injuries, we will incur substantial liabilities or be required to limit commercialization of our product candidates. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for any product candidates or drugs that we may develop;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- initiation of investigations by regulators;
- product recalls, withdrawals or labeling, marketing or promotional restrictions;
- significant costs to defend the related litigation;
- substantial monetary awards to trial participants or patients;

- loss of revenue;
- reduced resources of our management to pursue our business strategy;
- potential disputes, including litigation, with our insurance provider regarding coverage and
- the inability or significant limitations on the ability to commercialize any drugs that we may develop.

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.

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. The octreotide API is lyophilized, formulated with our TPE technology by Lyophilization Services of New England Inc., or LSNE, in Bedford, NH, and enteric-coated and blister packed by Capsugel, a division of Lonza, in Scotland. Almac Pharma Services Limited in Northern Ireland provides finished packaging and release services.

The facilities used by our contract manufacturers to manufacture octreotide capsules are evaluated by the FDA and other regulatory bodies. We 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. The third-party contract manufacturers that we utilize or plan to utilize for commercial supply have been subject to regulatory inspections from time to time that resulted in inspectional observations. 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. However, we were informed in late 2016 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. In addition, we did not reference in the NDA resubmission our planned primary commercial API manufacturer due to unresolved observations from a recent regulatory inspection. We expect that our suppliers will be subject to additional regulatory inspections in the future, including in connection with the FDA's review of the NDA we resubmitted seeking approval of octreotide

capsules as a treatment for acromegaly and in connection with the review of our planned prior approval manufacturing supplements. There can be no assurances that our suppliers will pass all necessary inspections, the failure of which could result in delays to our ability to receive regulatory approval for octreotide capsules.

Our NDA resubmission that was accepted by the FDA in January 2020 for review references one small-scale API manufacturer that was included in our original NDA and is owned by our planned secondary commercial API manufacturer. However, we do not expect to procure commercial API from this small-scale manufacturing site. Accordingly, even if we obtain approval of our NDA from the FDA, in order to commercially launch octreotide capsules, following the June 26, 2020 PDUFA date, we plan to submit to the FDA a prior approval manufacturing supplement to the NDA to provide for the approval of our primary API manufacturer and one of its large-scale manufacturing sites that was included in our original NDA. We also plan to concurrently file a second prior approval manufacturing supplement to the NDA to provide for a large-scale manufacturing site affiliated with the small-scale manufacturing site currently referenced in the NDA resubmission. If we are unable to obtain or delayed in obtaining regulatory approval of our NDA and either one of our two planned prior approval manufacturing supplements, we could be prevented from commercializing the product candidate in a timely manner or at all. The review of any prior approval manufacturing supplement to the NDA will require FDA review and approval of the manufacturing process, facility, equipment and procedures in place at each manufacturing site in accordance with the FDA's cGMP requirements and may require regulatory inspections of each manufacturing site, which could prevent or delay approval of any such prior approval manufacturing supplement and prevent or delay our planned commercial launch. The timing of the FDA's review process related to our planned prior approval manufacturing supplements and the outcome of such review are inherently uncertain, and we can provide no assurances that either planned prior approval manufacturing supplement will be approved in a timely manner or at all.

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 their inability to increase and maintain their capacity to meet our commercial demand, could impair our ability to supply octreotide capsules at required levels. Because of the significant regulatory requirements that are necessary to qualify a new API or finished product manufacturer or to qualify a new or existing site for a current manufacturer, which we plan to do by submitting prior approval manufacturing supplements for our planned sources of commercial API, we could experience significant interruptions in the supply of octreotide capsules if such regulatory qualifications are withheld or delayed, especially if we decided to transfer the manufacture of API or finished octreotide capsules to one or more alternative manufacturers in an effort to deal with any manufacturing, qualification or other difficulties.

Any manufacturing problem or the loss of a contract manufacturer or our failure to obtain FDA approval of at least one of our planned prior approval manufacturing supplements 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.

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 or increase, these costs may significantly impact our future operating results. In order to reduce costs and improve efficiencies, we plan to develop and implement process improvements and produce octreotide capsules at a larger scale. 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 produce sufficient quantities of octreotide capsules or reduce our costs over time, which could be detrimental to the profitability of octreotide capsules in any market, and particularly the EU market where substantially lower prices are expected if we are able to secure marketing approvals for octreotide capsules there.

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. Following our receipt of the CRL in 2016, we indefinitely suspended our commercial production commitments and only recently reinitiated commercial production planning with these suppliers and expect to amend our commercial supply agreement with Teva API. We have also more recently entered into commercial supply agreements with Lonza and Almac. 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 or commercial 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.

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 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 identified conditions that raise substantial doubt about our ability to continue as a going concern.

We may be forced to amend, delay, limit, reduce or terminate the scope of our development program or commercialization efforts or limit or cease our operations if we are unable to obtain additional funding. As of December 31, 2019, we had cash, cash equivalents and marketable securities totaling approximately $92.4 million. Based on our current operating plans, we do not have sufficient cash, cash equivalents and marketable securities to fund our operating expenses, inventory purchases and capital expenditures for at least the next 12 months from the filing date of this Annual Report. We will require additional capital to sustain our operations, including our potential commercial launch. Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity and debt financings, and we will also opportunistically consider license and collaboration agreements with potential partners and other non-dilutive financing arrangements. However, there can be no assurance that we will be able to complete any such transaction on acceptable terms or otherwise. 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 efforts or preparations for our anticipated commercial launch of oral octreotide capsules. The failure to obtain sufficient funds on commercially acceptable terms when needed would have a material adverse effect on our business, results of operations and financial condition. These factors raise substantial doubt about our ability to continue as a going concern.

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. As of December 31, 2019, our cash, cash equivalents and marketable securities were $92.4 million. Since inception, we have incurred significant operating losses. Our net loss was $36.3 million and $31.3 million for the years ended December 31, 2019 and 2018, respectively. As of December 31, 2019, we had an accumulated deficit of $272.9 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. We expect to incur significant additional costs conducting and completing our MPOWERED clinical trial, to fund our operations in support of this clinical trial, to pursue regulatory approvals,

to prepare for commercialization and to manufacture and commercialize octreotide capsules, if regulatory approval is obtained. In addition, we will continue to incur additional costs associated with operating as a public company. As a result of these and other factors, we expect to continue to incur significant operating losses for the foreseeable future. Because of the numerous risks and uncertainties associated with developing and commercializing pharmaceutical products, we are unable to predict the extent of any future losses, 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 the necessary regulatory approvals for marketing octreotide capsules or any future product candidates we may develop are obtained from the FDA, 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 obtain regulatory approval of our planned commercial contract manufacturers and manufacturing sites, to contract for the manufacture of commercial quantities of our product candidates at acceptable cost levels and establish sales, market access and marketing capabilities or identify and enter into one or more strategic collaborations to effectively market and sell any approved product candidate.

Even if we obtain regulatory approvals for octreotide capsules or any future product candidates and launch the commercial sale, any approved product may not gain market acceptance or achieve commercial success. In addition, we anticipate incurring significant costs associated with commercializing octreotide capsules if we obtain the necessary regulatory approvals and would anticipate incurring significant costs associated with commercializing any other approved product. We may not achieve profitability soon after generating product sales, if ever. If we are unable to generate sufficient levels of 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. Our oral octreotide capsules product candidate is our only product candidate for which we have conducted clinical trials. We have completed only two Phase 3 clinical trials to date with this product candidate, and we are currently conducting one additional Phase 3 clinical trial of octreotide capsules in acromegaly. We have not yet demonstrated our ability to successfully obtain regulatory approvals, manufacture a commercial-scale drug or arrange for a third party to do so on our behalf, or conduct sales, market access 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 all necessary regulatory approvals of octreotide capsules in acromegaly in the United States, we will need to transition from a company with a development focus to a company capable of supporting commercial activities. We may not be successful in such a transition in the United States, which is planned in 2020, or in the European Union or elsewhere.

As we continue to build our business, we expect our financial condition and operating results may fluctuate significantly from quarter to quarter and year to year due to a variety of factors, many of which are beyond our control. Accordingly, stockholders should not rely upon the results of any particular quarterly or annual periods as indications of future operating performance.

We will need additional capital to support our operations, including our product development efforts and preparations for our anticipated commercial launch, 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 establish the infrastructure and manufacture the commercial supply for a planned commercial launch of octreotide capsules in the United States in the fourth quarter of 2020 subject to obtaining the necessary regulatory approvals, and conduct and complete our MPOWERED clinical trial, for which we expect top-line data in the fourth quarter of 2020. Because the outcome of any clinical trial, regulatory approval process and commercialization efforts is highly uncertain, we cannot reasonably estimate the actual amounts necessary to successfully complete the development, regulatory approval process and commercialization of oral octreotide capsules. In addition, as noted above, we have identified conditions that raise substantial doubt as to our ability to continue as a going concern if we are unable to obtain funding on a timely basis. 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 efforts or preparations for our anticipated commercial launch of oral octreotide capsules.

Based on our current operating plans, we do not have sufficient cash, cash equivalents and marketable securities to fund our operating expenses, inventory purchases and capital expenditures for at least the next 12 months from the filing date of this Annual Report. We will require additional capital to sustain our operations, including our potential commercial launch. 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 as a treatment for acromegaly and obtain FDA approval of our planned prior approval manufacturing supplements for our commercial API manufacturing sources, and to conduct and complete our MPOWERED clinical trial;
- the amount of our future operating losses;
- the costs associated with establishing the infrastructure to support our planned commercial launch of octreotide capsules;
- 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 product 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 or commercialization of octreotide capsules, if approved, 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, debt financing, strategic collaboration agreements and other capital raising arrangements. 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 standalone business, materially impair our ability to remain in business and have a material adverse effect on our business, financial condition and results of operations.

Unstable market and economic conditions may have serious adverse consequences on our business, financial condition and stock price.

As widely reported, global credit and financial markets have experienced recent volatility and disruptions, including diminished liquidity and credit availability, predicted declines in economic growth, and uncertainty about economic stability. There can be no assurance that further deterioration in credit and financial markets and confidence in economic conditions will not occur. Our general business strategy may be adversely affected by any such economic downturn, volatile business environment or continued unpredictable and unstable market conditions. If the current equity and credit markets deteriorate, it may make any necessary debt or equity financing more difficult, more costly and more dilutive for us to achieve. Failure to secure any necessary financing in a timely manner and on favorable terms could have a material adverse effect on our growth strategy, financial performance and stock price and could require us to delay or abandon clinical development and commercialization plans. In addition, there is a risk that one or more of our current service providers, manufacturers and other partners may be negatively impacted or not survive an economic downturn, which could directly affect our ability to attain our operating goals.

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 transactions or other capital raising 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

Pandemics such as the coronavirus could have an adverse impact on our business and our financial condition.

In December 2019, a novel strain of coronavirus was first identified in Wuhan, Hubei Province, China. Any outbreak of contagious diseases, or other adverse public health developments, could have a material and adverse effect on our business operations. These could include disruption to our regulatory approval timelines due to diversion of government resources, delays in planned commercialization efforts due to manufacturing delays, slowed hiring of commercial personnel or other issues, restrictions on our ability to travel, participate in industry conferences, pursue partnerships and other business transactions, disruption of to our clinical trials, as well as impacts from the temporary closure of the facilities of suppliers and clinical trial sites or an overburdened healthcare system. Any disruption of regulators, physicians, suppliers, clinical trial sites or access to patients could impact our regulatory approval timing, commercialization efforts as well as our ability to access capital through the financial markets. The extent to which the coronavirus impacts our business will depend on future developments, which are highly uncertain and cannot be predicted, including new information which may emerge concerning the severity of the coronavirus and the actions to contain the coronavirus or treat its impact, among others.

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 March 9, 2020, we have a total of 48 full-time employees. In order to induce valuable employees to remain with us, we have provided employees with stock options that vest over time. The value to employees of stock options that vest over time is significantly affected by movements in our stock price that we cannot control and, together with our other compensation programs and benefits, may at any time be insufficient to counteract more lucrative offers from other companies.

We are highly dependent upon the principal members of our management team. These executives have significant commercial, research and development, regulatory, industry, operational, and/or corporate finance experience. 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.

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, products or technologies, 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 as a treatment for acromegaly. We cannot assure you that unforeseen problems will not develop with our TPE technology or applications thereof 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. We have 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. Cyber-attacks could include the deployment of harmful malware and key loggers, ransomware, a denial-of-service attack, a malicious website, the use of social engineering and other means to affect the confidentiality, integrity and availability of our technology systems and data. The risk of a security breach or disruption, particularly through cyber-attacks or cyber intrusion, including by computer hackers, foreign governments, and cyber terrorists, has generally increased as the number, intensity and sophistication of attempted attacks and intrusions from around the world have increased. In addition, our systems 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, our reputation or competitive position could be damaged and the further development and potential commercialization of octreotide capsules and any future product candidates we may develop could be delayed or halted. We may also be vulnerable to cyber-attacks by hackers, or other malfeasance. This type of breach of our cybersecurity may compromise our confidential information and/or our financial information and adversely affect our business and operations or result in financial, legal, business or reputational harm to us. In addition, the cost and operational consequences of implementing further data protection measures could be significant. Moreover, because the techniques used to obtain unauthorized access, disable or degrade service or sabotage systems change frequently and often are not recognized until launched against a target, we may be unable to anticipate these techniques or to implement adequate security measures. Our commercial insurance does not cover losses that may occur as a result of an event associated with cyber-attacks.

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

Our operations and those of our suppliers and other contractors could be subject to earthquakes, power shortages, telecommunications failures, water shortages, floods, hurricanes, typhoons, fires, extreme weather conditions, medical epidemics or pandemics, such as the recent outbreak of the novel coronavirus COVID-19, military conflicts, acts of terrorism and other natural or man-made disasters or business interruptions. For example, if the current novel coronavirus outbreak continues and results in a prolonged period of travel, commercial and other similar restrictions, we could experience business disruptions. In addition, some of our operations and our primary commercial supplier of octreotide acetate API 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 in multiple countries to produce octreotide capsules. Our ability to obtain 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, and 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.

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, data protection regulation is an area of increased focus and changing requirements. On April 27, 2016 the European Union adopted the General Data Protection Regulation 2016/679, or GDPR, which took effect on May 25, 2018, replacing the data protection laws of each European Union member state. The GDPR applies to any company that collects and uses personal data in connection with offering goods or services to, or monitoring the behavior of, individuals in the European Union. The GDPR enhances data protection obligations with respect to European personal data, including, for example, by requiring expanded disclosures about how personal data is to be used, by placing limitations on retention of information, by imposing mandatory data breach notification requirements, and by creating expansive data subject rights. Non-compliance with the GDPR can trigger fines of up to €20 million, or 4% of total worldwide annual revenue, whichever is higher. Given the breadth and depth of changes in data protection obligations, complying with the GDPR's requirements has caused us to expend significant resources and such expenditures are likely to continue into the near future as we respond to new interpretations and enforcement actions following the effective date.

The GDPR's restriction on transfers of personal data outside of Europe to countries that have not been found to provide adequate protection to personal data, such as the United States, poses particular compliance challenges. One of the transfer mechanisms that allows companies to transfer personal data from Europe to the United States is the EU-US Privacy Shield (see https://www.privacyshield.gov/welcome for more information). We conducted a self-assessment and subsequently self-certified under the Privacy Shield Framework in September 2016. We received a notice of acceptance of our self-certification in October 2016 and our registration became final on October 26, 2016. There continues to be concerns about whether the EU-US Privacy Shield will face successful legal challenges (as its predecessor the Safe Harbor framework did). If this does occur, we may need to identify and implement an alternative mechanism for legitimizing cross-border data transfers. This may entail additional cost and expense as well as changes to our business practices.

Separate European Union laws and regulations (and member states' implementations thereof) govern the protection of consumers and of electronic communications and these are also evolving. We cannot yet determine the impact that such future laws, regulations, and standards may have on our business. Such laws and regulations are often subject to differing interpretations and may be inconsistent among jurisdictions. 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. We may incur substantial expense in complying with the new obligations to be imposed by the GDPR and we may be required to make significant changes in our business operations and product development, all of which may adversely affect our revenues and our business overall. 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.

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

Risks Related to Our Intellectual Property

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

Our commercial success will depend in large part on our ability to obtain and maintain patent and other intellectual property protection in the United States and other countries with respect to our proprietary technology and products. We rely on trade secret, patent, copyright and trademark laws, and confidentiality and other agreements with employees and third parties, all of which offer only limited protection. Our strategy is to

seek patent protection for our product candidates and compositions, their methods of use and processes for their manufacture, and any other aspects of inventions that are commercially important to the development of our business.

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

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

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

from designing around our claims. Any of these outcomes could impair our ability to prevent competition from third parties.

Furthermore, the issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our owned and licensed patents may be challenged in the courts or patent offices in the United States and abroad. Such challenges may result in loss of exclusivity or freedom to operate or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical technology and drugs, or limit the duration of the patent protection of our technology and drugs. Given the amount of time required for the development, testing and regulatory review of new drug candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. For example, our patents covering our TPE platform technology expire in 2029. At least some of our patents covering MYCAPSA also expire in 2029. 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, 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.

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.

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 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 our confidential and unpatented know-how important to the maintenance of our competitive position. We protect our 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 the subject matter 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 the subject matter independently developed by a competitor, our competitive position would be harmed.

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

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

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

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

Risks Related to Our Operations in Israel

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

We 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. For example, we moved out of our Jerusalem location in 2016, which negatively impacted the local tax benefits we previously 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 octreotide acetate API manufacturers are located in Israel and, therefore, our business could be hurt by political and military instability affecting Israel.

Our development and certain administrative facilities and one of our octreotide acetate API manufacturer's 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.

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 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 December 31, 2019, we had federal operating loss, or NOL, carryforwards of approximately $217.1 million. The federal NOL carryforwards generated in 2017 and prior expire at various dates through 2037. The Federal NOL carryforwards generated in 2018 and after have an unlimited carryforward period. At December 31, 2019, we had state NOLs of approximately $167.2 million which expire at various dates through 2039. At December 31, 2019, 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 in August 2005 and May 2008. These ownership changes resulted in annual limitations to the amount of NOL carryforwards that can be utilized to offset future taxable income, if any, at the federal level. The annual limit related to these two ownership changes is approximately $0.1 million. 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. Management has also determined that we experienced an ownership change for purposes of Section 382 in February 2015. This ownership change resulted in annual limitations to the amount of the NOL carryforwards that can be utilized to offset future taxable income, if any, at the federal level; however, this ownership change did not result in a write-off of federal deferred tax assets. The annual limit related to the ownership change in 2015 is approximately $1.2 million. In addition, changes in our stock ownership, which are outside of our control, may have triggered an additional ownership change, as may future changes in our stock ownership. If additional ownership changes have occurred or occur in the future, our ability to utilize our net operating losses to offset income if we attain profitability may be substantially limited.

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

As of December 31, 2019, our executive officers, directors and principal stockholders collectively controlled approximately 38% of our outstanding common stock, excluding any shares of common stock that such persons may have the right to acquire upon exercise of outstanding options or warrants. As a result, these stockholders, if they act together, will be able to influence our management and affairs and all matters requiring stockholder approval, including the election of directors and approval of significant corporate transactions.

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

Provisions of Delaware law and our amended and restated certificate of incorporation and amended and restated bylaws, may discourage, delay or prevent a merger, acquisition or other change in control that stockholders may consider favorable, including transactions in which stockholders might otherwise receive a premium for their

shares. These provisions may also prevent or delay attempts by stockholders to replace or remove our current management or members of our board of directors. These provisions include:

- a classified board of directors;
- limitations on the removal of directors;
- advance notice requirements for stockholder proposals and nominations;
- the inability of stockholders to act by written consent or to call special meetings;
- the ability of our board of directors to make, alter or repeal our amended and restated bylaws; and
- the authority of our board of directors to issue preferred stock with such terms as our board of directors may determine.

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

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

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

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

Our amended and restated certificate of incorporation and amended and restated bylaws provide that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware shall be the sole and exclusive forum for any state law claim 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; provided, however, that this Delaware forum provision does not apply to any actions arising under the Securities Act or the Exchange Act. Although we believe this provision benefits us by providing increased consistency in the application of Delaware law in the types of lawsuits to which it applies, the provision may impose additional litigation costs on stockholders in pursuing such claims, particularly if the stockholders do not reside in or near the State of Delaware. Additionally, the 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 the filing of such lawsuits. The Court of Chancery of the State of Delaware may also reach different judgment or results than would other courts, including courts where a stockholder considering an action may be located or would otherwise choose to bring the action, and such judgments may be more or less favorable to us than our stockholders. Furthermore, the enforceability of similar exclusive forum provisions in other companies' certificates of incorporation has been challenged in legal proceedings, and it is possible that a court could rule

that this provision in our certificate of incorporation is inapplicable or unenforceable. 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 $1.20 per share through March 9, 2020. 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 efforts to secure FDA approval for octreotide capsules as a treatment for acromegaly and FDA approval of our planned prior approval supplements for our planned commercial manufacturers of API for octreotide capsules;
- the timing and results of our MPOWERED Phase 3 clinical trial of octreotide capsules or any future clinical trials we may conduct, or changes in the development status of octreotide capsules or any other product candidates we may develop;
- any delay in our regulatory filings for octreotide capsules or any other future product candidate and any adverse development or perceived adverse development with respect to the applicable regulatory authority's review of such filings;
- adverse results or delays in clinical trials;
- our decision to initiate a clinical trial, not to initiate a clinical trial or to terminate an existing clinical trial;
- adverse regulatory decisions, including failure to receive regulatory approval of octreotide capsules, such as occurred in April 2016 with the FDA's CRL to our original 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 acquire products or technologies or establish strategic collaborations, if needed;
- failure to successfully commercialize octreotide capsules or any other future product candidates, if approved;
- our ability to obtain market adoptions and 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;
- business disruptions due to natural disasters, epidemics or pandemics, such as the recent outbreak of the novel coronavirus COVID-19, military conflicts, acts of terrorism or other unanticipated catastrophes;
- 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, and developments related thereto;
- general political and economic conditions; and
- other events or factors, many of which are beyond our control.

We have been, and could become, 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*. An amended complaint was filed by the lead plaintiff on February 10, 2017 challenging our statements regarding our first 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 added as defendants current and former members of our board of directors, as well as the investment banks that underwrote our initial public offering on July 15, 2015. The plaintiff sought 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 on February 15, 2018, the court denied defendants' motion to dismiss. The defendants filed an answer to the amended complaint on March 30, 2018. On February 27, 2019, the parties agreed to a settlement of all legal claims in which defendants expressly denied that they have committed any act or omission giving rise to any liability under Sections 11 or 15 of the Securities Act of 1933. On March 14, 2019, the court issued an order of preliminary approval of the settlement. As a result of this settlement agreement, we have recorded a litigation settlement liability of $18.8 million as of December 31, 2018. Additionally, we have recorded a litigation insurance settlement recovery receivable of $18.3 million as of December 31, 2018 which represents the estimated insurance claim proceeds from our insurance carriers. On June 27, 2019, the court issued an order of final approval of the settlement. The litigation insurance settlement recovery and litigation settlement liability were settled during the three months ended June 30, 2019.

Future litigation and any matters arising out of any allegations 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 future claims and cannot provide assurance that insurance proceeds will be sufficient to cover any costs or liability under such claims.

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

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

We are an emerging growth company, as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, and may remain an emerging growth company through 2020. 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 will remain an emerging growth company until the earliest of (i) the last day of the fiscal year in which we have total annual gross revenues of $1.07 billion or more, (ii) December 31, 2020, (iii) the date on which we have issued more than $1.0 billion in nonconvertible debt during the previous three years, or (iv) the date on which we are deemed to be a large accelerated filer under the rules of the SEC based on market value of our common stock held by non-affiliates. 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, insurance and other expenses that we did not incur as a private company. The Sarbanes-Oxley Act of 2002, as well as rules subsequently implemented by the SEC and The NASDAQ Stock Market, has imposed various new requirements on public companies, including requiring establishment and maintenance of effective disclosure and financial controls and changes in corporate governance practices. Our management and other personnel are required to devote a substantial amount of time to these new compliance initiatives. Moreover, these rules and regulations have substantially increased our legal and financial compliance costs and have made some activities more time consuming and costly. These rules and regulations may make it more difficult and more expensive for us to maintain our existing director and officer liability insurance or to obtain similar coverage from an alternative provider.

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

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

We are subject to the reporting requirements of the Securities Exchange Act of 1934, as amended, or the Exchange Act, the Sarbanes-Oxley Act and the rules and regulations of the stock market on which our common stock is listed. The Sarbanes-Oxley Act requires, among other things, that we maintain effective disclosure controls and procedures and internal control over financial reporting. 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 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 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 December 31, 2019, we had 42,078,416 outstanding shares of common stock, assuming no exercise of outstanding options or warrants. In addition, the 6,489,692 shares subject to outstanding options under our stock option plans, the 1,021,108 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. 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. Shortly following our IPO, four securities analysts initiated coverage on our company. Following the receipt of the CRL to our original NDA from the FDA, each of these analysts downgraded their ratings on and lowered their price targets for our stock, and all four of the analysts either since dropped coverage or discontinued coverage following their departure from their employer. As of March 9, 2020, five securities analysts, including one of the original four analysts, initiated coverage on our company. In the event that one or more analysts who now, or in the future, cover us 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.

Item 1B. Unresolved Staff Comments

None.

Item 2. Properties

Our corporate headquarters, where our principal executive and administration functions are primarily located is, a subleased facility in Needham, Massachusetts. Our Needham sublease expires in October 2022. In addition, our international operations are headquartered in a leased facility located in Ness Ziona, Israel, where our development and supply chain operational functions are primarily based. Our Ness Ziona lease expires in December 2020. Based on our current operating plans, we believe our current facilities are adequate.

Item 3. 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*. An amended complaint was filed by the lead plaintiff on February 10, 2017 challenging our statements regarding our first 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 added as defendants current and former members of our board of directors, as well as the investment banks that underwrote our initial public offering on July 15, 2015. The plaintiff sought 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 on February 15, 2018, the court denied defendants' motion to dismiss. The defendants filed an answer to the amended complaint on March 30, 2018. On February 27, 2019, the parties agreed to a settlement of all legal claims in which defendants expressly denied that they have committed any act or omission giving rise to any liability under Sections 11 or 15 of the Securities Act of 1933. On March 14, 2019, the court issued an order of preliminary approval of the settlement. As a result of this settlement agreement, we have recorded a litigation settlement liability of $18.8 million as of December 31, 2018. Additionally, we have recorded a litigation insurance settlement recovery receivable of $18.3 million as of December 31, 2018 which represents the estimated insurance claim proceeds from our insurance carriers. On June 27, 2019, the court issued an order of final approval of the settlement. The litigation insurance settlement recovery and litigation settlement liability were settled during the three months ended June 30, 2019.

Item 4. Mine Safety Disclosures

Not applicable.

Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities

Market Information

Our common stock began trading on The NASDAQ Global Market under the symbol "CHMA" on July 16, 2015.

Holders of Record

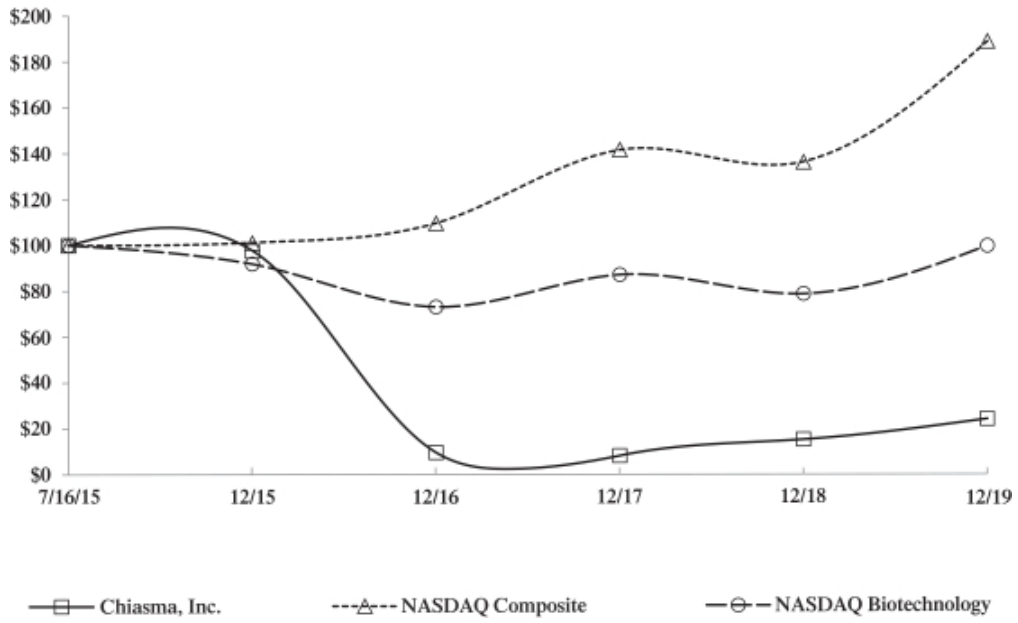
On March 9, 2020, the closing price per share of our common stock was $4.50 as reported on the NASDAQ Global Market, and we had approximately 14 stockholders of record. In addition, we believe that a significant number of beneficial owners of our common stock hold their shares in street name.

Stock Price Performance Graph

Set forth below is a graph comparing the cumulative total stockholder return on our common stock with the NASDAQ US Composite Index, the NASDAQ Biotechnology Index for the period covering from our IPO date of July 16, 2015, through the end of our fiscal year ended December 31, 2019. The graph assumes an investment

of $100.00 made on July 16, 2015, in (i) our common stock, (ii) the stocks comprising the NASDAQ US Composite Index, and (iii) stocks comprising the NASDAQ Biotechnology Index. This graph is not "soliciting material," is not deemed "filed" with the SEC and is not to be incorporated by reference into any filing by us under the Securities Act or the Exchange Act whether made before or after the date hereof and irrespective of any general incorporation language in any such filing. The graph assumes our closing sale price on July 16, 2015 of $20.00 per share as the initial value of our common stock and not the initial offering price to the public of $16.00 per share.

COMPARISON OF 54 MONTH CUMULATIVE TOTAL RETURN*
Among Chiasma, Inc., the NASDAQ Composite Index
and the NASDAQ Biotechnology Index



* $100 invested on July 16, 2015 in stock or June 30, 2015 in index, including reinvestment of dividends. Fiscal year ending December 31.

	12/31/2015	12/31/2016	12/31/2017	12/31/2018	12/31/2019
Chiasma, Inc.	97.85	9.75	8.50	15.55	24.80
NASDAQ Composite	101.22	109.77	141.85	136.68	189.33
NASDAQ Biotechnology	91.81	73.31	87.30	79.19	100.10

Our fiscal year ends on the last day of December each year; data in the above table reflects market values for our stock and NASDAQ and peer group indices as of the close of trading on the last trading day of the periods presented.

Securities authorized for issuance under equity compensation plans

Information about our equity compensation plans is incorporated herein by reference to Item 12 of Part III of this Annual Report on Form 10-K.

Recent Sales of Unregistered Securities

None.

Use of Proceeds from Registered Securities

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. As of December 31, 2019, we have used all of such net proceeds to fund the clinical development and regulatory approval efforts for our oral octreotide product candidate and for working capital and other general corporate purposes.

Issuer Purchases of Equity Securities

There were no repurchases of shares of common stock made during the year ended December 31, 2019.

Item 6. Selected Financial Data

You should read the following selected consolidated financial data in conjunction with our consolidated financial statements and the related notes which are included elsewhere in this Annual Report on Form 10-K and the "Management's Discussion and Analysis of Financial Condition and Results of Operations" section of this Annual Report on Form 10-K. We have derived the consolidated statement of operations data for the years ended December 31, 2019, 2018, and 2017 and the consolidated balance sheet data as of December 31, 2019 and 2018, from our audited consolidated financial statements, which are included elsewhere in this Annual Report. We have derived the statement of operations data for the years ended December 31, 2016 and 2015, and the consolidated balance sheet data as of December 31, 2017, 2016 and 2015 from our audited consolidated financial statements, which are not included in this Annual Report. Our historical results for any prior period are not necessarily indicative of results to be expected for any future period.

	For the Years Ended December 31,				
	2019	2018	2017	2016	2015
	(in thousands except share and per share data)				
Consolidated Statement of Operations Data					
Operating expenses:					
General and administrative	$ 15,122	$ 9,974	$ 9,146	$ 21,815	$ 16,456
Research and development	22,457	22,362	17,948	31,317	18,991
Restructuring charges	—	—	1,038	8,179	—
Total operating expenses	37,579	32,336	28,132	61,311	35,447
Loss from operations	(37,579)	(32,336)	(28,132)	(61,311)	(35,447)
Other expenses (income), net	(1,543)	(1,044)	(716)	(547)	300
Loss before income taxes	(36,036)	(31,292)	(27,416)	(60,764)	(35,747)
Provision (benefit) for income taxes	284	(31)	(590)	347	161
Net loss	(36,320)	(31,261)	(26,826)	(61,111)	(35,908)
Accretion of redeemable convertible preferred stock	—	—	—	—	(318)
Net loss attributable to common stockholders	$ (36,320)	$ (31,261)	$ (26,826)	$ (61,111)	$ (36,226)
Earnings per share attributable to common stockholders					
Basic	$ (1.06)	$ (1.28)	$ (1.10)	$ (2.51)	$ (3.25)
Diluted	$ (1.06)	$ (1.28)	$ (1.10)	$ (2.51)	$ (3.25)
Weighted-average shares outstanding:					
Basic	34,204,284	24,399,706	24,366,681	24,319,443	11,151,978
Diluted	34,204,284	24,399,706	24,366,681	24,319,443	11,151,978

	December 31,				
	2019	2018	2017	2016	2015
	(in thousands)				
Consolidated Balance Sheet Data					
Cash and cash equivalents	$27,855	$13,060	$14,603	$37,013	$ 41,039
Marketable securities	64,520	28,602	52,336	55,971	107,715
Current assets	96,256	62,187	68,707	95,094	151,085
Total assets	98,826	63,256	69,883	96,756	153,108
Current liabilities	11,375	28,627	6,745	8,400	6,514
Long-term liabilities	1,682	505	664	2,631	3,778
Total liabilities	13,057	29,132	7,409	11,031	10,292
Total stockholders' equity	85,769	34,124	62,474	85,725	142,816

Item 7. 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 together with our consolidated financial statements and the accompanying notes thereto included elsewhere in this Annual Report on Form 10-K. Some of the information contained in this discussion and analysis or set forth elsewhere in this Annual Report on Form 10-K, 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 Annual Report on Form 10-K, 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, late-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. In January 2020, the U.S. Food and Drug Administration, or the FDA, accepted for review our New Drug Application, or NDA, for our oral octreotide capsules product candidate, conditionally trade-named MYCAPSSA®, for the maintenance treatment of adults with acromegaly. We resubmitted our NDA following positive results from our CHIASMA OPTIMAL Phase 3 clinical trial, which was conducted under a Special Protocol Assessment, or SPA, agreement with the FDA and designed to support FDA approval. The FDA assigned a Prescription Drug User Fee Act, or PDUFA, target action date of June 26, 2020, which is a six-month review. Our primary focus is on developing and seeking the regulatory approval and subsequent commercialization of oral octreotide capsules, our sole TPE platform-based clinical product candidate, for the treatment of adult patients with acromegaly in the United States and European Union

Acromegaly is a rare and debilitating condition that results from the body's production of excess growth hormone, which in turn elevates insulin-like growth factor 1, or IGF-1. These elevated hormone levels result in a number of painful and disfiguring symptoms, including some acute, such as headaches, joint pain and fatigue, and some long-term, such as enlarged hands, feet and internal organs, as well as altered facial features. If not treated promptly, acromegaly can lead to serious illness and is associated with premature death, primarily due to cardiovascular disease. Octreotide is an analog of somatostatin, a natural inhibitor of growth hormone secretion. The current standard of care for patients diagnosed with acromegaly and not otherwise cured by surgical removal of the pituitary tumor consists of lifelong, once-monthly injections of an extended release somatostatin analog. We believe that octreotide capsules, if approved by regulatory authorities, will be the first somatostatin analog available for oral administration. Octreotide capsules have been granted orphan designation in the United States and the European Union for the treatment of acromegaly. The worldwide market for injectable somatostatin analogs is approximately $2.8 billion annually, of which we estimate approximately $800 million represents annual sales for the treatment of acromegaly. We retain worldwide rights to develop and commercialize octreotide capsules with no royalty obligations to third parties.

In September 2017, we initiated a third Phase 3 clinical trial for oral octreotide capsules for the maintenance therapy of adult patients with acromegaly following our agreement with the FDA on the design of the trial, reached through a SPA in August 2017. The trial, referred to as CHIASMA OPTIMAL, was a randomized, double-blind, placebo-controlled, nine-month trial expected to enroll 50 adult acromegaly patients designed to support regulatory approval of octreotide capsules in the United States. In October 2018, we completed enrollment in the CHIASMA OPTIMAL trial randomizing a total of 56 patients. In July 2019, we announced positive top-line results from this trial. In January 2020, the FDA accepted for review our resubmitted NDA for our oral octreotide capsules product candidate, conditionally trade-named MYCAPSSA®, for the maintenance treatment of adults with acromegaly. The FDA assigned a Prescription Drug User-Fee Act, or PDUFA, target action date of June 26, 2020, which is a six-month review.

We are also conducting an international Phase 3 clinical trial, referred to as MPOWERED, of oral octreotide capsules for the maintenance treatment of adult patients with acromegaly to support regulatory approval in the European Union. The MPOWERED trial is a randomized, open-label and active-controlled 15-month trial initially designed to enroll up to 150 patients. The European Medicines Agency, or EMA, requested that a minimum of at least 80 patients who are responders to octreotide capsules following the six-month run-in phase be randomized to either remain on octreotide capsules or return to injectable somatostatin receptor ligands (octreotide or lanreotide), and then followed for an additional nine months. In June 2019, we completed the enrollment of 146 total patients in MPOWERED. In January 2020, the randomization of patients was completed. Of the 146 patients that entered the six-month run-in phase of the trial, 92 of these patients (or 63%) completed the run-in phase and were deemed to be responders to octreotide capsules per protocol (IGF-1 <1.3 x ULN and GH<2.5 ng/mL). We expect to release top-line data from the MPOWERED trial in the fourth quarter of 2020.

We continue to believe that the data from the CHIASMA OPTIMAL trial alone is designed to address the clinical concerns raised by the FDA in its CRL to our original NDA submission and also that, with respect to our ongoing Phase 3 MPOWERED™ clinical trial (described below), the FDA only expects to review safety data from the MPOWERED trial as part of its review of our NDA resubmission. Any future requirement by the FDA to submit additional data, including the efficacy data from our MPOWERED clinical trial could delay or prevent the review or approval of our NDA.

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. In addition, we have initiated pre-commercial activities in anticipation of a potential mid-2020 FDA marketing approval of octreotide capsules. In July 2015, we completed our initial public offering, or IPO, in which we raised $106.5 million. In April 2019, we completed a follow-on public offering of common stock in which we raised an additional $32.2 million. In August 2019, we completed a follow-on public offering of common stock in which we raised an additional $52.3 million. As of December 31, 2019, our consolidated cash, cash equivalents and marketable securities were $92.4 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 $36.3 million and $31.3 million for the years ended December 31, 2019 and 2018, respectively. As of December 31, 2019, we had an accumulated deficit of $272.9 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 plan to invest in our commercial launch, if approved, manufacture octreotide capsules for market consumption, if approved, as well as invest in manufacturing scale-up activities, and continue the open label extension portion of our international Phase 3 CHIASMA OPTIMAL clinical trial of octreotide capsules in acromegaly and to continue to conduct our international Phase 3 MPOWERED clinical trial of octreotide capsules in acromegaly to support potential regulatory approval in the European Union. 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.

As of December 31, 2019, we had cash, cash equivalents and marketable securities totaling approximately $92.4 million. Based on our current operating plans, we do not have sufficient cash, cash equivalents and marketable securities to find our operating expenses, inventory purchases and capital expenditures for at least the next 12 months from the filing date of this Annual Report. We will require additional capital to sustain our operations, including our potential commercial launch. Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity and debt financings, and we will also opportunistically consider license and collaboration agreements with potential partners and other non-dilutive financing arrangements. However, 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 efforts or preparations for our anticipated commercial launch of oral octreotide capsules. These factors raise substantial doubt about our ability to continue as a going concern. We currently expect our existing cash, cash equivalents and marketable securities will be at least sufficient to fund our operations, as currently planned, through at least 2020. For more information, refer to "—Liquidity and Capital Resources" below and Note 2 to our condensed consolidated financial statements included elsewhere in this Annual Report.

Roche 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 octreotide capsules. In July 2014, Roche terminated the license agreement. 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 final $1.7 million annual payment in March 2018. Roche has no remaining rights to octreotide capsules and we retain all rights to octreotide capsules and all related intellectual property. We have no further financial or operational obligations to Roche.

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 and pre-approval 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.

We have limited research and discovery functions and are currently not materially investing in those areas. We have focused our resources on the clinical development of octreotide capsules, including our two international Phase 3 trials, CHIASMA OPTIMAL and MPOWERED. 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 plan to continue the open label extension portion of our international Phase 3 CHIASMA OPTIMAL clinical trial of octreotide capsules in acromegaly. We also expect to continue to conduct our international Phase 3 MPOWERED clinical trial of octreotide capsules in acromegaly to support potential regulatory approval in the European Union. The successful development of octreotide capsules is highly uncertain.

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, information technology 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, litigation, and intellectual property-related 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. Our marketing expenses for the six months ended June 30, 2019 and the year ended December 31, 2018 were immaterial. Following the positive top-line data from our CHIASMA OPTIMAL trial, which we released in July 2019, we have begun to incur additional pre-commercial marketing related expenses and we expect these expenses to substantially increase as we continue to prepare for the potential commercialization of octreotide capsules in the United States. In addition to anticipated future increases in marketing expenses, as we prepare for the potential commercialization of octreotide capsules and grow our operations, we have begun to incur additional other general and administrative expenses which we expect will continue to increase.

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, lease termination fees, and other expenses associated with restructuring our operations.

Other Income, Net

Other income, net consists primarily of interest income earned on our investments.

Provision (Benefit) 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 primarily affected by the mix of our foreign subsidiary permanent items, discrete items, and unrecognized tax benefits and to a lesser extent our taxable income (loss) in the United States.

Results of Operations

Comparison for the Years Ended December 31, 2019 and 2018

The following tables set forth, for the periods indicated, our results of operations and the change between the specified periods expressed as a percent increase or decrease:

Research and Development

	2019	2018	$ Change	% change
	($ in thousands)			
Research and development	$22,457	$22,362	$ 95	0%

During the year ended December 31, 2019, our total research and development expenses increased by $0.1 million to $22.5 million. This increase was primarily due to an increase in manufacturing and regulatory costs offset by a decrease in clinical trial costs.

General and Administrative

	2019	2018	$ Change	% change
	($ in thousands)			
General and administrative	$15,122	$9,974	$ 5,148	52%

For the year ended December 31, 2019, our general and administrative expenses increased by $5.1 million to $15.1 million. This increase was primarily due to the initiation of pre-commercial activities and an increase in compensation-related expenses primarily in the second half of 2019, which were partially offset by a decrease in legal costs.

Other Income, net

Other income totaled $1.5 million for the year ended December 31, 2019, compared to $1.0 million for the year ended December 31, 2018, an increase of approximately $0.5 million. The increase was driven by the increase of our cash equivalents and marketable securities and an increase in the interest yield on our cash equivalents and marketable securities.

Provision (Benefit) from Income Taxes

Our total tax provision was $0.3 million for the year ended December 31, 2019, representing an effective tax rate of (0.8%), as compared to a tax benefit of $31,000 for the year ended December 31, 2018, representing an effective tax rate of 0.10%.

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.

Comparison for the Years Ended December 31, 2018 and 2017

The following tables set forth, for the periods indicated, our results of operations and the change between the specified periods expressed as a percent increase or decrease:

Research and Development

	2018	2017	$ Change	% Change
	($ in thousands)			
Research and development	$22,362	$17,948	$ 4,414	25%

During the year ended December 31, 2018, our total research and development expenses increased by $4.4 million to $22.4 million. This increase was primarily due to increased costs related to the CHIASMA OPTIMAL clinical trial which we initiated in September 2017 and the MPOWERED trial and were partially offset by reduced personnel costs associated with the 2017 transition of our former Chief Development Officer from a full-time employee to a member of the board of directors of both our company and our Israeli subsidiary.

General and Administrative

	2018	2017	$ Change	Percent change
	($ in thousands)			
General and administrative	$9,974	$9,146	$ 828	9%

For the year ended December 31, 2018, our general and administrative expenses increased by $0.8 million to $10.0 million. This increase was primarily due to an increase in legal costs which were primarily offset by a reduction in facility costs.

Restructuring Charges

In November 2017, we finalized the termination of our lease agreement on our 24,000 square foot office facility in Waltham, MA which we no longer required following the 2016 workforce reductions. As a result, we recorded approximately $1.0 million of restructuring expenses during the year ended December 31, 2017, which consisted of a lease termination payment of $1.0 million, the write-off of office furniture and equipment of $0.4 million offset by the release of deferred rent liabilities of $0.4 million associated with the terminated lease. There were no restructuring charges incurred during the year ended December 31, 2018.

Other Income, net

Other income totaled $1.0 million for the year ended December 31, 2018, compared to $0.7 million for the year ended December 31, 2017, an increase of approximately $0.3 million. The increase was driven by interest income generated from increased yields on our cash equivalents and marketable securities and a decrease in the imputed interest associated with the lower remaining obligation related to the acquisition of API and trade name MYCAPSSA from Roche.

Benefit for Income Taxes

Our total tax benefit was $31,000 for the year ended December 31, 2018, representing an effective tax rate of 0.10%, as compared to a tax benefit of $0.6 million for the year ended December 31, 2017, representing an effective tax rate of 2.16%, which was primarily driven by the U.S. Federal alternative minimum tax credit of $1.0 million which was recorded as a benefit to the income tax provision as a result of the 2017 income tax reform.

At December 31, 2017, we had approximately $1.0 million of federal alternative minimum tax credit carryforwards that do not expire. Federal tax reform, enacted in December 2017, allows for U.S. federal alternative minimum tax credit carryforwards to be refunded between 2019 and 2022. We have a history of generating losses and are forecasting that they will not generate taxable income through 2022 which would otherwise limit our ability to realize the U.S. Federal alternative minimum tax credit. Accordingly, we have recorded the U.S. Federal alternative minimum tax credit as a benefit to the income tax provision for the year ended December 31, 2017.

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

In July 2015, we completed our IPO in which we raised $106.5 million by selling shares of common stock. In April 2019, to fund our operations, we completed a follow-on public offering of common stock in which we raised $34.5 million in gross proceeds, or $32.2 million in net proceeds after underwriting fees and offering expenses. In August 2019, to fund our operations, we completed a follow-on public offering of common stock in which we raised $55.9 million in gross proceeds, or $52.3 million in net proceeds after underwriting fees and offering expenses. We filed a $200.0 million shelf registration statement on Form S-3 with the SEC in September 2019, which the SEC declared effective in September 2019. As of December 31, 2019, our cash and cash equivalents were $27.9 million, of which $0.6 million was held by our Israeli subsidiary. In addition, as of December 31, 2019, we have $64.5 million invested in short-term marketable securities.

Plan of Operations, Future Funding Requirements and Going Concern

We expect that our primary uses of capital will be associated with the planned commercialization of octreotide capsules in the United States, if approved, and the manufacturing of octreotide capsules for market consumption, if approved, seeking regulatory approval of octreotide capsules in the United States and European Union, including clinical trial costs (including our international Phase 3 MPOWERED clinical trial to support regulatory approval of octreotide capsules in the European Union and our international Phase 3 CHIASMA OPTIMAL clinical trial open label extension), medical affairs activities, legal and regulatory expenses related to seeking regulatory approval of octreotide capsules in the United States and European Union, compensation and related expenses, third-party clinical development services, and other general operating costs.

As of December 31, 2019, we had cash, cash equivalents and marketable securities totaling approximately $92.4 million. Based on our current operating plans, we do not have sufficient cash, cash equivalents and marketable securities to fund our operating expenses, inventory purchases and capital expenditures for at least the next 12 months from the filing date of this Annual Report. We will require additional capital to sustain our operations, including our potential commercial launch. Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity and debt financings, and we will also opportunistically consider license and collaboration agreements with potential partners and other non-dilutive financing arrangements. 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. These factors raise substantial doubt about our ability to continue as a going concern. We currently expect our existing cash, cash equivalents and marketable securities will be at least sufficient to fund our operations, as currently planned, through at least 2020. 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 and our planned prior approval manufacturing supplements;
- the progress and results of our ongoing clinical trials 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;
- 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 develop, acquire or in-license other product candidates and technologies or explore or consummate other strategic transactions.

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 or other financing 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, debt or other 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 years ended December 31, 2019 and 2018:

	2019	2018
	($ in thousands)	
Cash flows provided by (used in):		
Operating activities	$(35,012)	$(24,091)
Investing activities	(35,657)	24,211
Financing activities	85,464	(1,663)

Operating Activities

Net cash used in operating activities was $35.0 million in 2019, and primarily consisted of $36.3 million in net loss, adjusted for non-cash items of $3.1 million (primarily stock-based compensation of $3.3 million and partially offset by amortization of premium on marketable securities) and was offset by working capital decreases of $1.8 million (primarily driven by the increase in prepaid expenses and other current assets which was partially offset by an increase in accounts payable and accrued expenses). Net cash used in operating activities was $24.1 million in 2018, and primarily consisted of $31.3 million in net loss, adjusted for non-cash items of $2.4 million (primarily stock-based compensation of $2.7 million and partially offset by amortization of premium on marketable securities) and was offset by working capital decreases of $4.8 million (primarily driven by the increase in accounts payable and accrued expenses and the decreases in prepaid and other current assets and other assets).

Investing Activities

Net cash used in investing activities was $35.7 million in 2019, primarily related to the net purchases of marketable securities driven by the net proceeds received from the follow-on public offerings that were completed in April and August 2019. Net cash provided by investing activities was $24.2 million in 2018, primarily related to the net maturities of marketable securities.

Financing Activities

Net cash provided by financing activities was $85.5 million in 2019, primarily related to the net proceeds received from the follow-on public offerings that were completed in April and August 2019 and the net proceeds from a short-term borrowing. Net cash used in financing activities was $1.7 million in 2018 related to the third and final $1.7 million installment payment on the termination of the Roche license agreement and was partially offset by the proceeds resulting from the exercise of stock options.

Contractual Obligations and Contingent Liabilities

The following summarizes our significant contractual obligations as of December 31, 2019:

Contractual Obligations	Total	Less than 1 Year	1 to 3 Years	3 to 5 Years	More than 5 Years
		($ in thousands)			
Purchase obligations	$11,604	$11,604	$ —	$—	$ —
Operating leases	1,757	609	1,148	—	—
Total contractual obligations	$13,361	$12,213	$1,148	$—	$ —

Purchase Obligations. This amount represents API purchase commitments under non-cancelable agreements.

Operating Leases. This amount represents future minimum lease payments under non-cancelable operating leases in effect as of December 31, 2019 for our current and future facilities in the U.S. and Israel. The minimum lease payments do not include common area maintenance charges or real estate taxes.

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

Critical Accounting Policies and Use of Estimates

Our management's discussion and analysis of financial condition and results of operations is based on our consolidated financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States, or GAAP. The preparation of consolidated financial statements in conformity with GAAP requires us to make estimates and assumptions that affect the amounts reported in the consolidated financial statements and accompanying notes. 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 consolidated financial statements include, but are not limited to, accounting for stock-based compensation, and accounting for certain accruals. We assess these estimates on an ongoing basis; however, actual results could materially differ from those estimates.

While our significant accounting policies are described in more detail in the notes to our consolidated financial statements included elsewhere in this Annual Report on Form 10-K, we believe that the following accounting policies are critical to the process of making significant judgments and estimates in the preparation of our consolidated financial statements and understanding and evaluating our reported financial results.

Clinical trial costs

Clinical trial costs are a component of research and development expenses. We accrue and expense clinical trial activities performed by third parties on an evaluation of the progress to completion of specific tasks using data such as hours spent in performance of services, patient enrollment, clinical site activation, and other information provided to us by our vendors. We make estimates of our clinical trial accrued expenses as of each balance sheet date in our financial statements based on facts and circumstances known to us. If timelines or contracts are modified based upon changes in the clinical trial protocol or scope of work to be performed, we assess our estimates of accrued expenses accordingly.

If we do not identify costs that we have begun to incur, or if we underestimate or overestimate the level of services performed or the costs of these services, our actual expenses could differ from our estimates. To date, there have not been any material adjustments to our prior estimates of accrued research and development expenses.

Stock-based Compensation

We account for all stock-based compensation to employees and nonemployees based on their fair values on the date of grant. For stock-based awards with only service conditions, we recognize compensation on a straight-line basis over the requisite service period, which is usually the vesting period of the award, net of any actual forfeitures.

We determine the fair value of stock options by using the Black-Scholes option pricing model. This model requires the input of several assumptions such as the expected option term, the expected risk-free interest rate over the expected option term, the expected volatility of our stock price over the expected option term, and the expected dividend yield over the expected option term. The computation of expected volatility is based on an

average historical share price volatility based on an analysis of reported data for a peer group of comparable publicly traded companies, which were selected based upon industry similarities. The interest rate for periods within the expected term of the award is based on the U.S. Treasury risk-free interest rate in effect at the time of grant. The expected lives of the options were estimated using the simplified method.

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 7A. 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 December 31, 2019, we had $27.9 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 and short-term corporate notes. In addition, we had $64.5 million of marketable securities. 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 short-term investments of $0.2 million. As of December 31, 2019, we did not have any outstanding variable interest rate nor long-term 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 work to maintain all balances in U.S. dollars until payment in other currencies is required to minimize this currency risk. Fluctuations in the exchange rate between the U.S. dollar and each of the Euro, GBP and NIS over the past 24 months has been approximately (7)%, (2)% and 1%, respectively. As of December 31, 2019, we held $0.6 million in Israeli banks and petty cash funds to support our Israeli operations, the majority of which is denominated in U.S. dollars. We contract with CROs internationally, primarily for the execution of clinical trials and manufacturing activities. Transactions with these providers are settled in U.S. dollars, Euros or GBP and, therefore, we believe that we have only minimal exposure to foreign currency exchange risks. We do not hedge against foreign currency risks.

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

Item 8. Financial Statements and Supplementary Data

See the consolidated financial statements filed as part of this Annual Report on Form 10-K as listed under Item 15 below.

Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure

Not Applicable.

Item 9A. Controls and Procedures

Evaluation of Disclosure Controls and Procedures

Disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) are designed only to provide reasonable assurance that they will meet their objectives. Under the supervision and with the participation of our management, including our principal executive officer and principal financial officer, we conducted an evaluation of the effectiveness, as of December 31, 2019, of the design and operation of our disclosure controls and procedures, as such term is defined in Exchange Act Rules 13a-15(e) and 15d-15(e). Based on this evaluation, our principal executive officer and principal financial officer have concluded that, as of such date, our disclosure controls and procedures are effective to ensure that information required to be disclosed by us in our Exchange Act reports is recorded, processed, summarized, and reported within the time periods specified in the SEC's rules and forms, and that such information is accumulated and communicated to our management, including our principal executive officer and principal financial officer, as appropriate to allow timely decisions regarding required disclosure.

Management's Annual Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting, as such term is defined in Exchange Act Rule 13a-15(f). Our internal control over financial reporting is designed to provide reasonable assurance to our management and board of directors regarding the preparation and fair presentation of published financial statements. A control system, no matter how well designed and operated, can only provide reasonable, not absolute, assurance that the objectives of the control system are met. Because of these inherent limitations, management does not expect that our internal controls over financial reporting will prevent all error and all fraud. Under the supervision and with the participation of our management, including our principal executive officer and principal financial officer, we conducted an evaluation of the effectiveness of our internal control over financial reporting based on the framework in Internal Control-Integrated Framework issued in 2013 by the Committee of Sponsoring Organizations of the Treadway Commission. Based on our evaluation under the framework in Internal Control-Integrated Framework, our management concluded that our internal control over financial reporting was effective as of December 31, 2019.

Changes in Internal Control over Financial Reporting

There were no changes in our internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) or 15d-15(d)) during the quarter ended December 31, 2019 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information

Not Applicable.

PART III

Item 10. Directors, Executive Officers and Corporate Governance

The information required under this item is incorporated herein by reference to the Company's definitive proxy statement pursuant to Regulation 14A under the Exchange Act, which proxy statement will be filed with the Securities and Exchange Commission not later than 120 days after the close of the Company's fiscal year ended December 31, 2019.

We intend to disclose on our website any amendments to, or waivers from, our Code of Business Conduct and Ethics that are required to be disclosed pursuant to the rules of the SEC. Information contained on, or connected to, our website is not incorporated by reference into this Form 10-K and should not be considered part of this report or any other filing that we make with the SEC.

Item 11. Executive Compensation

The information required under this item is incorporated herein by reference to the Company's definitive proxy statement pursuant to Regulation 14A under the Exchange Act, which proxy statement will be filed with the Securities and Exchange Commission not later than 120 days after the close of the Company's fiscal year ended December 31, 2019.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters

The information required under this item is incorporated herein by reference to the Company's definitive proxy statement pursuant to Regulation 14A under the Exchange Act, which proxy statement will be filed with the Securities and Exchange Commission not later than 120 days after the close of the Company's fiscal year ended December 31, 2019.

Item 13. Certain Relationships and Related Transactions, and Director Independence

The information required under this item is incorporated herein by reference to the Company's definitive proxy statement pursuant to Regulation 14A under the Exchange Act, which proxy statement will be filed with the Securities and Exchange Commission not later than 120 days after the close of the Company's fiscal year ended December 31, 2019.

Item 14. Principal Accounting Fees and Services

The information required under this item is incorporated herein by reference to the Company's definitive proxy statement pursuant to Regulation 14A under the Exchange Act, which proxy statement will be filed with the Securities and Exchange Commission not later than 120 days after the close of the Company's fiscal year ended December 31, 2019.

PART IV

Item 15. Exhibits and Financial Statement Schedules

(a) 1. Consolidated Financial Statements.

For a list of the consolidated financial statements included herein, see Index on page F-1 of this report.

2. Financial Statement Schedules.

All required information is included in the financial statements or notes thereto.

3. List of Exhibits.

See the Exhibit Index in Item 15(b) below.

(b) Exhibit Index.

EXHIBIT INDEX

Exhibit No.	
3.1	Amended and Restated Certificate of Incorporation of the Company, incorporated by reference from our Current Report on Form 8-K filed on July 21, 2015
3.2	Amended and Restated Bylaws of the Company, incorporated by reference from our Current Report on Form 8-K filed on July 21, 2015
4.1	Form of Common Stock certificate of the Company, incorporated by reference from our Amendment No. 1 to Registration Statement on Form S-1/A filed on July 6, 2015 (File No. 333-204949)
4.2	Amended and Restated Investors' Rights Agreement, by and between the Company and the Investors named therein, dated as of December 16, 2014, incorporated by reference from our Registration Statement on Form S-1 filed on June 15, 2015 (File No. 333-204949)
4.3	Form of Warrant to Purchase Shares of Common Stock (issued in connection with the Company's Series D preferred stock financing), incorporated by reference from our Registration Statement on Form S-1 filed on June 15, 2015 (File No. 333-204949)
4.4	Form of Warrant to Purchase Shares of Common Stock (issued in connection with the Company's Series E preferred stock financing), incorporated by reference from our Registration Statement on Form S-1 filed on June 15, 2015 (File No. 333-204949)
4.5*	Description of Capital Stock
10.1†	Israeli Stock Option Plan 2003 and forms of agreements thereunder, incorporated by reference from our Registration Statement on Form S-1 filed on June 15, 2015 (File No. 333-204949)
10.2†	2015 Stock Option and Incentive Plan and forms of agreement thereunder, incorporated by reference from our Amendment No. 1 to Registration Statement on Form S-1/A filed on July 6, 2015 (File No. 333-204949)
10.3†	2015 Employee Stock Purchase Plan, incorporated by reference from our Amendment No. 1 to Registration Statement on Form S-1/A filed on July 6, 2015 (File No. 333-204949)
10.4†	Senior Executive Cash Incentive Bonus Plan, incorporated by reference from our Registration Statement on Form S-1 filed on June 15, 2015 (File No. 333-204949)
10.5†	Employment Agreement dated as of May 31, 2019 by and between the Company and Raj Kannan, incorporated by reference from our Current Report on Form 8-K filed on June 5, 2019, as amended on February 14, 2020, which amendment is incorporated by reference from our Current Report on Form 8-K filed on February 21, 2020
10.6†	Amended and Restated Employment Agreement dated as of May 31, 2019 by and between the Company and Mark J. Fitzpatrick, incorporated by reference from our Current Report on Form 8-K filed on June 5, 2019, as amended on February 14, 2020, which amendment is incorporated by reference from our Current Report on Form 8-K filed on February 21, 2020
10.7†	Amended and Restated Employment Agreement dated as of February 23, 2018 by and between the Company and Drew Enamait, incorporated by reference from our Current Report on Form 8-K filed on February 28, 2018, as amended on February 14, 2020, which amendment is incorporated by reference from our Current Report on Form 8-K filed on February 21, 2020
10.8†	Amended and Restated Employment Agreement dated as of February 23, 2018 by and between the Company and William Ludlam, incorporated by reference from our Quarterly Report on Form 10-Q filed on May 10, 2018, as amended on February 14, 2020, which amendment is incorporated by reference from our Current Report on Form 8-K filed on February 21, 2020

10.9†*	Amended and Restated Employment Agreement dated as of February 14, 2020 by and between the Company and Lee G. Giguere
10.10	Form of Indemnification Agreement, to be entered into between the Company and its directors and officers, incorporated by reference from our Amendment No. 1 to Registration Statement on Form S-1/A filed on July 6, 2015 (File No. 333-204949)
10.11†	Amended and Restated Non-Employee Director Compensation Policy, incorporated by reference from our Quarterly Report on Form 10-Q filed on May 5, 2017
10.12	Lease dated as of November 15, 2017 by and between the Company and NWALP TPOP Property Owner LLC, incorporated by reference from our Annual Report on Form 10-K filed on March 20, 2018
10.13*	Sublease dated as of October 11, 2019 by and between the Company and PTC, Inc.
21.1*	Subsidiaries of the Company
23.1*	Consent of Deloitte & Touche LLP
31.1*	Certification of the Principal Executive Officer Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002
31.2*	Certification of the Principal Financial Officer Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002
32.1**	Certification of the Principal Executive Officer and Principal Financial Officer Pursuant to 18 U.S.C. Section 1350 as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
101	Interactive Data Files regarding (a) our Consolidated Balance Sheets as of December 31, 2019 and 2018, (b) our Consolidated Statements of Operations and Comprehensive Income (Loss) for the Years Ended December 31, 2019, 2018 and 2017, (c) our Consolidated Statement of Stockholders' Equity for the Years Ended December 31, 2019 and 2018, (d) our Consolidated Statements of Cash Flows for the Years Ended December 31, 2019, 2018 and 2017 and (e) the Notes to such Consolidated Financial Statements

† Indicates a management contract or compensatory plan.
* Filed herewith.
** Furnished herewith.

Item 16. Form 10-K Summary

None.

SIGNATURES

Pursuant to the requirements of the Section 13 or 15(d) 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.

By: /s/ *Raj Kannan*
Raj Kannan
Chief Executive Officer and Director
(Principal Executive Officer)

By: /s/ *Mark J. Fitzpatrick*
Mark J. Fitzpatrick
President
(Principal Financial Officer)

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated.

Name	Title	Date
/s/ Raj Kannan Raj Kannan	Chief Executive Officer and Director *(Principal Executive Officer)*	March 16, 2020
/s/ *Mark J. Fitzpatrick* Mark J. Fitzpatrick	President *(Principal Financial Officer)*	March 16, 2020
/s/ Drew Enamait Drew Enamait	Vice President, Finance and Administration *(Principal Accounting Officer)*	March 16, 2020
/s/ *David Stack* David Stack	Director	March 16, 2020
/s/ *Todd Foley* Todd Foley	Director	March 16, 2020
/s/ *Bard Geesaman, M.D., Ph.D.* Bard Geesaman, M.D., Ph.D.	Director	March 16, 2020
/s/ *Roni Mamluk, Ph.D.* Roni Mamluk, Ph.D.	Director	March 16, 2020
/s/ *Scott Minick* Scott Minick	Director	March 16, 2020
/s/ *John Scarlett, M.D.* John Scarlett, M.D.	Director	March 16, 2020
/s/ *John F. Thero* John F. Thero	Director	March 16, 2020

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REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the stockholders and the Board of Directors of Chiasma, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Chiasma, Inc. and subsidiaries (the "Company") as of December 31, 2019 and 2018, the related consolidated statements of operations, comprehensive income (loss), stockholders' equity, and cash flows, for each of the three years in the period ended December 31, 2019, and the related notes (collectively referred to as the "financial statements"). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2019 and 2018, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2019, in conformity with accounting principles generally accepted in the United States of America.

Going Concern

The accompanying financial statements have been prepared assuming that the Company will continue as a going concern. As discussed in Note 2 to the financial statements, the Company has incurred losses since inception that raise substantial doubt about its ability to continue as a going concern. Management's plans in regard to this matter are also described in Note 2. The financial statements do not include any adjustments that might result from the outcome of this uncertainty.

Change in Accounting Principle

As discussed in Note 2 to the financial statements, effective January 1, 2019, the Company adopted FASB Accounting Standards Codification Topic 842, *Leases*, using the modified retrospective approach and utilizing the effective date as its date of adoption.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits, we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ Deloitte & Touche LLP

Boston, Massachusetts
March 16, 2020

We have served as the Company's auditor since 2016.

CHIASMA, INC.

CONSOLIDATED BALANCE SHEETS

	As of December 31,	
	2019	2018
	(in thousands except share data)	
Assets		
Current Assets		
Cash and cash equivalents	$ 27,855	$ 13,060
Marketable securities	64,520	28,602
Insurance recovery (Note 12)	—	18,288
Prepaid expenses and other current assets	3,881	2,237
Total current assets	96,256	62,187
Property and equipment, net	334	111
Other assets	2,236	958
Total assets	$ 98,826	$ 63,256
Liabilities and Stockholders' Equity		
Current liabilities		
Accounts payable	$ 3,253	$ 2,029
Estimated settlement liability (Note 12)	—	18,750
Accrued expenses	7,576	7,848
Other current liabilities	546	—
Total current liabilities	11,375	28,627
Long-term liabilities	1,682	505
Total liabilities	13,057	29,132
Commitments and Contingencies (Note 12)		
Stockholders' equity:		
Common stock, $0.01 par value; authorized 125,000,000 shares at December 31, 2019 and December 31, 2018; issued and outstanding 42,078,416 shares at December 31, 2019 and 24,456,120 shares at December 31, 2018	421	245
Preferred stock, $0.01 par value; authorized 5,000,000 shares; none outstanding	—	—
Additional paid-in capital	358,245	270,509
Accumulated other comprehensive income (loss)	37	(16)
Accumulated deficit	(272,934)	(236,614)
Total stockholders' equity	85,769	34,124
Total liabilities and stockholders' equity	$ 98,826	$ 63,256

See accompanying notes to consolidated financial statements.

CHIASMA, INC.

CONSOLIDATED STATEMENTS OF OPERATIONS

	For the Years Ended December 31,		
	2019	2018	2017
	(in thousands except share and per share data)		
Operating expenses:			
General and administrative	$ 15,122	$ 9,974	$ 9,146
Research and development	22,457	22,362	17,948
Restructuring charges	—	—	1,038
Total operating expenses	37,579	32,336	28,132
Loss from operations	(37,579)	(32,336)	(28,132)
Other income, net	(1,543)	(1,044)	(716)
Loss before income taxes	(36,036)	(31,292)	(27,416)
Provision (benefit) for income taxes	284	(31)	(590)
Net loss	$ (36,320)	$ (31,261)	$ (26,826)
Earnings per share			
Basic	$ (1.06)	$ (1.28)	$ (1.10)
Diluted	$ (1.06)	$ (1.28)	$ (1.10)
Weighted-average shares outstanding:			
Basic	34,204,284	24,399,706	24,366,681
Diluted	34,204,284	24,399,706	24,366,681

See accompanying notes to consolidated financial statements.

CHIASMA, INC.

CONSOLIDATED STATEMENTS OF COMPREHENSIVE INCOME (LOSS)

	For the Years Ended December 31,		
	2019	2018	2017
	(in thousands)		
Net loss	$(36,320)	$(31,261)	$(26,826)
Other comprehensive income (loss):			
Unrealized gain (loss) on available for sale securities, net	53	43	(50)
Total other comprehensive income (loss):	53	43	(50)
Comprehensive loss	$(36,267)	$(31,218)	$(26,876)

See accompanying notes to consolidated financial statements.

CHIASMA, INC.

CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY

	Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount				
	(in thousands except share data)					
Balance, December 31, 2016	24,359,584	$ 244	$264,017	$ (9)	$ (178,527)	$ 85,725
Stock-based compensation	—	—	3,522	—	—	3,522
Exercise of stock options	22,021	—	2	—	—	2
Additional paid-in capital on account of vested portion of restricted stock	—	—	101	—	—	101
Other comprehensive loss	—	—	—	(50)	—	(50)
Net loss	—	—	—	—	(26,826)	(26,826)
Balance, December 31, 2017	24,381,605	244	267,642	(59)	(205,353)	62,474
Stock-based compensation	—	—	2,730	—	—	2,730
Exercise of stock options	74,515	1	36	—	—	37
Additional paid-in capital on account of vested portion of restricted stock	—	—	101	—	—	101
Other comprehensive income	—	—	—	43	—	43
Net loss	—	—	—	—	(31,261)	(31,261)
Balance, December 31, 2018	24,456,120	245	270,509	(16)	(236,614)	34,124
Stock-based compensation	—	—	3,270	—	—	3,270
Exercise of stock options	192,711	2	48	—	—	50
Issuance of common stock in follow-on offerings, net	17,429,585	174	84,402	—	—	84,576
Additional paid-in capital on account of vested portion of restricted stock	—	—	16	—	—	16
Other comprehensive income	—	—	—	53	—	53
Net loss	—	—	—	—	(36,320)	(36,320)
Balance, December 31, 2019	42,078,416	$ 421	$358,245	$ 37	$ (272,934)	$ 85,769

See accompanying notes to consolidated financial statements.

CHIASMA, INC.

CONSOLIDATED STATEMENTS OF CASH FLOWS

	For the Years Ended December 31,		
	2019	2018	2017
	(in thousands)		
Operating Activities:			
Net loss	$(36,320)	$(31,261)	$(26,826)
Adjustments to reconcile net loss to net cash provided by (used in) operating activities:			
Depreciation	55	88	152
Stock-based compensation	3,270	2,730	3,522
Amortization of premium on marketable securities, net	(515)	(440)	(150)
Amortization of right-of-use asset	319	—	—
Provision (benefit) for deferred income taxes	(22)	16	(884)
Non-cash interest expense	—	5	131
Loss on disposal of property and equipment	29	—	—
Changes in operating assets and liabilities:			
Prepaid expenses and other current assets	(1,420)	471	820
Insurance recovery (Note 12)	18,288	—	—
Accounts payable and accrued expenses	111	4,349	(1,616)
Settlement liability (Note 12)	(18,750)	—	—
Other assets	(107)	9	402
Other current and long-term liabilities	50	(58)	25
Net cash used in operating activities	(35,012)	(24,091)	(24,424)
Investing Activities:			
Purchase of marketable securities	(99,726)	(38,010)	(89,163)
Maturities of marketable securities	64,376	62,227	92,898
Purchases of property and equipment	(307)	(6)	(23)
Net cash provided by (used in) investing activities	(35,657)	24,211	3,712
Financing Activities:			
Proceeds from the issuance of common stock, net	84,576	—	—
Exercise of stock options	50	37	2
Payments under license termination agreement	—	(1,700)	(1,700)
Proceeds from short-term borrowing	1,675	—	—
Payments of short-term borrowing	(837)	—	—
Net cash provided by (used in) financing activities	85,464	(1,663)	(1,698)
Net increase (decrease) in cash and cash equivalents	14,795	(1,543)	(22,410)
Cash and cash equivalents, beginning of year	13,060	14,603	37,013
Cash and cash equivalents, end of year	$ 27,855	$ 13,060	$ 14,603
Supplemental disclosures of cash flow information:			
Cash paid for income taxes	$ 380	$ 333	$ 51

See accompanying notes to consolidated financial statements.

CHIASMA, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

1. Nature of Business

Chiasma, Inc. is a clinical, late-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 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 ("TPE") technology platform, we seek to develop oral medications that are currently available only as injections. We are currently developing oral octreotide capsules, conditionally trade-named "MYCAPSSA", our TPE platform-based clinical product candidate, for the treatment of acromegaly. In July 2019, we reported positive top-line data from our second completed Phase 3 clinical trial of octreotide capsules in adult patients for the treatment of acromegaly. The trial, referred to as CHIASMA OPTIMAL, was a randomized, double-blind, placebo-controlled, nine-month trial that enrolled 56 adult acromegaly patients. We initiated this trial following our agreement with the United States Food and Drug Administration ("FDA") on the design of the trial, reached through a Special Protocol Assessment in August 2017. In December 2019, we resubmitted our New Drug Application ("NDA") and in early January 2020 the FDA accepted it for review and assigned a Prescription Drug User Fee Act, ("PDUFA") target action date of June 26, 2020.

Acromegaly is a rare and debilitating condition that results in the body's production of excess growth hormone. Octreotide is an analog of somatostatin, a natural inhibitor of growth hormone secretion. Octreotide capsules have 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.

We are also currently conducting an international Phase 3 clinical trial, referred to as MPOWERED, of oral octreotide capsules for the maintenance treatment of adult patients with acromegaly to support regulatory approval in the European Union by the European Medicines Agency ("EMA"). The MPOWERED trial is a global, randomized, open-label and active-controlled 15-month trial initially designed to enroll up to 150 patients. The EMA requested that a minimum of 80 patients who are responders to octreotide capsules per the protocol following the six-month run-in phase be randomized to either remain on octreotide capsules or return to injectable somatostatin receptor ligands (octreotide or lanreotide), and then followed for an additional nine months. In June 2019, we completed the enrollment of 146 total patients in MPOWERED and in January 2020 completed the randomization in the trial.

On April 2, 2019, we completed a follow-on underwritten public offering of 6,315,790 shares of common stock at a public offering price of $4.75 per share, before underwriting discounts and commissions, and on April 3, 2019, we closed on the sale of an additional 947,368 shares of common stock pursuant to the underwriters' option at a public offering price of $4.75 per share, before underwriting discounts and commissions. Aggregate gross proceeds were $34.5 million while net proceeds received after underwriting fees and offering expenses were approximately $32.2 million.

On July 30, 2019, we completed a follow-on underwritten public offering of 10,000,000 shares of common stock at a public offering price of $5.50 per share, before underwriting discounts and commissions and on August 23, 2019, we closed on the sale of an additional 166,427 shares of common stock pursuant to the underwriters' option at a public offering price of $5.50 per share, before underwriting discounts and commissions. Aggregate gross proceeds were $55.9 million while net proceeds received after underwriting fees and offering expenses were approximately $52.3 million.

These offerings were made pursuant to a prospectus dated March 22, 2018 and prospectus supplements dated March 29, 2019 and July 26, 2019, respectively, in connection with drawdowns from our shelf registration statement on Form S-3, which the U.S. Securities and Exchange Commission ("SEC") declared effective on May 3, 2018.

2. Summary of Significant Accounting Policies

Principles of Consolidation and Basis of Presentation

The accompanying consolidated financial statements include the accounts of Chiasma, Inc. and its subsidiaries and are prepared in conformity with accounting principles generally accepted in the United States of America ("U.S. GAAP") and are stated in U.S. dollars. The consolidated financial statements have been prepared on the basis of continuity of operations, realization of assets and the satisfaction of liabilities in the ordinary course of business. All intercompany balances and transactions have been eliminated in consolidation.

Consideration of Going Concern and Management's Plans

Under the existing accounting guidance, management must evaluate whether there are conditions or events, considered in the aggregate, that raise substantial doubt about the Company's ability to continue as a going concern within one year after the date the consolidated financial statements are issued. This evaluation initially does not take into consideration the potential mitigating effect of management's plans that have not been fully implemented as of the date the consolidated financial statements are issued. When substantial doubt is determined to exist, management evaluates whether the mitigating effect of its plans sufficiently alleviates substantial doubt about the Company's ability to continue as a going concern. The mitigating effect of management's plans; however, is only considered if both (1) it is probable that the plans will be effectively implemented within one year after the date the consolidated financial statements are issued, and (2) it is probable that the plans, when implemented, will mitigate the relevant conditions or events that raise substantial doubt about the entity's ability to continue as a going concern within one year after the date the consolidated financial statements are issued.

We have incurred substantial operating losses since inception, and we expect our operating losses and negative operating cash flows to continue for the foreseeable future. For the year ended December 31, 2019, we had a net loss of $36.3 million and used $35.0 million of cash in operations. At December 31, 2019, we had cash, cash equivalents and marketable securities of $92.4 million and an accumulated deficit of $272.9 million. We expect to continue to incur significant costs in the upcoming year as we prepare for the potential approval and commercial launch of octreotide capsules in the United States. The FDA has assigned a PDUFA target date of June 26, 2020 to our NDA resubmission. We also plan to continue to fund our international Phase 3 MPOWERED clinical trial of octreotide capsules in acromegaly to support potential regulatory approval in the European Union. Our current combined cash, cash equivalents and marketable securities are not sufficient to fund these activities, as currently planned, for one year after the date these consolidated financial statements are issued. Accordingly, we believe these conditions, in the aggregate, raise substantial doubt regarding our ability to continue as a going concern for a period of one year from the date the consolidated financial statements are issued.

In order to fund these efforts, we expect to finance our cash needs through a combination of equity and debt financings, and we will also opportunistically consider license and collaboration agreements with potential partners and other non-dilutive financing arrangements to the extent such sources are identified and available. If FDA approval is obtained, we plan to use revenues, if any, generated from the sale of octreotide capsules in the U.S. to fund our operations. While we believe our plans to raise additional funds and generate product sales will alleviate the conditions that raise substantial doubt, these plans are not entirely within our control and cannot be assessed as being probable of occurring. Further, while we have received a PDUFA date from the FDA, there can be no assurances that FDA approval of octreotide capsules will be received.

Use of estimates

The preparation of consolidated financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the amounts reported in the consolidated financial statements and accompanying notes. 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 consolidated financial statements include, but are not limited to, accounting for stock-based compensation, income taxes, and accounting for certain accruals. We assess these estimates on an ongoing basis; however, actual results could materially differ from those estimates.

Cash Equivalents

Cash equivalents consist of highly liquid instruments which mature within three months or less from 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 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 and accretion, together with interest on securities, are included in other income, net, on our 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.

Foreign currency translation

We use the U.S. dollar as our functional currency. Monetary assets and liabilities denominated in foreign currency are re-measured at current rates and non-monetary assets denominated in foreign currency are recorded at historical exchange rates. Realized and unrealized exchange gains or losses from transactions and re-measurement adjustments are reflected in other income, net, in the accompanying consolidated statements of operations.

Comprehensive income (loss)

Comprehensive income (loss) is defined as the change in equity of a business enterprise during a period from transactions and other events and circumstances from non-owner sources. Other than reported net income, comprehensive income (loss) includes unrealized gains and losses on available for sale securities, which are disclosed in the accompanying consolidated statements of comprehensive income. There were no reclassifications out of comprehensive income (loss) for the years ended December 31, 2019, 2018 or 2017.

Segment information

Operating segments are identified as components of an enterprise about which separate discrete financial information is available for evaluation by the chief operating decision maker, our Chief Executive Officer, in making decisions regarding resource allocation and assessing performance. We view our operations and manage our business in one operating segment.

Other assets

Other assets consist of right of use assets, long-term restricted deposits, prepayments, and deferred tax assets. Long-term restricted deposits represent interest-bearing money market accounts held as security deposits against bank guarantees.

Concentrations of credit risk

Financial instruments that potentially subject us to significant concentration of credit risk consist primarily of cash, cash equivalents, and marketable securities. 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 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.

Property and equipment

Property and equipment are stated at cost, net of accumulated depreciation and amortization. Expenditures for maintenance and repairs are charged to operations as incurred, whereas major betterments are capitalized as additions to property and equipment. Depreciation and amortization are recorded using the straight-line method over the estimated useful lives of the assets, as follows:

Asset Category	Estimated Useful Lives
Computer equipment and software	3 years
Office furniture and equipment	7—17 years (mainly 7)
Machinery and equipment	5—7 years
Leasehold improvements	The lesser of lease term or estimated useful lives

Impairment of long-lived assets

We review long-lived assets for impairment whenever events or changes in circumstances indicate that the carrying amount of the asset may not be recoverable. When such events occur, we compare the carrying amounts of the assets to their undiscounted expected future cash flows the assets are expected to generate and to be recognized. The amount of impairment loss to be recognized is the excess of the carrying value over the fair value of the related asset. We did not record any impairments during the years ended December 31, 2019, 2018 and 2017.

Employment termination costs

We accrue employment termination liabilities when (a) management, having the authority to approve the action, commits to a plan of termination; (b) the plan identifies the number of employees to be terminated, their job classifications or functions, their locations, and the expected completion date; (c) the plan establishes the terms of the arrangement, including the benefits that employees will receive upon termination, in sufficient detail to enable employees to determine the type and amount of benefits they will receive upon involuntary termination; (d) it is unlikely that significant changes to the plan will be made or withdrawn; and (e) the plan has been communicated to the affected employees. When employees are required to render services beyond the minimum retention period through the involuntary termination date in order to receive the termination benefits, a liability is measured initially at the communication date based on the fair value of the liability and is recognized ratably over the future service period through expected termination date. We reverse the liability when events or circumstances occur that discharge or remove its responsibility to settle the termination liability.

Research and development

Research and development costs are expensed as incurred. Research and development costs include payroll and personnel expense, consulting costs, external contract research and development expenses, raw materials, drug product manufacturing costs, and allocated overhead including depreciation and amortization, rent, and utilities. Research and development costs that are paid in advance of performance are capitalized as a prepaid expense and amortized over the service period as the services are provided.

Clinical trial costs

Clinical trial costs are a component of research and development expenses. We accrue and expense clinical trial activities performed by third parties on an evaluation of the progress to completion of specific tasks using data such as hours spent in performance of services, patient enrollment, clinical site activation, and other information provided to us by our vendors. We make estimates of our clinical trial accrued expenses as of each balance sheet date in our financial statements based on facts and circumstances known to us. If timelines or contracts are modified based upon changes in the clinical trial protocol or scope of work to be performed, we assess our estimates of accrued expenses accordingly.

Patent costs

Patent costs are expensed as incurred as their realization is uncertain. These costs are classified as general and administrative in the accompanying consolidated statements of operations.

Stock-based compensation

We account for all stock-based compensation to employees and nonemployees based on their fair values on the date of grant. For stock-based awards with only service conditions, we recognize compensation on a straight-line basis over the requisite service period, which is usually the vesting period of the award, net of any actual forfeitures.

We determine the fair value of stock options by using the Black-Scholes option pricing model. This model requires the input of several assumptions such as the expected option term, the expected risk-free interest rate over the expected option term, the expected volatility of our stock price over the expected option term, and the expected dividend yield over the expected option term. The computation of expected volatility is based on an average historical share price volatility based on an analysis of reported data for a peer group of comparable publicly traded companies, which were selected based upon industry similarities. The interest rate for periods within the expected term of the award is based on the U.S. Treasury risk-free interest rate in effect at the time of grant. The expected lives of the options were estimated using the simplified method.

Income taxes

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

We determine whether it is more likely than not that a tax position will be sustained upon examination. If it is not more likely than not that a position will be sustained, none of the benefit attributable to the position is recognized. The tax benefit to be recognized for any tax position that meets the more likely than not recognition threshold is calculated as the largest amount that is more than 50% likely of being realized upon resolution of the contingency. We account for interest and penalties related to uncertain tax positions as part of our other expenses in the accompanying consolidated financial statements.

Contingent liabilities

In the normal course of business, we are subject to proceedings, lawsuits, and other claims and assessments. We assess the likelihood of any adverse judgments or outcomes to these matters as well as potential ranges of probable losses. A determination of the amount of reserves required, if any, for these contingencies is made after careful analysis of each individual issue. The required reserves may change in the future due to new developments in each matter or changes in approach such as a change in settlement strategy in dealing with these matters. We record charges for the losses we anticipate incurring in connection with litigation and claims against us when we conclude a loss is probable and we can reasonably estimate these losses.

Earnings per share

We compute basic earnings per share by dividing net loss by the weighted average number of common shares outstanding for the period. We compute diluted earnings per common share after giving consideration to all potentially dilutive common shares, including stock options and warrants outstanding during the period, except where the effect of such non-participating securities would be antidilutive.

Recently issued accounting pronouncements

In February 2016, the Financial Accounting Standards Board ("FASB") issued new guidance which establishes a right-of-use model that requires a lessee to record an asset and a lease liability on the balance sheet for all leases with terms longer than 12 months. Leases will be classified as either finance or operating, with classification affecting the pattern of expense recognition in the income statement. The new standard is effective for annual periods beginning after December 15, 2018, including interim periods within those annual reporting periods. A modified retrospective approach, which includes a number of optional practical expedients that we have elected to apply, 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. On January 1, 2019, we adopted this standard using a modified retrospective approach. As of January 1, 2019, we recorded a right-of-use asset of $0.3 million and an operating lease liability of $0.3 million.

In June 2018, the FASB issued new guidance which changes certain aspects of the accounting for share-based payments granted to nonemployees. Under this guidance, most of the treatment for share-based payments granted to nonemployees would be aligned with the requirements for share-based payments granted to employees. The new standard is effective beginning January 1, 2019. Early adoption of this standard is permitted. We adopted this standard on January 1, 2019 and thus ceased the re-measurement of non-employee awards. The adoption of this standard did not have a material impact on our condensed consolidated financial statements.

In June 2016, the FASB issued new guidance which will require more timely recording of credit losses on loans and other financial instruments held by financial institutions and other organizations. The new guidance requires the measurement of all expected credit losses for financial assets held at the reporting date based on historical experience, current conditions and reasonable and supportable forecasts. The new guidance also requires enhanced disclosures regarding significant estimates and judgments used in estimating credit losses. This guidance is effective January 1, 2020 and early adoption of this standard is permitted. We plan to adopt this standard on January 1, 2020. We believe the adoption of this standard will not have a material impact on our consolidated financial statements.

3. Investments

Our investments consisted of the following as of December 31, 2019 and 2018:

	As of December 31, 2019			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
	($ in thousands)			
Money market funds	$ 23,012	$ —	$ —	$ 23,012
Corporate notes	45,584	20	—	45,604
Commercial paper	20,899	17	—	20,916
Total	$ 89,495	$ 37	$ —	$ 89,532

	As of December 31, 2018			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
	($ in thousands)			
Money market funds	$ 11,612	$ —	$ —	$ 11,612
Corporate notes	7,234	—	(3)	7,231
Commercial paper	21,384	—	(13)	21,371
Total	$ 40,230	$ —	$ (16)	$ 40,214

As of December 31, 2019, 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 years ended December 31, 2019, 2018 or 2017.

The fair values of our investments by classification in our consolidated balance sheets as of December 31, 2019 and 2018 were as follows:

	As of December 31,	
	2019	2018
	($ in thousands)	
Cash and cash equivalents	$25,012	$11,612
Marketable securities	64,520	28,602
Total	$89,532	$40,214

Cash and cash equivalents in the table above exclude cash of $2.8 million and $1.4 million as of December 31, 2019 and 2018, respectively. The contractual maturity dates of all of our investments are less than one year.

4. Fair Value Measurements and Fair Value of Financial Instruments

Certain assets and liabilities are reported at fair value on a recurring basis. 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 following tables summarize the fair value measurements of our financial instruments as of December 31, 2019 and 2018:

	Fair Value Measurements at December 31, 2019			
	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	$ 23,012	$ —	$ —	$23,012
Corporate notes	—	2,000	—	2,000
Total cash equivalents	$ 23,012	$ 2,000	$ —	$25,012
Marketable securities:				
Corporate notes	$ —	$ 43,604	$ —	$43,604
Commercial paper	—	20,916	—	20,916
Total marketable securities	$ —	$ 64,520	$ —	$64,520
Total	$ 23,012	$ 66,520	$ —	$89,532

	Fair Value Measurements at December 31, 2018			
	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	$ 11,612	$ —	$ —	$11,612
Total cash equivalents	$ 11,612	$ —	$ —	$11,612
Marketable securities:				
Corporate notes	$ —	$ 7,231	$ —	$ 7,231
Commercial paper	—	21,371	—	21,371
Total marketable securities	$ —	$ 28,602	$ —	$28,602
Total	$ 11,612	$ 28,602	$ —	$40,214

Our cash equivalents are classified as Level 1 assets under the fair value hierarchy as these assets have been valued using quoted market prices in active markets and do not have any restrictions on redemption. Our marketable securities are classified as Level 2 assets under the fair value hierarchy as these assets were primarily determined from independent pricing services, which normally derive security prices from recently reported trades for identical or similar securities, making adjustments based upon other significant observable market transactions. At the end of each reporting period, we perform quantitative and qualitative analysis of prices received from third parties to determine whether prices are reasonable estimates of fair value. After completing

our analysis, we did not adjust or override any fair value measurements provided by our pricing services as of December 31, 2019 or 2018. We did not have any Level 3 assets being measured at fair value on a recurring basis as of December 31, 2019 or 2018. There were no transfers between measurement levels during the years ended December 31, 2019 and 2018.

5. Earnings per Share

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 years ended December 31, 2019, 2018 and 2017. Since we have reported a net loss for the years ended December 31, 2019, 2018 and 2017, diluted net loss per share is the same as basic net loss per share for those periods.

6. Property and Equipment

Property and equipment consisted of the following as of December 31, 2019 and 2018:

	As of December 31,	
	2019	2018
	($ in thousands)	
Computer equipment and software	$ 431	$ 357
Office furniture and equipment	108	155
Machinery and equipment	115	—
Property and equipment, at cost	654	512
Less accumulated depreciation	(320)	(401)
Property and equipment, net	$ 334	$ 111

Depreciation expense was $0.1 million, $0.1 million and $0.2 million for the years ended December 31, 2019, 2018 and 2017, respectively.

7. Accrued Expenses

Accrued expenses consisted of the following as of December 31, 2019 and 2018:

	As of December 31,	
	2019	2018
	($ in thousands)	
Accrued general and administrative expenses	$ 647	$2,120
Accrued research and development expenses	4,219	4,557
Accrued payroll and employee benefits	1,872	1,171
Short-term borrowing	838	—
Total accrued expenses	$7,576	$7,848

8. 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 octreotide capsules. In July 2014, Roche terminated the license agreement. 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 final $1.7 million annual payment in March 2018. Roche has no remaining rights to octreotide capsules and we retain all rights to octreotide capsules and all related intellectual property. We have no further financial or operational obligations to Roche.

9. Warrants

As of December 31, 2019, there are warrants for the purchase of 3,567,015 shares of common stock outstanding, with exercise prices ranging from $0.09 to $9.13. Such warrants were issued between October 2012 and February 2015 and have expiration dates ranging from March 2022 through December 2024. There were no warrants issued or exercised during the year ended December 31, 2019.

10. Stock Incentive Plan

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 our employees, directors, and nonemployees up to 3,547,741 shares of common stock. Option awards expire 10 years from the grant date and generally vest over four years; however, vesting conditions can vary at the discretion of our Board of Directors.

In July 2015, we approved a 2015 Stock Option and Incentive Plan (the "2015 Plan"), which became effective upon our IPO. The 2015 Plan allows the grant of incentive stock options, nonqualified stock options, restricted stock, and other stock-based awards to employees, directors, and nonemployees of Chiasma 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, 2020 and 2019, the number of shares reserved and available for issuance under the 2015 Stock Plan increased by 1,683,136 and 978,245 shares of common stock, respectively, 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. The Board of Directors determined there would be no increase to the shares reserved and available under the 2015 Stock Plan on January 1, 2018. As of December 31, 2019, the total number of shares authorized for stock award plans is 8,092,282 of which 1,021,108 remain available for grant. There are 6,489,692 stock options outstanding as of December 31, 2019. 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:

	For the Years Ended December 31,		
	2019	2018	2017
Expected volatility	97%	77%	74%
Expected term (years)	6.0	6.2	5.7
Risk-free interest rate	1.93%	2.72%	1.81%
Expected dividend yield	0%	0%	0%

A summary of option activity as of December 31, 2019 and the year then ended is presented below:

	Number of Stock Options	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term (Years)	Aggregate Intrinsic Value
Outstanding, December 31, 2018	4,373,674	$ 4.16	7.0	$ 3,140,879
Exercised	(192,711)	$ 0.26		
Granted	2,336,233	$ 6.17		
Forfeited / Expired	(27,504)	$ 2.62		
Outstanding, December 31, 2019	6,489,692	$ 5.01	7.3	$ 8,166,882
Exercisable, December 31, 2019	3,537,464	$ 4.82	5.8	$ 5,433,126
Vested and expected to vest, December 31, 2019	6,489,692	$ 5.01	7.3	$ 8,166,882

The weighted-average grant date per-share fair value of stock options granted during 2019, 2018 and 2017 was $4.79, $1.06 and $0.95, respectively. The aggregate intrinsic value of stock options exercised during the years ended December 31, 2019, 2018 and 2017 was approximately $1.0 million, $0.2 million and $40,000, respectively.

At December 31, 2019, there was $10.1 million of unrecognized compensation cost related to stock options, which is expected to be recognized over a weighted-average period of 3.0 years.

Stock-based compensation expense for 2019, 2018 and 2017 consisted of the following:

	For the Years Ended December 31,		
	2019	2018	2017
	($ in thousands)		
General and administrative	$2,243	$1,412	$1,510
Research and development	1,027	1,318	2,012
Total	$3,270	$2,730	$3,522

During 2015, two directors exercised options to purchase an aggregate of 122,644 shares of common stock of which 116,258 of the shares were issued as restricted stock as they were exercised prior to full vesting. The proceeds from the issuance of the restricted stock was historically presented as a liability within the consolidated balance sheet, since we had the right to repurchase the unvested portion of the restricted stock following termination of the services of their holder. The liability was released to additional paid-in capital per the original vesting schedule of the options. As of December 31, 2019, the restricted shares were fully vested.

11. Income Taxes

Our loss before provision (benefit) for income taxes for the years ended December 31, 2019, 2018 and 2017 consisted of the following:

	For the Years Ended December 31,		
	2019	2018	2017
	($ in thousands)		
Domestic	$(36,407)	$(31,477)	$(27,703)
Foreign	371	185	287
Total	$(36,036)	$(31,292)	$(27,416)

The components of income tax provision (benefit) consisted of the following for the years ended December 31, 2019, 2018 and 2017:

	For the Years Ended December 31,		
	2019	2018	2017
	($ in thousands)		
Current provision for income taxes:			
U.S.	$ 18	$ 12	$ 13
Foreign	288	(59)	281
Total current provision for income taxes	306	(47)	294
Deferred tax benefit—U.S. Federal	—	—	(956)
Deferred tax provision (benefit)—foreign	(22)	16	72
Total deferred provision (benefit) for income taxes	(22)	16	(884)
Total provision (benefit) for income taxes	$284	$ (31)	$(590)

A reconciliation setting forth the differences between our effective tax rates and the U.S. federal statutory tax rate is as follows:

	For the Years Ended December 31,		
	2019	2018	2017
U.S. federal tax provision at statutory rate	21.0%	21.0%	34.0%
State and local tax, net of federal benefit	5.6%	5.3%	4.4%
Foreign rate differences	0.1%	0.2%	0.8%
Non-deductible foreign stock compensation	(0.3%)	(0.4%)	(1.7%)
Effect of other permanent differences	(0.5%)	(0.3%)	(0.7%)
Uncertain tax positions	(0.4%)	0.2%	0.1%
Change in valuation allowance	(26.1%)	(26.0%)	33.2%
Federal Tax Reform Rate Change	0.0%	0.0%	(68.5%)
Other adjustments	(0.2%)	0.1%	0.6%
Effective tax rate	(0.8%)	0.1%	2.2%

Deferred income taxes reflect the net tax effects of temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income and for tax carryforwards. Significant components of our deferred tax assets and liabilities as of December 31, 2019 and 2018 are as follows:

	As of December 31,	
	2019	2018
	($ in thousands)	
Deferred tax assets:		
Federal and state net operating loss carryforwards	$ 54,269	$ 45,722
Intangible and other related assets	379	333
Accrued expenses	710	482
Stock compensation	2,180	1,513
Lease liability	325	—
Other	18	77
Total deferred tax assets	57,881	48,127
Deferred tax liabilities:		
Right of use asset	(291)	—
Total deferred tax liabilities	(291)	—
Valuation allowance	(57,560)	(48,119)
Net deferred tax assets	$ 30	$ 8

When realization of a deferred tax asset is more likely than not to occur, the benefit related to the deductible temporary differences attributable to operations is recognized as a reduction of income tax expense. Valuation allowances are provided against deferred tax assets when, based on all available evidence, it is considered more likely than not that some portion or all of the recorded deferred tax assets will not be realized in future periods. We cannot be certain that future U.S. taxable income will be sufficient to realize our deferred tax assets. Accordingly, a full valuation allowance has been provided against our U.S. net deferred tax assets. The valuation allowance increased by $9.4 million and $8.1 million in 2019 and 2018, respectively. The increases in 2019 and 2018 were primarily the result of an increase in net operating loss (“NOL”) carryforwards.

At December 31, 2019, we had U.S. Federal and state NOL carryforwards totaling approximately $217.1 million and $167.2 million, respectively, that expire at various dates through 2037 with the exception of the Federal NOLs generated after December 31, 2017 of approximately $61.3 million which have an unlimited carryover period. At December 31, 2019, we had no Israeli NOL carryforwards.

We expect, our U.S. Federal alternative minimum tax credit to go unutilized and become refundable in future periods. The tax reform also allows us to receive the U.S. Federal alternative minimum tax credit carryforward in the form of a refund on our 2018 through 2021 Federal tax returns. We have a history of generating losses and are forecasting that we will not generate taxable income through 2021 which would otherwise limit our ability to realize our U.S. Federal alternative minimum tax credit. Accordingly, we have recorded a receivable of $0.5 million and $1.0 million for the U.S. Federal alternative minimum tax credit refund in the accompanying consolidated balance sheet as of December 31, 2019 and 2018, respectively.

Under Section 382 of the Internal Revenue Code of 1986, as amended, substantial changes in our ownership may limit the amount of NOL carryforwards that can be utilized annually in the future to offset our U.S. Federal taxable income. Specifically, this limitation may arise in the event of a cumulative change in our ownership of more than 50% within any three-year period. We have determined that we experienced an ownership change for purposes of Section 382 in August 2005, May 2008, and February 2015. 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 U.S. Federal level. The annual limit is approximately $1.2 million for 2015, and each year thereafter.

If we perform a Section 382 study in the future and conclude that have in fact undergone an ownership change, our NOL carryforwards may be substantially limited.

Our Israeli subsidiary has been recognized as a research and development company by the Head of the Israeli Administration of Industrial Research and Development and is entitled to tax benefits by virtue of the "beneficiary enterprise" status granted to part of its business activities under the Israeli Law for the Encouragement of Capital Investments 1959. The tax benefits include reduced tax rates on the research and development portion of its income during the first ten years of the benefit period (commenced in 2008). We benefit from a 16% tax rate for its income derived from research and development activities. Our tax rate on income from non-research and development activities is 23.0%. The continued application of the tax benefits is subject to certain conditions as defined by Israeli law.

As part of the transition tax provision, we have a deemed repatriation of all of our undistributed earnings as of December 31, 2019. However, our subsidiary's earnings, if distributed, would still be subject to local withholding tax and state income taxes. The subsidiary has undistributed earnings of approximately $1.7 million as of December 31, 2019, which is considered to be permanently reinvested in the operations of the subsidiary. If the earnings were to be distributed to the U.S. parent, they would be subject to Israeli withholding and state income tax liabilities. The unrecognized deferred tax liability is approximately $0.2 million.

We file U.S. federal, various state and Israeli income tax returns. The associated tax filings remain subject to examination by applicable tax authorities for a certain length of time following the tax year to which those filings relate. As we are in a loss carry-forward position, we are generally subject to U.S. Federal and state examinations for all years for which the Company generated losses that are included in the available losses carried forward to the current period. As of December 31, 2019, a summary of the tax years that remain subject to examination in our taxing jurisdictions is as follows:

United States	2003 and forward
Israel	2014 and forward

We have reviewed the tax positions taken, or to be taken, in our tax returns for all tax years currently open to examination by a taxing authority. We have recorded minimal interest or penalties related to uncertain tax positions. We remain subject to examination until the statute of limitations expires for each respective tax jurisdiction. The statute of limitations will be open with respect to these tax positions until 2021. A reconciliation of the beginning and ending amount of our unrecognized tax benefits is as follows:

	For the Years Ended December 31,		
	2019	2018	2017
	($ in thousands)		
Uncertain tax position at the beginning of year	$391	$471	$460
Additions for uncertain tax positions of prior year	177	—	45
Additions for uncertain tax positions of current year	—	—	—
Reductions for settlements with taxing authorities	—	—	—
Reductions for lapses of the applicable statutes of limitations	—	(80)	(34)
Uncertain tax position at the end of the year	$568	$391	$471

12. Commitments and Contingencies

Manufacturing Commitments

As of December 31, 2019, we had outstanding purchase orders for the acquisition of API in the aggregate amount of $11.6 million. The payments on these orders will occur following the deliveries of the API which are anticipated during 2020.

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*. An amended complaint was filed by the lead plaintiff on February 10, 2017 challenging our statements regarding our first 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 added as defendants current and former members of our board of directors, as well as the investment banks that underwrote our initial public offering on July 15, 2015. The plaintiff sought 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 on February 15, 2018, the court denied defendants' motion to dismiss. The defendants filed an answer to the amended complaint on March 30, 2018. On February 27, 2019, the parties agreed to a settlement of all legal claims in which defendants expressly denied that they have committed any act or omission giving rise to any liability under Sections 11 or 15 of the Securities Act of 1933. On March 14, 2019, the court issued an order of preliminary approval of the settlement. As a result of this settlement agreement, we recorded a litigation settlement liability of $18.8 million as of December 31, 2018. Additionally, we recorded a litigation insurance settlement recovery receivable of $18.3 million as of December 31, 2018 which represents the estimated insurance claim proceeds from our insurance carriers. On June 27, 2019, the court issued an order of final approval of the settlement. The litigation insurance settlement recovery and litigation settlement liability were settled during the three months ended June 30, 2019.

13. Leases

We adopted the new lease standard on January 1, 2019. We elected a package of practical expedients, which include: (i) an entity need not reassess whether any expired or existing contracts are or contain leases; (ii) an entity need not reassess the lease classification for any expired or existing leases; and (iii) an entity need not reassess any initial direct costs for any existing leases. Another practical expedient allows us to use hindsight in determining the lease term when considering lessee options to extend or terminate the lease and to purchase the underlying asset. We have elected to utilize this package of practical expedients and have not elected the hindsight methodology in its implementation of the lease standard. We elected to adopt this standard using the optional modified retrospective transition method and therefore comparative periods have not been restated. We have elected to not recognize right-of-use assets and lease liabilities arising from short-term leases, which are leases that, at the commencement date, have a lease term of 12 months or less and do not include an option to purchase the underlying asset that the lessee is reasonably certain to exercise.

We determine if an arrangement is a lease at inception. We have operating leases for our office spaces and certain automobiles. Right-of-use assets and lease liabilities are recognized based on the present value of the future minimum lease payments over the lease term at the commencement date. The operating lease right-of-use asset also includes direct costs incurred and is reduced by lease incentives. Lease agreements with lease and non-lease components are accounted for separately. As our leases do not provide an implicit rate, we use an estimated incremental borrowing rate based on the information available at the commencement date in determining the present value of future payments. We recognize operating lease expense on a straight-line basis over the lease term.

In October 2019, we entered into a sublease agreement for our new corporate headquarters in Needham, Massachusetts with a three-year term commencing on December 7, 2019. We were required to provide the sublandlord with a security deposit in the amount of $0.1 million.

	Year Ending December 31, 2019 ($ in thousands)
The components of lease expense were as follows:	
Operating lease expense	$ 366
Supplemental cash flow information related to leases was as follows:	
Cash paid for amounts included in the measurement of lease liabilities:	
Operating cash flows from operating leases	$ 219
Right-of-use assets obtained in exchange for lease obligations:	
Operating leases	$ 1,690

For the years ended December 31, 2018 and 2017, we recognized rent expense of $0.2 million and $1.0 million, respectively.

Our operating lease right-of-use assets are recorded within other assets on our consolidated balance sheets.

	December 31, 2019 ($ in thousands)
Supplemental balance sheet information related to leases was as follows:	
Operating lease right-of-use assets	$ 1,371
Other current liabilities	$ 465
Long-term liabilities	1,036
Total operating lease liabilities	$ 1,501
Weighted average remaining lease term—operating leases	31 Months
Weighted average discount rate—operating leases	10.8%

Future lease payments under noncancelable leases as of December 31, 2019 are as follows:

	($ in thousands)
2020	$ 609
2021	661
2022	487
Total future minimum lease payments	1,757
Less: imputed interest	(256)
Total	$ 1,501

14. Related Party Transactions

In August 2014, we signed a consulting agreement, which was most recently amended in March 2018, with one of our investors and a representative of this investor to serve as our head of clinical. Payments for services

rendered by the head of clinical were $0.3 million, $0.3 million and $0.2 million for the years ended December 31, 2019, 2018 and 2017, respectively. Related to this consulting agreement, there were $0.1 million of accrued liabilities as of December 31, 2019 and 2018, respectively, recorded in our consolidated balance sheets.

15. Employee Benefit Plans

Pursuant to the Israeli Severance Pay Law 1963, Israeli employees are entitled to severance pay equal to one month's salary for each year of employment, or a portion thereof. The employees of Chiasma (Israel) Ltd. are included under Section 14 of the Severance Pay Law, under which these employees are entitled to monthly deposits, which relieve us from future obligations under this law. As a result, no assets or liabilities are recorded in the accompanying consolidated balance sheets. In addition, we make mandated monthly contributions to an Israeli government retirement benefit plan for our Israeli employees. Beginning in 2016, we provide a 401(k) profit-sharing plan covering eligible U.S. employees to make tax deferred contributions, a portion of which are matched by us. All matching contributions and participant contributions vest immediately. During the years ended December 31, 2019, 2018 and 2017, we recorded expenses of $0.2 million, $0.2 million and $0.2 million, respectively, related to these employee benefit plans.

16. Restructuring Charges

In August 2016, we announced a corporate restructuring plan which included an immediate reduction of approximately 44% of our workforce. In November 2017, we finalized the termination of our lease agreement on our 24,000 square foot office facility in Waltham, MA which we no longer required following the 2016 workforce reductions. As a result, we recorded approximately $1.0 million of restructuring expenses during the year ended December 31, 2017, which consisted of a lease termination payment of $1.0 million, the write-off of office furniture and equipment of $0.4 million offset by the release of deferred rent liabilities of $0.4 million associated with the terminated lease.

We did not incur any restructuring expenses during the years ended December 31, 2019 and 2018.

Activity related to accrued restructuring costs during the year ended December 31, 2017 is as follows:

	2017
Balance at beginning of year	$ 283
Plus:	
Current year restructuring costs	1,038
Less:	
Lease termination costs	(1,038)
Payment of employee severance costs	(283)
Balance at end of year	$ —

17. Other Income, net

Other income, net is as follows:

	For the Years Ended December 31,		
	2019	2018	2017
	($ in thousands)		
Loss / (gain) on foreign currency transactions, net	$ 75	$ (37)	$ 81
Interest income	(1,573)	(1,013)	(928)
Interest expense	19	6	131
Other income	(64)	—	—
Total	$(1,543)	$(1,044)	$(716)

18. Quarterly Financial Data (unaudited)

	Three Months Ended			
	March 31, 2019	June 30, 2019	September 30, 2019	December 31, 2019
	($ in thousands, except for per share data)			
Loss from operations	$ (8,921)	$(8,166)	$ (8,226)	$ (12,266)
Net loss	(8,750)	(7,840)	(7,683)	(12,047)
Earnings per share				
Basic	$ (0.36)	$ (0.25)	$ (0.20)	$ (0.29)
Diluted	$ (0.36)	$ (0.25)	$ (0.20)	$ (0.29)

	Three Months Ended			
	March 31, 2018	June 30, 2018	September 30, 2018	December 31, 2018
	($ in thousands, except for per share data)			
Loss from operations	$ (7,297)	$(8,932)	$ (7,718)	$ (8,389)
Net loss	(7,043)	(8,673)	(7,470)	(8,075)
Earnings per share				
Basic	$ (0.29)	$ (0.36)	$ (0.31)	$ (0.32)
Diluted	$ (0.29)	$ (0.36)	$ (0.31)	$ (0.32)

DESCRIPTION OF CAPITAL STOCK

The following description of the capital stock of Chiasma, Inc. ("us," "our," "we" or the "Company") is a summary of the rights of our common stock and certain provisions of our amended and restated certificate of incorporation and our amended and restated bylaws currently in effect. This summary does not purport to be complete and is qualified in its entirety by the provisions of our amended and restated certificate of incorporation, as amended, and amended and restated bylaws, each previously filed with the Securities and Exchange Commission and incorporated by reference as an exhibit to the Annual Report on Form 10-K of which this Exhibit 4.5 is a part, as well as to the applicable provisions of the Delaware General Corporation Law (the "DGCL"). We encourage you to read our certificate of incorporation, bylaws and the applicable portions of the DGCL carefully.

Authorized Capital Stock

Our authorized capital stock consists of 125,000,000 shares of common stock, par value $0.01 per share, and 5,000,000 shares of preferred stock, par value $0.01 per share, all of which shares of preferred stock are undesignated.

Common Stock

The holders of our common stock are entitled to one vote for each share held on all matters submitted to a vote of the stockholders. The holders of our common stock do not have any cumulative voting rights. Holders of our common stock are entitled to receive ratably any dividends declared by the board of directors out of funds legally available for that purpose, subject to any preferential dividend rights of any outstanding preferred stock. Our common stock has no preemptive rights, conversion rights or other subscription rights or redemption or sinking fund provisions.

In the event of our liquidation, dissolution or winding up, holders of our common stock will be entitled to share ratably in all assets remaining after payment of all debts and other liabilities and any liquidation preference of any outstanding preferred stock. The shares to be issued by us in this offering will be, when issued and paid for, validly issued, fully paid and non-assessable.

Preferred Stock

Our board of directors has the authority, without further action by our stockholders, to issue up to 5,000,000 shares of preferred stock in one or more series and to fix the rights, preferences, privileges and restrictions thereof. These rights, preferences and privileges could include dividend rights, conversion rights, voting rights, terms of redemption, liquidation preferences, sinking fund terms and the number of shares constituting, or the designation of, such series, any or all of which may be greater than the rights of common stock. The issuance of our preferred stock could adversely affect the voting power of holders of common stock and the likelihood that such holders will receive dividend payments and payments upon our liquidation. In addition, the issuance of preferred stock could have the effect of delaying, deferring or preventing a change in control of our Company or other corporate action. No shares of preferred stock are outstanding, and we have no present plan to issue any shares of preferred stock.

Registration Rights

The holders of our registrable shares, as described in our Amended and Restated Investor Rights Agreement, dated December 16, 2014 (the "Investor Rights Agreement") are entitled to rights with respect to the registration of such shares under the Securities Act. These rights are provided under the terms of the Investor Rights Agreement, and include demand registration rights, short-form registration rights and piggyback registration rights. All fees, costs and expenses of underwritten registrations will be borne by us and all selling expenses, including underwriting discounts and selling commissions, will be borne by the holders of the shares being registered.

Demand registration rights

Certain holders of shares of our common stock are entitled to demand registration rights. Under the terms of the Investor Rights Agreement, we are required, upon the written request of holders of at least 25% of the shares of our common stock issued upon conversion of our Series E Preferred Stock, to use our best efforts to effect the registration of such shares, subject to certain exceptions. We are required to effect only two registrations pursuant to this provision.

Form S-3 Registration Rights

Certain holders of shares of our common stock are also entitled to short form registration rights. If we are eligible to file a registration statement on Form S-3, upon the written request of certain holders of our common stock to register shares with an anticipated aggregate offering price of at least $3,000,000, we are required to use our best efforts to effect a registration of such shares, subject to certain exceptions.

Piggyback registration rights

Certain holders of shares of our common stock are entitled to piggyback registration rights. If we propose to register any of our securities, either for our own account or for the account of other security holders, the holders of these shares are entitled to include their shares in the registration, and if such holders exercise their right to be included in such registration, we will be required to use our best efforts to include them in the registration. Subject to certain exceptions, the managing underwriter may limit the number of shares included in the underwritten offering if it concludes that marketing factors require such a limitation.

Indemnification

The Investor Rights Agreement contains customary cross-indemnification provisions, under which we are obligated to indemnify holders of registrable securities in the event of material misstatements or omissions in the registration statement attributable to us, and they are obligated to indemnify us for material misstatements or omissions attributable to them.

Expiration of registration rights

The registration rights granted under the Investor Rights Agreement will terminate on the earliest of (i) the fifth anniversary of our initial public offering, (ii) the date on which no stockholder party to the Investor Rights Agreement holds any Registrable Shares (as defined therein) or (iii) a Company Sale (as defined therein).

Anti-Takeover Effects of Our Certificate of Incorporation and Bylaws and Delaware Law

Our certificate of incorporation and bylaws contain certain provisions that are intended to enhance the likelihood of continuity and stability in the composition of the board of directors and which may have the effect of delaying, deferring or preventing a future takeover or change in control of the company unless such takeover or change in control is approved by the board of directors. These provisions include the items described below.

Classified Board

Our certificate of incorporation provides that our board of directors will be divided into three classes of directors, with the classes as nearly equal in number as possible. As a result, approximately one-third of our board of directors will be elected each year. The classification of directors will have the effect of making it more difficult for stockholders to change the composition of our board. Our certificate of incorporation also provides that, subject to any rights of holders of preferred stock to elect additional directors under specified circumstances, the number of directors will be fixed exclusively pursuant to a resolution adopted by our board of directors. Our board of directors currently has eight members.

Action by Written Consent; Special Meetings of Stockholders

Our certificate of incorporation provides that stockholder action can be taken only at an annual or special meeting of stockholders and cannot be taken by written consent in lieu of a meeting. Our certificate of incorporation and the bylaws also provide that, except as otherwise required by law, special meetings of the stockholders can be called only by or at the direction of the board of directors pursuant to a resolution adopted by a majority of the total number of directors. Stockholders are not permitted to call a special meeting or to require the board of directors to call a special meeting.

Removal of Directors

Our certificate of incorporation provides that our directors may be removed only for cause by the affirmative vote of at least 75% of the votes that all our stockholders would be entitled to cast in an annual election of directors, voting together as a single class, at a meeting of the stockholders called for that purpose. This requirement of a supermajority vote to remove directors could enable a minority of our stockholders to prevent a change in the composition of our board.

Advance Notice Procedures

Our bylaws provide an advance notice procedure for stockholder proposals to be brought before an annual meeting of our stockholders, including proposed nominations of persons for election to the board of directors. Stockholders at an annual meeting may only consider proposals or nominations specified in the notice of meeting or brought before the meeting by or at the direction of the board of directors or by a stockholder who was a stockholder of record on the record date for the meeting, who is entitled to vote at the meeting and who has given our Secretary timely written notice, in proper form, of the stockholder's intention to bring that business before the meeting. Although the bylaws do not give the board of directors the power to approve or disapprove stockholder nominations of candidates or proposals regarding other business to be conducted at a special or annual meeting, the bylaws may have the effect of precluding the conduct of certain business at a meeting if the proper procedures are not followed or may discourage or deter a potential acquirer from conducting a solicitation of proxies to elect its own slate of directors or otherwise attempting to obtain control of the company.

Super Majority Approval Requirements

The Delaware General Corporation Law generally provides that the affirmative vote of a majority of the shares entitled to vote on any matter is required to amend a corporation's certificate of incorporation or bylaws, unless either a corporation's certificate of incorporation or bylaws requires a greater percentage. A majority vote of our board of directors or the affirmative vote of holders of at least 75% of the total votes of the outstanding shares of our capital stock entitled to vote with respect thereto, voting together as a single class, will be required to amend, alter, change or repeal the bylaws. In addition, the affirmative vote of the holders of at least 75% of the total votes of the outstanding shares of our capital stock entitled to vote with respect thereto, voting together as a single class, is required to amend, alter, change or repeal, or to adopt any provisions inconsistent with, any of the provisions in our certificate of incorporation relating to amendments to our certificate of incorporation and bylaws and as described under "Action by Written Consent; Special Meetings of Stockholders", "Classified Board" and "Removal of Directors" above. This requirement of a supermajority vote to approve amendments to our bylaws and certificate of incorporation could enable a minority of our stockholders to exercise veto power over any such amendments.

Authorized but Unissued Shares

Our authorized but unissued shares of common stock and preferred stock are available for future issuance without stockholder approval. These additional shares may be utilized for a variety of corporate purposes, including future public offerings to raise additional capital and corporate acquisitions. The existence of authorized but unissued shares of common stock and preferred stock could render more difficult or discourage an attempt to obtain control of a majority of our common stock by means of a proxy contest, tender offer, merger or otherwise.

Exclusive Forum

Our certificate of incorporation provides that, subject to limited exceptions, the state or federal courts located in the State of Delaware is the sole and exclusive forum for (i) any derivative action or proceeding brought on our behalf, (ii) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers or other employees to us or our stockholders, (iii) any action asserting a claim against us arising pursuant to any provision of the Delaware General Corporation Law, our certificate of incorporation or our bylaws, or (iv) any other action asserting a claim against us that is governed by the internal affairs doctrine. Any person or entity purchasing or

otherwise acquiring any interest in shares of our capital stock shall be deemed to have notice of and to have consented to the provisions of our certificate of incorporation described above. Although we believe these provisions benefit us by providing increased consistency in the application of Delaware law for the specified types of actions and proceedings, the provisions may have the effect of discouraging lawsuits against our directors and officers. The enforceability of similar choice of forum provisions in other companies' certificates of incorporation has been challenged in legal proceedings, and it is possible that, in connection with one or more actions or proceedings described above, a court could find the choice of forum provisions contained in our certificate of incorporation to be inapplicable or unenforceable.

Section 203 of the Delaware General Corporation Law

We are subject to the provisions of Section 203 of the Delaware General Corporation Law. In general, Section 203 prohibits a publicly held Delaware corporation from engaging in a "business combination" with an "interested stockholder" for a three-year period following the time that this stockholder becomes an interested stockholder, unless the business combination is approved in a prescribed manner. Under Section 203, a business combination between a corporation and an interested stockholder is prohibited unless it satisfies one of the following conditions:

- before the stockholder became interested, our board of directors approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder;
- upon consummation of the transaction which resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the voting stock outstanding, shares owned by persons who are directors and also officers, and employee stock plans, in some instances, but not the outstanding voting stock owned by the interested stockholder; or
- at or after the time the stockholder became interested, the business combination was approved by our board of directors and authorized at an annual or special meeting of the stockholders by the affirmative vote of at least two-thirds of the outstanding voting stock which is not owned by the interested stockholder.

Section 203 defines a business combination to include:

- any merger or consolidation involving the corporation and the interested stockholder;
- any sale, transfer, lease, pledge or other disposition involving the interested stockholder of 10% or more of the assets of the corporation;
- subject to exceptions, any transaction that results in the issuance or transfer by the corporation of any stock of the corporation to the interested stockholder;
- subject to exceptions, any transaction involving the corporation that has the effect of increasing the proportionate share of the stock of any class or series of the corporation beneficially owned by the interested stockholder; and
- the receipt by the interested stockholder of the benefit of any loans, advances, guarantees, pledges, or other financial benefits provided by or through the corporation.

In general, Section 203 defines an interested stockholder as any entity or person beneficially owning 15% or more of the outstanding voting stock of the corporation and any entity or person affiliated with or controlling or controlled by the entity or person.

Nasdaq Global Select Market Listing

Our common stock is listed on the Nasdaq Global Select Market under the trading symbol "CHMA".

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is American Stock Transfer & Trust Company, LLC.

Chiasma, Inc.
140 Kendrick Street
Building C East
Needham, MA 02494

February 14, 2020

Lee G. Giguere

Re: Amended and Restated Executive Employment Letter

Dear Lee:

This amended and restated letter agreement (the "Agreement") confirms the revised terms and conditions of your employment with Chiasma, Inc. (the "Company") effective February 14, 2020 (the "Effective Date"). This Agreement amends, restates and supersedes in all respects your offer letter with the Company dated September 16, 2019 (the "Prior Agreement") as of the Effective Date, *provided* that your Non-Competition, Non-Solicitation, Confidentiality and Assignment Agreement with the Company dated September 30, 2019 (the "Restrictive Covenant Agreement") shall remain unaltered and in full effect.

1. **Position**. You will continue to serve as the Company's Vice President, General Counsel and report to the Company's Chief Executive Officer. This is a full-time exempt position. It is understood and agreed that, while you render services to the Company, you will not engage in any other employment, consulting or other business activities (whether full-time or part-time), unless you first obtain the Company's approval. You also may engage in religious, charitable and other community activities, so long as such activities do not interfere or conflict with your obligations to the Company. Upon the ending of your employment, you shall immediately resign from any other position(s) to which you were elected or appointed in connection with your employment.

2. **Salary**. Effective January 1, 2020, the Company will pay you a base salary at a rate equivalent to $355,875.00 per year, payable in accordance with the Company's standard payroll schedule and subject to applicable deductions and withholdings. Your base salary will be subject to periodic review and adjustment at the Company's discretion.

3. **Annual Bonus**. You will be eligible to receive an annual performance bonus. The Company will target the bonus at up to 30% of your annual salary rate (the "Bonus Target"). The actual bonus amount and percentage are discretionary and will be subject to the Company's assessment of your performance, as well as business conditions at the Company. The bonus also will be subject to your employment for the full period covered by the bonus, approval by and adjustment at the discretion of the Board and the terms of any applicable bonus plan. The Company expects to review your job performance on an annual basis and to discuss with you the criteria which the Company will use to assess your performance for bonus purposes. The Board may also make adjustments in the targeted amount of your annual performance bonus. The Company will pay any bonus no later than 75 days after the end of the period covered by the bonus.

4. **Signing Bonus.** In addition to the bonus under Section 3 above, in connection with your commencement of employment with the Company on September 30, 2019, you became eligible to receive a one-time cash sign-on bonus in the amount of $50,000 (the "Signing Bonus"), of which $25,000 was paid to you within 30 days of the date you commenced employment with the Company (the "Start Date") and the final $25,000 will be paid to you on the date that is 6 months from the Start Date. You must be employed by the Company at the time of payment of the Signing Bonus in order to receive the Signing Bonus or any portion thereof. The Signing Bonus shall be subject to deductions and withholdings as required by law. If, prior to the 12-month anniversary of the Start Date, you voluntarily terminate your employment or are terminated by the Company for Cause (as defined below), then you agree to repay to the Company the net amount of the initial Signing Bonus of $25,000 that you received, after deduction of state and federal withholding tax, social security, FICA, and all other employment taxes and authorized payroll deductions, within 30 days of your Date of Termination (as defined below). If, prior to the 18-month anniversary of the Start Date, you voluntarily terminate your employment or are terminated by the Company for Cause, then you agree to repay to the Company the net amount of the second installment of the Signing Bonus of $25,000 that you received, after deduction of state and federal withholding tax, social security, FICA, and all other employment taxes and authorized payroll deductions, within 30 days after your Date of Termination.

5. **Business Travel/Expenses**. The Company will reimburse you for travel and other business expenses consistent with the terms and conditions of the Company's expense reimbursement policies.

6. **Benefits/Vacation**. You will continue to be eligible to participate in the employee benefits and insurance programs generally made available to the Company's full-time employees. You will be eligible for up to three (3) weeks of vacation per year, which shall accrue on a prorated basis. Other provisions of the Company's vacation policy are set forth in the policy itself.

7. **Stock Options**. The Board has granted you an option for the purchase of 75,000 shares of common stock of the Company, with an exercise price equal to the closing trading price on the date of the grant (the "Option"). The Option shall vest in equal quarterly installments over the 4-year period following the date of the grant, as described in more detail in the applicable stock option agreement to be provided by the Company, *provided* that you remain employed by the Company on each such vesting date. Your eligibility for stock options will be governed by the Company's 2015 Stock Incentive Plan and the associated stock option agreement required to be entered into by you and the Company (the "Equity Documents"). Your stock options granted prior to the date of this letter shall also remain subject to the applicable Equity Documents.

8. **At-Will Employment**. Your employment is "at will," meaning you or the Company may terminate it at any time for any or no reason.

9. **Termination Benefits.**

a. In the event of the termination of your employment for any reason, the Company shall pay you your base salary through your last day of employment (the "Date of Termination"), for any accrued but unused vacation and the amount of any documented expenses properly incurred by you on behalf of the Company prior to any such termination and not yet reimbursed (the "Accrued Obligations").

b. "Cause" means: (i) conduct by you in connection with your service to the Company that is fraudulent, unlawful or grossly negligent; (ii) your material breach of your material responsibilities to the Company, or your willful failure to comply with the lawful directives of the Board or written policies of the Company; (iii) breach by you of your representations, warranties, covenants and/or obligations under this Agreement (including the Restrictive Covenant Agreement); (iv) material misconduct by you which seriously discredits or damages the Company or any of its affiliates, and/or (v) nonperformance or unsatisfactory performance of your duties or responsibilities to the Company as determined in good faith by the Company after (in the case of subsection (v) only) written notice to you and a reasonable opportunity to cure that shall not exceed thirty (30) days.

c. A "Change in Control" means the sale of all or substantially all of the outstanding shares of capital stock, assets or business of the Company, by merger, consolidation, sale of assets or otherwise (other than a merger or consolidation in which all or substantially all of the individuals and entities who were beneficial owners of the Company's voting securities immediately prior to such transaction beneficially own, directly or indirectly, more than 50% (determined on an as-converted basis) of the outstanding securities entitled to vote generally in the election of directors of the resulting, surviving or acquiring corporation in such transaction). Notwithstanding the foregoing, where required to avoid extra taxation under Section 409A of the Internal Revenue Code, a Change in Control must also satisfy the requirements of Treas. Reg. Section l. 409A-3(a)(5).

d. "Good Reason" means that you have complied with the "Good Reason Process" (hereinafter defined) following the occurrence of any of the following events: (i) a material diminution in your responsibilities, authority or duties; (ii) a material diminution in your base salary except for across-the-board salary reductions based on the Company's financial performance similarly affecting all or substantially all senior management employees of the Company; or (iii) change of more than 60 miles in the geographic location at which you provide services to the Company (each a "Good Reason Condition"). Notwithstanding the foregoing, a suspension of your responsibilities, authority and/or duties for the Company during any portion of a bona fide internal investigation or an investigation by regulatory or law enforcement authorities shall not be a Good Reason Condition. Good Reason Process shall mean that (i) you reasonably determine in good faith that a Good Reason Condition has occurred; (ii) you notify the

Company in writing of the occurrence of the Good Reason Condition within 30 days of the occurrence of such condition; (iii) you cooperate in good faith with the Company's efforts, for a period not less than 30 days following such notice (the "Cure Period"), to remedy the Good Reason Condition; (iv) notwithstanding such efforts, the Good Reason condition continues to exist; and (v) you terminate employment within 30 days after the end of the Cure Period. If the Company cures the Good Reason Condition during the Cure Period, Good Reason shall be deemed not to have occurred.

e. In the event the Company terminates your employment without Cause or you terminate your employment for Good Reason, in either case within 12 months after the occurrence of the first event constituting a Change in Control (a "Change in Control Termination") and provided you (i) enter into, do not revoke and comply with the terms of a separation agreement in a form provided by the Company which shall include a general release of claims against the Company and related persons and entities (the "Release"), within the time period required by the Release but in no event later than 60 days after the Date of Termination; (ii) resign from any and all positions, including, without implication of limitation, as a director, trustee or officer, that you then hold with the Company or any affiliate of the Company; and (iii) return all Company property and comply with any instructions related to deleting and purging duplicates of such Company property, the Company will provide you with the following "Termination Benefits": (a) continuation of your base salary for the six (6) month period that immediately follows the Date of Termination; (b) payment of one-half (1/2) of your Bonus Target for the year in which the Change in Control occurs; (c) your accrued bonus (if any) with respect to the calendar year in which the Date of Termination occurs, subject to the Board's assessment of applicable bonus criteria and prorated from the beginning of such year to the Date of Termination ((a), (b) and (c), the "Severance Payments"); (d) all of the unvested shares subject to time based vesting pursuant to the stock options granted to you by the Company shall immediately vest and become exercisable as of the Date of Termination; and (d) if elected, continuation of group health plan benefits to the extent authorized by and consistent with 29 U.S.C. *§* 1161 et seq. (commonly known as "COBRA"), with the cost of the regular premium for such benefits shared in the same relative proportion by the Company and you as in effect on the Date of Termination until the earlier of (i) the date that is six (6) months after the Date of Termination; and (ii) the date you become eligible for health benefits through another employer or otherwise become ineligible for COBRA. This Section 9(e) shall terminate and be of no further force or effect beginning 12 months after the occurrence of a Change in Control.

f. In the event the Company terminates your employment without Cause or you terminate your employment for Good Reason, in either case other than a Change in Control Termination, and in either case provided you (i) enter into, do not revoke and comply with the terms of the Release within 60 days after the Date of Termination; (ii) resign from any and all positions, including, without implication of limitation, as a director, trustee or officer, that you then hold with the Company and any affiliate of the Company; and (iii) return all Company property and comply with any instructions related to deleting and purging duplicates of such Company property, the Company will provide you with the following "Termination Benefits": (a) continuation of your then current base salary for the six (6) month period that immediately follows the Date of Termination (the "Severance Payments"); and (b) if elected, continuation of group health plan benefits to the extent authorized by and consistent with 29 U.S.C. § 1161 et seq. (commonly known as "COBRA"), with the cost of the regular premium for such benefits shared in the same relative proportion by the Company and you as in effect on the Date of Termination until the earlier of (i) the date that is six (6) months after the Date of Termination; and (ii) the date you become eligible for health benefits through another employer or otherwise become ineligible for COBRA.

g. The Severance Payments shall commence within 60 days after the Date of Termination and shall be made on the Company's regular payroll dates; provided, however, that if the 60-day period begins in one calendar year and ends in a second calendar year, the Severance Payments shall begin to be paid in the second calendar year. In the event you miss a regular payroll period between the Date of Termination and first Severance Payment date, the first Severance Payment shall include a "catch up" payment. Solely for purposes of Section 409A of the Internal Revenue Code of 1986, as amended, each Severance Payment is considered a separate payment.

10. **Termination of Employment as a Result of Death, Disability, Termination by the Company for Cause or Resignation without Good Reason.** In the event your employment is terminated as a result of your (i) death, (ii) Disability, (iii) termination for Cause by the Company; or (iv) resignation without Good Reason, you will be entitled to the Accrued Obligations but you will not be entitled to Termination Benefits. "Disability" means that, as a result of your mental or physical illness, you are unable to perform (with or without reasonable accommodation in accordance with the Americans with Disabilities Act) the duties of your position pursuant to this Agreement for a period of a minimum of ninety (90) consecutive days.

11. **Confidential Information and Restricted Activities.** The Restrictive Covenant Agreement remains in full effect, is incorporated by reference herein. You agree without reservation that the restraints in the Restrictive Covenant Agreement are necessary for the reasonable and proper protection of the Company and its affiliates, and that each and every one of the restraints is reasonable in respect to subject matter, length of time and geographic area. You further agree that, were you to breach any of the covenants contained in this Agreement or the Restrictive Covenant Agreement, in addition to the Company's other legal and equitable remedies, the Company may suspend or cease any Termination Benefits to which you might otherwise be entitled. Any such suspension or termination of the Termination Benefits by the Company in the event of a breach by you shall not affect your ongoing obligations to the Company.

12. **Taxes; Section 409A; Section 280G; Section 4099.**

a. All forms of compensation referred to in this Agreement are subject to reduction to reflect applicable withholding and payroll taxes and other deductions required by law. You hereby acknowledge that the Company does not have a duty to design its compensation policies in a manner that minimizes your tax liabilities, and you will not make any claim against the Company or its board of directors related to tax liabilities arising from your compensation.

b. Anything in this Agreement to the contrary notwithstanding, if at the time of your separation from service within the meaning of Section 409A of the Code, the Company determines that you are a "specified employee" within the meaning of Section 409A(a)(2)(B)(i) of the Code, then to the extent any payment or benefit that you become entitled to under this Agreement on account of your separation from service would be considered deferred compensation subject to the 20 percent additional tax imposed pursuant to Section 409A(a) of the Code as a result of the application of Section 409A(a)(2)(B)(i) of the Code, such payment shall not be payable and such benefit shall not be provided until the date that is the earlier of (A) six months and one day after your separation from service, or (B) your death. If any such delayed cash payment is otherwise payable on an installment basis, the first payment shall include a catch-up payment covering amounts that would otherwise have been paid during the six-month period but for the application of this provision, and the balance of the installments shall be payable in accordance with their original schedule. All in-kind benefits provided and expenses eligible for reimbursement under this Agreement shall be provided by the Company or incurred by you during the time periods set forth in this Agreement. All reimbursements shall be paid as soon as administratively practicable, but in no event shall any reimbursement be paid after the last day of the taxable year following the taxable year in which the expense was incurred. The amount of in-kind benefits provided or reimbursable expenses incurred in one taxable year shall not affect the in-kind benefits to be provided or the expenses eligible for reimbursement in any other taxable year. Such right to reimbursement or in-kind benefits is not subject to liquidation or exchange for another benefit. To the extent that any payment or benefit described in this Agreement constitutes "non-qualified deferred compensation" under Section 409A of the Code, and to the extent that such payment or benefit is payable upon your termination of employment, then such payments or benefits shall be payable only upon your "separation from service." The determination of whether and when a separation from service has occurred shall be made in accordance with the presumptions set forth in Treasury Regulation Section l. 409A- l (h). The Company and you intend that this Agreement will be administered in accordance with Section 409A of the Code. To the extent that any provision of this Agreement is ambiguous as to its compliance with Section 409A of the Code, the provision shall be read in such a manner so that all payments hereunder comply with Section 409A of the Code. The Company makes no representation or warranty and shall have no liability to you or any other person if any provisions of this Agreement are determined to constitute deferred compensation subject to Section 409A of the Code but do not satisfy an exemption from, or the conditions of, such Section.

c. Anything in this Agreement to the contrary notwithstanding, in the event that the amount of any compensation, payment or distribution by the Company to or for your benefit, whether paid or payable or distributed or distributable pursuant to the terms of this Agreement or otherwise, calculated in a manner consistent with Section 280G of the Code and the applicable regulations thereunder (the "Aggregate Payments"), would be subject to the excise tax imposed by Section 4999 of the Code, then the Aggregate Payments shall be reduced (but not below zero) so that the sum of all of the Aggregate Payments shall be $1.00 less than the amount at which you become subject to the excise tax imposed by Section 4999 of the Code; provided that such reduction shall only occur if it would result in you receiving a higher After Tax Amount (as defined below) than you would receive if the Aggregate Payments were not subject to such reduction. In such event, the Aggregate Payments shall be reduced in the following order, in each case, in reverse chronological order beginning with the Aggregate Payments that are to be paid the furthest in time from consummation of the transaction that is subject to Section 280G of the Code: (1) cash payments not subject to Section 409A of the Code; (2) cash payments subject to Section 409A of the Code; (3) equity-based payments and acceleration; and (4) non-cash forms of benefits; provided that in the case of all the foregoing Aggregate Payments all amounts or payments that are not subject to calculation under Treas. Reg. §1.2800-1, Q&A-24(b) or (c) shall be reduced before any amounts that are subject to calculation under Treas. Reg. §1.280G-l, Q&A-24(b) or (c).

(i) For purposes of this subsection (c), the "After Tax Amount" means the amount of the Aggregate Payments less all federal, state, and local income, excise and employment taxes imposed on you as a result of your receipt of the Aggregate Payments. For purposes of determining the After Tax Amount, you shall be deemed to pay federal income taxes at the highest marginal rate of federal income taxation applicable to individuals for the calendar year in which the determination is to be made, and state and local income taxes at the highest marginal rates of individual taxation in each applicable state and locality, net of the maximum reduction in federal income taxes which could be obtained from deduction of such state and local taxes.

(ii) The determination as to whether a reduction in the Aggregate Payments shall be made pursuant to subsection(c) shall be made by a nationally recognized accounting firm selected by the Company (the "Accounting Firm"), which shall provide detailed supporting calculations both to the Company and you within 15 business days of the Date of Termination, if applicable, or at such earlier time as is reasonably requested by the Company or you. Any determination by the Accounting Firm shall be binding upon the Company and you.

13. **Interpretation, Amendment and Enforcement.** This Agreement, including the Restrictive Covenant Agreement and the Equity Documents, constitutes the complete agreement between you and the Company, contains all of the terms of your employment with the Company and supersedes any prior agreements, representations or understandings (whether written, oral or implied) between you and the Company, including without limitation the Prior Agreement. The terms of this Agreement and the resolution of any disputes as to the meaning, effect, performance or validity of this Agreement or arising out of, related to, or in any way connected with this Agreement, your employment with the Company or any other relationship between you and the Company (the "Disputes") will be governed by Massachusetts law, excluding laws relating to conflicts or choice of law. You and the Company submit to the exclusive personal jurisdiction of the federal and state courts located in the Commonwealth of Massachusetts in connection with any Dispute or any claim related to any Dispute.

14. **Assignment.** Neither you nor the Company may make any assignment of this Agreement or any interest in it, by operation of law or otherwise, without the prior written consent of the other; *provided, however,* that the Company may assign its rights and obligations under this Agreement (including the Restrictive Covenant Agreement) without your consent to any affiliate at any time, or to any person or entity with whom the Company shall hereafter effect a reorganization, consolidate with, or merge into or to whom it transfers all or substantially all of its properties or assets. This Agreement shall inure to the benefit of and be binding upon you and the Company, and each of your and its respective successors, executors, administrators, heirs and permitted assigns.

15. **Miscellaneous.** This Agreement may not be modified or amended, and no breach shall be deemed to be waived, unless agreed to in writing by you and the CEO of the Company. The headings and captions in this Agreement are for convenience only and in no way define or describe the scope or content of any provision of this Agreement. The words "include," "includes" and "including" when used herein shall be deemed in each case to be followed by the words "without limitation." This Agreement may be executed in two or more counterparts, each of which shall be an original and all of which together shall constitute one and the same instrument.

16. **Other Terms.** By signing this Agreement, you represent to the Company that you have no contractual commitments or other legal obligations that would or may prohibit you from performing your duties for the Company.

Please acknowledge, by signing below, that you have accepted this Agreement.

Very Truly Yours,

/s/ Raj Kannan
Raj Kannan
Chief Executive Officer
Chiasma, Inc.

I have read and accept this amended and restated employment offer:

/s/ Lee G. Giguere
Lee G. Giguere
Dated: February 14, 2020

Execution Version

SUBLEASE

By and Between

PTC INC.

(“Sublandlord”)

and

CHIASMA, INC.

(“Subtenant”)

140 Kendrick Street
Needham, Massachusetts

THIS SUBLEASE (the **"Sublease"**) is made and entered into as of this 11th day of October, 2019 by and between **PTC INC.**, a corporation organized under the laws of the State of Delaware (**"Sublandlord"**) and **CHIASMA, INC.**, a corporation organized under the laws of the state of Delaware (**"Subtenant"**).

1. BASIC LEASE PROVISIONS.

A. "**Building**": The building designated as Building C located at:

140 Kendrick Street
Needham, Massachusetts 02494

B. **Subtenant's Address**:

Chiasma, Inc.
460 Totten Pond Rd.
Waltham MA 02451
Attn: Drew Enamait

with a copy to:

Langer & McLaughlin, LLP
535 Boylston Street
Boston, MA 02116

C. **Sublandlord's Address (for notices)**:

PTC, Inc.
121 Seaport Boulevard
Boston, Massachusetts 02210
Attention: VP, Corporate Real Estate;

and

PTC, Inc.
121 Seaport Boulevard
Boston, Massachusetts 02210
Attention: VP, General Counsel

With copies to:
Cresa
200 State Street
Boston, Massachusetts 02109
Attention: Lease Administration (PTC Inc.);

and

Choate, Hall & Stewart LLP
Two International Place
Boston, Massachusetts 02110
Attention: Paul Laudano, Esq./Adam M. Zaiger, Esq.

D. **"Prime Landlord"**: BP 140 Kendrick Street LLC

E. **Prime Landlord's Address (for notices)**:

BP 140 Kendrick Street LLC
c/o Boston Properties Limited Partnership
Prudential Center
800 Boylston Street, Suite 1900
Boston, Massachusetts 02199-8103

with a copy to:

BP 140 Kendrick Street LLC
c/o Boston Properties Limited Partnership
Prudential Center
800 Boylston Street, Suite 1900
Boston, Massachusetts 02199-8103
Attention: Regional General Counsel

F. **Identification of Prime Lease and all presently-existing amendments thereto as of the date hereof**:

Indenture of Lease dated as of December 14, 1999 (the "**Original Lease**"), by and between Boston Properties Limited Partnership ("**Original Prime Landlord**") and Parametric Technology Corporation ("**Original Tenant**"), respecting the real property at 140 Kendrick Street, Needham, Massachusetts (as more-fully described herein, the "**Property**"), as amended and affected by the following: (i) that certain letter agreement by and between Original Prime Landlord and Original Tenant dated as of April 25, 2000 (the "**First Amendment**"); (ii) that certain Second Amendment to Lease agreement by and between Original Prime Landlord and Original Tenant dated as of November 30, 2001 (the "**Second Amendment**"); (iii) that certain Agreement by and between Original Prime Landlord and Original Tenant dated July 6, 2006 (the "**July 2006 Letter Agreement**"); (iv) that certain Third Amendment to Lease by and between Original Prime Landlord and Original Tenant dated October 27, 2010 (the "**Third Amendment**"); (v) that certain letter agreement dated as of April 13, 2012 (the "**April 2012 Letter Agreement**") by and between Original Tenant and Prime Landlord, as successor to BP 140 Kendrick Street LLC and Original Landlord pursuant to a certain Second Assignment of Lease dated as of June 11, 2001 (the "**Second Assignment**"); (vi) that certain Fourth Amendment to Lease by and between Prime Landlord and Original Tenant dated July 20, 2012 (the "**Fourth Amendment**"); (vii) that certain Acknowledgement of Merger and Change of Name by and between Prime

Landlord and Sublandlord, as successor-by-merger to Original Tenant, dated as of February 19, 2013 (the "**Acknowledgment of Merger**"); and (viii) that certain letter agreement by and between Master Landlord and Sublandlord dated as of June 23, 2014 (the "**June 2014 Letter Agreement**").

G. **"Term"**: The period of time beginning on the Delivery Date and ending on the Expiration Date, subject to earlier termination as provided in this Sublease.

H. **"Delivery Date"**: The date on which Sublandlord delivers exclusive possession of the Premises to Subtenant in the condition required by the provisions contained in Section 5.1 of this Sublease. It is estimated that the Delivery Date will occur approximately ten (10) days after the date of this Sublease.

I. **"Commencement Date"**: the Delivery Date, or the date the Delivery Date would have occurred in the absence of any Tenant Delay, in accordance with the terms set forth in *Section 5.3*.

J. **"Guarantor"**: None.

K. **"Expiration Date"**: October 31, 2022. However, notwithstanding the foregoing, in the event Subtenant notifies Sublandlord that Subtenant has executed and delivered a direct lease with Prime Landlord for occupancy of the entire Premises commencing on December 1, 2022, and as part of the documentation thereof Prime Landlord releases Sublandlord in writing from any obligation to remove property or otherwise restore the Premises or cause Subtenant to vacate any portion of the Premises upon expiration of the Prime Lease (a "**Direct Lease**"), the Term hereunder shall be deemed extended through November 30, 2022, subject to earlier termination as provided in this Sublease.

L. **"Annual Fixed Rent"**: For the period commencing on the Commencement Date and ending on the Expiration Date, as set forth in the table below. Annual Fixed Rent for any partial month shall be pro-rated.

Period	Annual Fixed Rent	Monthly Installment
Commencement Date through the December 31, 2020.	$510,806.00	$42,567.17
January 1, 2021 through December 31, 2021.	$528,420.00	$44,035.00
January 1, 2022 through the Expiration Date.	$546,034.00	$45,502.83

Notwithstanding the foregoing or anything contained in this Sublease to the contrary, no Annual Fixed Rent or Additional Rent (other than the electricity charge in Section 9(a)) shall be due from Subtenant hereunder for the period of time beginning on the Commencement Date and ending on the date which is one

hundred twenty (120) days thereafter (the "**Abated Rent Period**"), provided, however, that the abated Rent provided for herein is conditioned upon no Event of Default occurring hereunder, and in the event of any Event of Default hereunder Subtenant's right to the abatement of Rent described herein shall terminate and any Rent previously abated hereunder shall be come immediately due and payable to Sublandlord in addition to all other rights and remedies available to Sublandlord on account thereof.

M. **Payee of Rent**: Sublandlord.

N. **Base Years**:

"Base Operating Year": Calendar Year 2020.

"Base Tax Year": Fiscal Year 2020 (i.e., July 1, 2019 through June 30, 2020).

Taxes and Operating Expenses for the applicable Base Years shall be grossed up to full occupancy in accordance with *Section 8.2*.

Taxes and Operating Expenses for the current year are presently estimated to be Ten and 33/100 Dollars ($10.33) per rentable square foot of Landlord's Property, but Sublandlord makes no representations, warranty or guarantee to Subtenant that such amount will not be exceeded.

O. **Address for Payment of Rent**:

By electronic funds transfer to the following account:

Bank Name: JPMorgan Chase, N.A.
Bank Address: New York, NY
Routing Number: 021-000-021
SWIFT Code: CHASUS33
Account Name: PTC Inc.
Account Number: 937216422

P. **"Subtenant's Share"**: 5.493%, subject to the provisions of *Section 8.3*. Such percentage represents a fraction, the numerator of which is the rentable square footage of the Premises (i.e., 17,614 rentable square feet), and the denominator is the rentable square footage of the Property (i.e., 320,655 rentable square feet, as set forth on Page 1 of the Third Amendment).

Q. **Description of Premises**: A stipulated 17,614 rentable square feet, consisting of those portions of the first floor of the Building containing a stipulated 16,587 and 1,027 rentable square feet, respectively, as depicted on **Exhibit A** attached hereto.

R. **Security Deposit**: As provided in *Section 38*.

S. **"Permitted Use"**: general office use in keeping with a first class office building and for no other purpose.

T. **"Broker(s)"**: Cresa Boston (representing Sublandlord) and Colliers International (representing Subtenant).

U. **Exhibits**:

Exhibit A – Description of Premises

Exhibit B – Plans Showing Fitness Center, Common Conference Facility and Cafeteria Seating Area

Exhibit C – INTENTIONALLY OMITTED

Exhibit D - Description of Sublandlord's Work

2. PRIME LEASE. Sublandlord is the tenant under a Prime Lease (as described and amended as specified in *Section 1(F)*, collectively, and as the same may be further amended and/or supplemented from time to time, the **"Prime Lease"**) with the Prime Landlord (identified in *Section 1(D)*). Sublandlord represents to Subtenant that such copy of the Prime Lease delivered to Subtenant (with the redactions as included therein) is true, correct and complete in all material respects that could reasonably be expected to affect Subtenant's rights or obligations under this Sublease. Subtenant hereby acknowledges that Sublandlord has delivered to Subtenant a copy of the Prime Lease, except that portions of the Prime Lease have been redacted with respect to terms and provisions proprietary to Sublandlord. The premises leased to Sublandlord under the Prime Lease, as same may be modified from time to time, are referred to herein as the "**Prime Lease Premises**".

3. SUBLEASE. Sublandlord, for and in consideration of the Rent herein reserved and of the covenants and agreements herein contained on the part of the Subtenant to be performed, hereby subleases to the Subtenant, certain space within the Prime Lease Premises and described in *Section 1(Q)* (the **"Premises"**) and Subtenant hereby subleases the Premises from Sublandlord upon the terms, covenants and agreements herein contained. As appurtenant to its use of the Premises, and at no additional cost or expense, Subtenant shall have the right, on a non-exclusive and first-come, first served basis with Sublandlord and other subtenants of Sublandlord in the Building and in the Property, to use the common facilities and areas of the Building and the Property for their intended purposes, in each case so long as such common facilities and areas shall exist. Such common facilities shall include (a) the Property's fitness center which is located in the Building and part of the common areas under the Prime Lease (the "**Fitness Center**"), (b), the common conference rooms on the first and second floors of the building at the Property designated as Building "A", which are located within the Prime Lease Premises (the "**Common Conference Facilities**"), and (c) if and when operated by the Prime Landlord, the Property's cafeteria also located in the building at the Property designated as Building "A" and within the common areas under the Prime Lease (the "**Cafeteria**"). Plans showing the location of the Fitness Center, the Common Conference Facilities and the Cafeteria are attached hereto as **Exhibit B**. Sublandlord shall provide non-exclusive interior access for Subtenant to access the Fitness Center, the Common Conference Facilities and the Cafeteria, subject to the provisions of this Sublease. Subtenant acknowledges and agrees that its right to use the Common Conference Facilities and the Cafeteria's seating area shall be subject to an electronic or other booking system operated by Sublandlord, as in effect from time to time. A description of such booking systemshall be provided to Subtenant upon written request promptly following Subtenant's commencement of business operations in the Premises. Notwithstanding the foregoing, Sublandlord reserves the right, in its sole and absolute discretion, to eliminate, diminish, re-equip, and/or close,

temporarily or permanently, any and all such common facilities, areas and amenities at any time and from time to time, provided (i) Subtenant's utilities are not permanently discontinued, (ii) Subtenant continues to have reasonable means of ingress to and egress from the Premises, and (iii) the Fitness Center is not permanently eliminated unless replaced with facilities substantially the same or better quality, and (iv) Sublandlord shall not permanently eliminate the Common Conference Facilities (which are located within the Prime Lease Premises) unless and to the extent Sublandlord or Prime Landlord leases portions thereof to a third party, which Sublandlord and Prime Landlord reserve the right to do their respective sole and unlimited discretion. Sublandlord shall not voluntarily modify or amend the terms of the Prime Lease so as to eliminate the Fitness Center and/or Cafeteria from the Building, unless there is a replacement made therefor of substantially similar or better quality. Sublandlord agrees to use commercially reasonable efforts to minimize any interruption in Subtenant's use of or access to the Cafeteria and/or the Fitness Center in connection with any relocation of the same or other exercise of Sublandlord's rights reserved hereunder

4. TERM.

4.1 The Term of this Sublease shall commence on the Commencement Date, provided, however, that upon reasonable prior written notice to Sublandlord, Subtenant shall be permitted to have reasonable access to the Premises commencing on a date reasonably designated by Sublandlord (the "**Early Access Date**") prior to the Commencement Date for the purpose of architect's inspections, design and installation of cabling, and similar activities preparatory to Subtenant's commencement of business operations in the Premises, which activities shall be conducted by Subtenant in such a manner so as to not interfere with or delay the performance of Sublandlord's Work (and any such interference or delay caused by such early access shall be deemed a "Tenant Delay" under *Section 5.3*). All of the terms and conditions of this Sublease (including, without limitation, the obligations to maintain insurance) shall apply to Subtenant's occupancy of the Premises from and after the Early Access Date, except that Subtenant shall have no obligation to pay Annual Fixed Rent (or Additional Rent or other charges) for any period prior to the Commencement Date. The Term shall expire on the Expiration Date unless sooner terminated as otherwise provided elsewhere in this Sublease. If Sublandlord fails to give Subtenant possession of the Premises on the Commencement Date, Sublandlord shall have no liability to Subtenant, and this Sublease shall remain in full force and effect according to its terms, but the Term and the Rent shall not commence until the Commencement Date occurs hereunder.

4.2 Anything herein to the contrary notwithstanding, if the Prime Lease shall be terminated during the Term hereof for any reason whatsoever, this Sublease shall terminate upon such termination with the same force and effect as if such termination date had been named herein as the date of expiration hereof; provided, however, that Sublandlord covenants and agrees that it shall not voluntarily terminate the Prime Lease (or surrender to Prime Landlord any portion of the Prime Lease Premises that is sublet to Subtenant hereunder or is necessary for utility service and/or access to and from the Premises) during the Term unless the then owner of the Building has entered into a direct lease with Subtenant on substantially the same net economic terms and conditions as this Sublease (or where Sublandlord agrees in writing to compensate Subtenant for the difference); and provided, further, that the foregoing shall not be interpreted to prohibit Sublandlord from modifying the Prime Lease in any manner that does not materially adversely affect the rights or materially increase the obligations of Subtenant under this Sublease.

5. PREPARATION OF PREMISES FOR OCCUPANCY.

5.1 Except as expressly provided herein, but without reducing or derogating from Sublandlord's repair and maintenance obligations under the Prime Lease respecting the Premises, Sublandlord shall have no obligation to do any work in the Premises preparatory to Subtenant's occupancy, and Subtenant agrees that all portions of the Premises shall, other than performance of Sublandlord's Work, be delivered "AS IS" on the Delivery Date. Except as expressly set forth in this Sublease, no representations

or warranties are made herein by Sublandlord regarding the Premises or the Property, including, without limitation, as to the physical condition thereof and/or the suitability of the Premises or the Property for Subtenant's use, or any compliance with applicable law. Sublandlord shall, at its sole cost and expense and in a good and workmanlike manner in accordance with all applicable building codes and other legal requirements, perform the work to the Premises described in **Exhibit D** attached hereto ("**Sublandlord's Work**"). Upon Substantial Completion of Sublandlord's Work, Sublandlord shall notify Subtenant of the date such Sublandlord's Work was Substantially Completed, and the date of Substantial Completion and delivery of possession shall be the Delivery Date under this Sublease. Sublandlord shall permit Subtenant's construction representatives an opportunity to walk through the Premises with Sublandlord and its construction representatives for the purpose of inspecting the Premises and developing the punchlist for Sublandlord's Work.

5.2 Except for Sublandlord's Work, Subtenant shall be responsible for the performance of any leasehold improvements in the Premises required for its use and occupancy, which shall be performed in compliance with the provisions hereof and with all applicable provisions of the Prime Lease applicable to the making of improvements, additions or alterations in the Premises. Such work shall be performed at Subtenant's sole cost and expense, except as provided herein. Any leasehold improvements to be made by Subtenant shall be subject to obtaining the prior approval of the Prime Landlord (where required by the prime Lease) and Sublandlord, which approval Sublandlord will not unreasonably withhold, delay or condition. Without limitation, Sublandlord acknowledges that Subtenant plans to enhance the main entry to the Premises with additional glass walls in place of drywall and to construct a new reception area Sublandlord agrees to submit Subtenant's request for any such approval to Prime Landlord and will convey to Subtenant any requests from Prime Landlord for further information in respect thereof. Subtenant accepts responsibility, at its sole cost and expense, for complying with all laws applicable to the interior of the Premises including, without limitation, the Americans With Disabilities Act (42 U.S.C. §1201 et seq.) (the "**ADA**") and obtaining all required permits and licenses as they relate to Subtenant's use of the Premises and any leasehold improvements, alterations or additions therein to be made by Subtenant.

Sublandlord and Subtenant acknowledge that the ADA establishes requirements for business operations, accessibility and barrier removal, and that such requirements may or may not apply to the Premises and the Building depending on, among other things: (1) whether Subtenant's business is deemed a "public accommodation" or "commercial facility", (2) whether such requirements are "readily achievable", and (3) whether a given alteration affects a "primary function area" or triggers "path of travel" requirements. The parties hereby agree that: (a) Sublandlord shall be responsible for compliance with ADA Title III in the portions of the Prime Lease Premises (excluding the Premises) and the entrances and exits of the Premises as existing on the Delivery Date, except as provided below, (b) Subtenant shall be responsible for ADA Title III compliance within the Premises (specifically excluding the entrances and exits therefrom as existing on the Delivery Date), (c) Sublandlord may perform, or require that Subtenant perform, and Subtenant shall be responsible for the cost of, ADA Title III "path of travel" requirements triggered by alterations in the Premises made by Subtenant, and (d) Sublandlord may perform, or require Subtenant to perform, and Subtenant shall be responsible for the cost of, ADA Title III compliance in the Prime Lease Premises or common areas of the Building not within the Prime Lease Premises necessitated by the Building being deemed to be a "public accommodation" instead of a "commercial facility" as a result of Subtenant's use of the Premises for other than general office purposes. Subtenant shall be solely responsible for requirements under Title I of the ADA relating to Tenant's employees.

5.3 For purposes of this Sublease, "**Substantial Completion**" of Sublandlord's Work (and terms correlative thereto) shall mean the completion of construction thereof (which completion shall be reasonably determined by Sublandlord) and (if legally required) issuance of a certificate of occupancy for the Premises (or applicable legal equivalent), with the exception of (i) any punch list items that can be completed after Subtenant has taken occupancy of the Premises without unreasonably interfering with Subtenant's operation of its business in the Premises, and (ii) any leasehold improvements, furnishings, fixtures and equipment not included in Sublandlord's Work, all of which shall be the responsibility of Subtenant to purchase and install at Subtenant's sole cost and expense in accordance with the requirements hereof. Sublandlord shall complete all punch list items with respect to Sublandlord's Work as soon as reasonably practicable following Substantial Completion of Sublandlord's Work. To the extent there shall be a delay or delays in the Substantial Completion of Sublandlord's Work as a result of any of the following (each, a "**Tenant Delay**") then, notwithstanding anything to the contrary set forth in this Sublease, and regardless of the actual date of Substantial Completion of the Sublandlord's Work, the date of Substantial Completion of Sublandlord's Work shall be deemed to be the date the Substantial Completion of Sublandlord's Work would have occurred if no Tenant Delay had occurred:

(a) Subtenant's failure to timely approve any matter with respect to which Subtenant's approval is required hereunder or requested by Sublandlord;

(b) A breach by Subtenant of the terms of this Sublease;

(c) Subtenant's request for changes to the Sublandlord's Work after the date hereof;

(d) Subtenant's request, after the date hereof, for materials, components, finishes or improvements which are not available in a commercially reasonable time given the estimated date of Substantial Completion; or

(e) Any other acts or omissions of Subtenant or its agents, employees, contractors or representatives after the date hereof.

Sublandlord agrees that upon obtaining actual knowledge of any facts or circumstances that constitute a Tenant Delay (other than a Tenant Delay under clause (b) of this *Section 5.3*), Sublandlord will notify Subtenant thereof in writing as promptly as is reasonably practicable.

6. SUBTENANT'S USE; ACCESS. The Premises shall be used and occupied only for the Permitted Use set forth in *Section 1(S).* Anything herein to the contrary notwithstanding, uses prohibited under the Prime Lease are not permitted hereunder and all restrictions on use in the Prime Lease shall be applicable to any use of the Premises by Subtenant. Subject to security procedures instituted by the Sublandlord or Prime Landlord, or both, from time to time to prevent unauthorized access to the Building and appurtenant areas, and subject to the terms and provisions contained in this Sublease, Subtenant shall have access to the Premises elevator twenty four (24) hours per day, seven (7) days per week, fifty two (52) weeks per year. Sublandlord agrees that any such security procedures it imposes will be commercially reasonable. To the extent not included as part of Substantial Completion, Subtenant shall be responsible, at its own cost and expense, for obtaining prior to commencement of its business operations at the Premises any and all licenses, permits and renewals thereof required by any governmental or other authority having jurisdiction for such business operations.

7. RENT. Beginning on the Commencement Date, but subject to the Abated rent Period described above, Subtenant agrees to pay the Annual Fixed Rent set forth in *Section 1(L)* to the Payee specified in *Section 1(M)*, by ACH transfer in accordance with the instructions provided in *Section 1(O)*), or to such other payee or at such other address as may be designated by notice in writing from Sublandlord

to Subtenant, without prior demand therefor and without any deduction or set off whatsoever (except as expressly set forth herein or in the Prime Lease as incorporated herein). Annual Fixed Rent shall be paid in monthly installments (as set forth in *Section 1(L)*) in advance on the first day of each month of the Term after the Commencement Date. Annual Fixed Rent shall be pro-rated for any partial calendar month at the beginning and end of the Term, All charges, costs and sums required to be paid by Subtenant under this Sublease in addition to Annual Fixed Rent, shall be deemed **"Additional Rent"** and Annual Fixed Rent and Additional Rent shall hereinafter collectively be referred to as **"Rent"**. Subtenant's covenant to pay Rent shall be independent of every other covenant in this Sublease. Any amount due from Subtenant to Sublandlord under this Sublease that is not paid when due shall bear annual interest from the due date at the lesser of (i) three percent (3%) above the prime rate as reported in *The Wall Street Journal* on the date closest to the date such payment was required to be made hereunder and (ii) the highest legal rate permitted under the laws of the Commonwealth of Massachusetts (the "**Interest Rate**"), such interest to accrue from the date due until paid unless otherwise specifically provided herein, but the payment of such interest shall not excuse or cure any default by Subtenant under this Sublease. Notwithstanding the foregoing, Sublandlord agrees to waive the payment of interest as provided in the immediately preceding sentence with respect to the first late payment of Rent during any twelve-month period. Sublandlord shall also be entitled, on account of a failure by Subtenant to make any payment of Rent when due (except with respect to a first late payment of Rent during any twelve-month period), to charge as Additional Rent a fee equal to five percent (5%) of the amount due as compensation for Sublandlord's administrative costs in investigating and collecting such late payment.

8. ADDITIONAL RENT.

8.1 Subtenant shall pay to Sublandlord, as Additional Rent, the percentage that is set forth in *Section 1(P)* as Subtenant's Share of (i) Operating Expenses, to the extent in excess of Operating Expenses for the Base Operating Year, and (ii) Taxes, to the extent in excess of Taxes for the Base Tax Year.

For purposes hereof, "**Taxes**" shall mean Landlord's Tax Expenses as described in Article VI of the Prime Lease.

Likewise, for purposes hereof, "**Operating Expenses**" shall mean the aggregate of the following: (i) Operating Expenses" as defined in Section 6.2 of the Prime Lease; (ii) the management fee payable by Sublandlord to Prime Landlord pursuant to Section 6.5 of the Prime Lease; and (iii) all costs and expenses incurred by Sublandlord in performing its obligations as required by the terms of the Prime Lease which are not an obligation of and performed by Subtenant hereunder (excluding payment of regular installments of "Annual Fixed Rent," "Real estate taxes," "Landlord's Tax Expenses" and "Operating Expenses" under the Prime Lease), provided, however, that (A) costs for security services and shuttle bus service described in *Section 40* and *Section 41* hereof shall not be included in this clause (iii), (B) costs and expenses related to items which are for the benefit of only a specific tenant or occupant of the Property, as opposed to Property tenants and occupants generally, shall be excluded from Operating Expenses, (C) any Operating Expenses which benefit the various buildings at the Property shall be equitably allocated among such buildings such that each building's tenants and occupants are only responsible for their pro rata equitable share thereof, as reasonably determined by Sublandlord from time-to-time, (D) any management fee included in this clause (iii) shall be fair and reasonable under the circumstances, accounting for those management services provided by Prime Landlord under the Prime Lease, and (E) capital expenditures shall only be included by Sublandlord in this clause (iii) where the same are depreciated over the useful life of the item in question and the portion thereof included in Operating Expenses is limited to annual depreciation thereof over the number of years of useful life of the capital item in question, reasonably determined by Sublandlord in accordance with generally-accepted accounting principles, including an interest factor at a rate not to exceed the rate Prime Landlord would be permitted to include for depreciation of capital expenditures included in "Operating Expenses" under the Prime Lease.

Subtenant shall pay to Sublandlord estimated payments on account of Subtenant's Share of excess Operating Expenses, commencing January 1, 2021, and excess Taxes, commencing July 1, 2020, as reasonably estimated by Sublandlord (where applicable, based on estimates provided by Prime Landlord) from time to time, monthly with payments of Annual Fixed Rent. Beginning with Subtenant's first such payment, which shall be due no less than thirty (30) days after Subtenant's receipt of notice, Subtenant shall make monthly installment payments to Sublandlord on account of Operating Expenses and Taxes on the date each installment of Annual Fixed Rent is due, or in the event of any adjustment thereof no later than thirty (30) days after submission by Sublandlord to Subtenant of an invoice setting forth the adjustment and corresponding amount due.

Within ten (10) days after receipt by Sublandlord of the Prime Landlord's annual statement under the Prime Lease respecting Operating Expenses and/or Taxes, Sublandlord shall provide Subtenant with an itemized invoice (which shall include a copy of the Prime Landlord's statement) of the actual amount of Operating Expenses and/or Taxes due and such supporting materials or documentation as reasonably necessary to substantiate the same (**"Adjustment Notice"**). Any overpayment by Subtenant in excess of its obligations hereunder shall be returned to Subtenant or applied to the following year's Annual Fixed Rent payments, at the option of Sublandlord. Any underpayment by Subtenant n account of its obligations shall be paid by Subtenant within thirty (30) days of receiving the Adjustment Notice documenting such underpayment. Any required adjustment and adjusting payment or reimbursement shall survive the expiration or termination of this Sublease.

8.2 Notwithstanding anything contained herein to the contrary, if the occupancy level of the Building for the Base Operating Year or the Base Tax Year (or any subsequent calendar year or fiscal year, as applicable) is less than one hundred percent (100%), Taxes and Operating Expenses for the applicable period shall be determined by extrapolation of Taxes and those items of Operating Expenses which are affected by changes in occupancy levels of the Property to the costs of such Taxes and/or Operating Expenses which would have been incurred if the Property were one hundred percent (100%) occupied and such services reflected by such items were being supplied to one hundred percent (100%) of the rentable area of the Property for such period, and as if the Property were fully assessed at full occupancy, and such projected amounts shall, for the purposes hereof, together with items of Operating Expenses which are not affected by occupancy levels, be deemed to be the Operating Expenses and Taxes for the applicable period (as applicable).

8.3 Subtenant's Share provided for in *Section 1(P)* is a fraction (expressed as a percentage) of which the numerator is the Rentable Square Feet of the Premises as set forth in *Section 1(Q)* and the denominator is the rentable square feet of the Prime Lease Premises. In the event that the Rentable Square Feet in the Premises is increased pursuant to any of the provisions hereof, such numerator shall be adjusted accordingly and Subtenant's Share shall be recalculated. In the event that the rentable square feet of the Prime Lease Premises (exclusive of Storage Space) is increased or decreased, such denominator shall be adjusted accordingly and Subtenant's Share shall be recalculated.

8.4 Payments of all other monetary obligations of Subtenant hereunder, including, without limitation, charges incurred by or for the account of Subtenant pursuant to *Sections 9* and *27* hereof, are also deemed Additional Rent, whether or not specified as such hereunder. Such payments shall be made no later than thirty (30) days after submission by Sublandlord of an invoice setting forth the amount due. If requested by Subtenant in writing, Sublandlord shall provide commercially reasonable back-up documentation for such invoice. Such charges may be included on invoices with respect to Operating Expenses (or estimated payments) submitted pursuant to *Section 8.1* hereof. For the purposes of clarification, Subtenant shall have no liability on account of Operating Expenses attributable to the period of time prior to January 1, 2021, or Taxes attributable to the period of time prior to July 1, 2020.

8.5 Upon written request from Subtenant delivered within ninety (90) days following its receipt of Sublandlord's annual reconciliation statement relating to Taxes or Operating Expenses, Sublandlord shall furnish to Subtenant copies of all tax bills, invoices and such back-up documentation with respect to the Operating Expenses and/or Taxes included in the statement in question, as Subtenant may reasonably request (but if related to Taxes or Operating Expenses payable by Sublandlord pursuant to the Prime Lease only to the extent such information has been received by Sublandlord from the Prime Landlord).

8.6 Subtenant shall have no right to audit Operating Expenses or Taxes under the Prime Lease or right to require that Sublandlord do so. Refunds with respect to any overpayments by Subtenant of Operating Expenses attributable to the Premises resulting from any audit conducted by Sublandlord (if any) shall be made to Subtenant within thirty (30) days after Sublandlord shall have received payment from the Prime Landlord pursuant to the Prime Lease. Subtenant shall have no liability for any costs incurred by Sublandlord to audit Operating Expenses or Taxes under the Prime Lease, except that Sublandlord may deduct from any refund to Subtenant arising from an audit the Subtenant's Share of the actual and reasonable costs thereof .

9. SUBTENANT'S OBLIGATIONS. From and after the Commencement Date, Subtenant shall also be responsible for the following at its own cost and expense:

(a) All utility consumption costs relating to electricity, water and sewer, and condenser water services consumed by Subtenant in the Premises, in each case in an amount not greater than the actual cost for the same incurred by Sublandlord, as follows: (i) electric and other charges incurred in connection with lighting and providing electrical power to the Premises, which the parties agree shall be charged to Tenant at a fixed rate of One and 75/100 Dollars ($1.75) per rentable square foot of the Premises per annum, payable in equal monthly installments of Two Thousand Five Hundred Sixty-Eight and 71/100 Dollars ($2,568.71) at the same time and in the same manner as Tenant's payment of Annual Fixed Rent, provided, Tenant uses electricity for ordinary general office purposes only and without exceeding the standard electricity service provided by Landlord as set forth in Exhibit C to the Prime Lease (and if Tenant uses electricity for any other purpose, equipment other than ordinary office machines, or otherwise exceeds such standards, then Landlord may require that Tenant pay to install a check meter(s) or submeter(s) to measure Subtenant's usage, and in such event Tenant shall be obligated to pay the actual cost of its electricity consumption as shown on such meter or meters), (ii) water and sewer costs, payable as part of Operating Expenses, and (iii) charges for condenser water from Building's system (if available) at Sublandlord's actual cost thereof..

(b) maintenance, repairs and replacements as to the Premises and its equipment performed by the Prime Landlord at the expense of Sublandlord, if and to the extent required by reason of Subtenant's failure to perform repairs or maintenance required of it under this Sublease.

(c) The cost of any license or roof rights for Subtenant in connection with telecommunications equipment as provided in *Section 31* hereof.

(d) The cost of any after-hours HVAC (i.e., outside of the standard hours described in Exhibit C to the Prime Lease) and utility costs that are requested by Subtenant as provided in *Section 27* hereof.

(e) special cleaning services for removal of rubbish and for other non-routine cleaning of the Premises, in either case as requested by Tenant (or as reasonably required by Sublandlord with regard for the first class nature of the Building) and over and above cleaning services required to be provided by Prime Landlord, as more fully described in Exhibit C of Prime Lease.

10. QUIET ENJOYMENT. Sublandlord represents that it has full power and authority to enter into this Sublease, subject to the obtaining of the consent of the Prime Landlord, if and to the extent required under the Prime Lease. So long as Subtenant is not in default in the performance of its covenants and agreements in this Sublease (continuing beyond the expiration of any applicable notice and cure periods), Subtenant's quiet and peaceable enjoyment of the Premises shall not be disturbed or interfered with by Sublandlord, or by any person claiming by, through, or under Sublandlord, subject to the terms of this Sublease and the Prime Lease as incorporated herein.

11. SUBTENANT'S INSURANCE. Subtenant shall procure and maintain, at its own cost and expense and unless the Prime Landlord shall agree to lesser limits and coverage, such commercial general liability and other insurance as is required to be carried by Sublandlord under the Prime Lease as it relates to the Premises, naming as additional insureds Sublandlord as well as Prime Landlord, Prime Landlord's managing agent, Sublandlord's managing agent, and any mortgagee designated in writing by Sublandlord or the Prime Landlord of which Subtenant shall have had notice, in the manner required therein. However, for purposes hereof it is agreed that the limit of Subtenant's commercial general liability insurance shall be $5 million per annum, combined single limit. Unless the Prime Landlord agrees to waive or permit lesser coverage and limits, Subtenant shall also procure and maintain, at its own cost and expense, such property insurance, including, without limitation, on Subtenant's furniture, trade fixtures and equipment within the Premises (and any leasehold improvements made by Subtenant after the date of this Lease) as is required to be carried by Sublandlord under the Prime Lease with respect to the Premises. Sublandlord will be responsible for maintaining or causing to maintain property insurance on any leasehold betterments or improvements made in or to the Premises prior to the date hereof, with the cost thereof being part of Operating Expenses hereunder. Subtenant shall furnish to Sublandlord a certificate evidencing Subtenant's insurance coverage required hereunder not later than ten (10) days prior to Subtenant's taking possession of the Premises and thereafter, when and as amended or replaced, following Sublandlord's written request therefor from time to time in connection with the adjustment of any claim relating to Subtenant or the Premises. Subtenant agrees to obtain, for the benefit of Sublandlord, the Prime Landlord, its managing agent, any mortgagee or other Additional Insureds designated by the Prime Landlord of which Subtenant shall have had notice, such waivers of subrogation rights from its insurers) as are required of Sublandlord under the Prime Lease. Sublandlord agrees to obtain for the benefit of Subtenant a waiver from its insurer(s) of their respective right of subrogation, subject to and in accordance with the terms and provisions of the Prime Lease. Sublandlord agrees to use commercially reasonable efforts to obtain from the Prime Landlord a waiver of claims for insurable property damage losses and an agreement from the Prime Landlord to obtain a waiver of subrogation rights in the Prime Landlord's property insurance, to the extent that the Prime Landlord waives such claims against Sublandlord under the Prime Lease or is required under the Prime Lease to obtain such waiver of subrogation rights. Each party hereby waives claims against the other for property damage provided such waiver shall not invalidate the waiving party's property insurance. Subtenant hereby waives claims against the Prime Landlord and Sublandlord for property damage to the Premises or its contents if and to the extent that Sublandlord waives such claims against the Prime Landlord under the Prime Lease. Anything herein to the contrary notwithstanding, Subtenant shall obtain and maintain in force such additional insurance coverage, including terrorism insurance, and shall increase the limits of coverage herein provided as the Prime Landlord may from time to time require pursuant to the Prime Lease.

12. ASSIGNMENT OR SUBLETTING.

12.1 Except as provided herein, Subtenant shall not, without the express written consent of Sublandlord (which consent shall not be unreasonably withheld, delayed or conditioned, it being agreed by Subtenant that failure of the Prime Landlord to provide its consent is a reasonable basis for Sublandlord to withhold its consent) and of the Prime Landlord (to the extent required pursuant to the Prime Lease), (i) assign, convey or mortgage this Sublease or any interest under it; (ii) allow any transfer thereof or any lien

upon Subtenant's interest by operation of law; (iii) further sublet the Premises or any part thereof; or (iv) permit the occupancy of the Premises or any part thereof by anyone other than Subtenant. In addition, for the purposes of this Sublease, unless the stock or other ownership interests in Subtenant is traded on a regulated securities exchange (and excepting any future additional stock issuance or any "going private" transaction), the sale or transfer (which term shall include, without limitation, the exchange, issuance and redemption) of fifty-one percent (51%) or more, or such smaller percentage as would result in a change in the voting control of Subtenant (whether such sale or transfer occurs at one time or at intervals so that, in the aggregate, over the Term of this Sublease, such transfer shall have occurred) shall be treated as if such sale or transfer or transaction(s) were, for all purposes, an assignment of this Sublease and shall be governed by the provisions of this *Article 12*. If Sublandlord consents thereto, and Sublandlord would have the right to enter into such assignment or sublease under the terms and conditions of the Prime Lease, Sublandlord shall use commercially reasonable efforts to obtain the consent of the Prime Landlord if and to the extent required by the terms of the Prime Lease. Any actual and reasonable out-of-pocket cost of obtaining the Prime Landlord's consent and Sublandlord's consent including, without limitation, attorneys fees and disbursements, shall be borne by Subtenant. The granting by Sublandlord and the Prime Landlord of consent to a sublease, assignment or other transfer or occupancy in any one instance shall not relieve the Subtenant of the obligation to obtain such consent to any further such transaction.

12.2 No assignment or transfer by Subtenant shall release Subtenant or Subtenant's Guarantor (if any) from its obligations under this Sublease or the Guaranty (as applicable).

12.3 No permitted assignment or transfer of the subleasehold interest, whether or not consent is required, shall be effective and no permitted sublease, occupancy or other transfer shall commence if an Event of Default (as hereinafter defined) by Subtenant shall have occurred or (ii) if a condition or event then exists which, with or without notice or the lapse of time, or both, would if not cured constitute an Event of Default by Subtenant, unless and until such condition or event shall have been cured within the applicable cure period, if any. No assignment, subletting, other transfer or occupancy shall relieve Subtenant from Subtenant's obligations and agreements hereunder and Subtenant shall continue to be liable as a principal and not as a guarantor or surety to the same extent as though no assignment, subletting, other transfer or occupancy had been made.

Notwithstanding the foregoing provisions of this Sublease, unless the Prime Landlord's consent is required pursuant to the provisions of the Prime Lease, Sublandlord's prior consent shall not be required for a sublease or assignment by Subtenant (including, without transactions deemed an assignment under Section 12.1 above) to a parent, affiliate or successor entity to Subtenant, provided the assignee (or surviving entity under any such deemed assignment transaction) has a net worth not less than Subtenant's net worth as of the date of this Sublease, and Subtenant furnishes reasonable documentation thereof to Sublandlord at least five (5) days prior to the applicable assignment or sublease date (or, if disclosure not then permitted by applicable law, within five (5) days following such time as disclosure thereof is lawfully permitted) (each, a "**Permitted Transferee**")

12.4 If Subtenant desires to assign, sublet, permit another to occupy or transfer (except to a Permitted Transferee) as of a date certain (the **"Termination Date"**) the entire Premises or a portion thereof (the **"Offered Premises**") for all or substantially all of the balance of the Term (collectively, to **"Sublet"**). Subtenant shall so inform Sublandlord in writing (a **"Notice of Intent to Sublet"**). Sublandlord shall have the right, by notice given within thirty (30) days after receipt of a Notice of Intention to Sublet, to require Subtenant to surrender the Offered Premises upon the Termination Date. Subtenant shall not be required to have entered into a definitive agreement with the proposed transferee as a condition to delivering a Notice of Intent to Sublease. Failure by Sublandlord to respond within such thirty (30) day period shall be deemed a waiver of Sublandlord's right to require surrender. If Sublandlord shall elect to require surrender of the Offered Premises, then the Sublease with respect to such Offered Premises shall expire on the Termination

Date and the Sublease shall be amended as of the Termination Date to reflect the surrender. Subtenant shall be responsible for the cost of constructing or reconstructing of demising walls and a public corridor and code required entrances and egresses to the public corridor and other modifications, if necessitated by reason of the surrender of the Offered Premises or as otherwise required by law.

12.5 If Sublandlord shall not exercise its right to require surrender of the Offered Premises or is deemed not to have done so, then Subtenant shall have the right, subject to obtaining Sublandlord's and the Prime Landlord's consent (if required by the Prime Lease) for the proposed transaction pursuant to paragraph 12.1 hereof, and for a period of six (6) months thereafter (failing which the provisions of Section 12.4 shall again apply) to assign, sublease, permit occupancy by another or otherwise transfer the portion of the Premises proposed to be assigned, sublet, transferred or occupied. In the event of any such assignment, sublease or other transfer, Subtenant shall pay to Sublandlord, as Additional Rent each month, fifty percent (50%) of the entire amount of the Excess Income (as hereinafter defined), received by Subtenant with respect thereto, other than from any Permitted Transferee. Subtenant shall be responsible, at its own expense, for payment of all costs and expenses related to the assignment, sublease, occupancy or other transfer, including, without limitation, broker's and legal fees and the cost of fixing up the space, including, without limitation, the cost of constructing demising walls, corridors and code required entrances and egresses and such other modifications, if necessary or as may be required by law or by reason of the demise of space. The term **"Excess Income"** shall be calculated in the same manner as "Assignment/Sublease Profits" as set forth in Section 12.6(B) of the Prime Lease. Subtenant shall furnish Sublandlord upon request with a detailed statement certified by an officer of Subtenant showing the amount of rental or other consideration received and such additional documentation of Excess Income as Sublandlord may reasonably request.

12.6 Any transferee of Subtenant must be of a character, creditworthiness and engaged in a business which is of a first class nature. There shall not be more than two (2) subtenants (including Subtenant) (or such lesser number as Prime Landlord may require) in the Premises.

12.7 If this Sublease be assigned or if the Premises or any part thereof be sublet or occupied by any person other than the Subtenant, Sublandlord may, upon an Event of Default by Subtenant at any time and from time to time, and while the same is continuing, collect Annual Fixed Rent and Additional Rent from the assignee, subtenant or occupant and apply the net amount collected to the amounts then due and thereafter becoming due hereunder, but the collection of such rental shall in no event be construed as consent to any assignment, sublease or other transfer or acceptance of the assignee, subtenant, or occupant nor the release of Subtenant from the performance by Subtenant of covenants on its part herein contained nor the waiver of any right or remedy of Sublandlord.

12.8 The provisions of this *Section 12* shall survive termination or expiration of this Sublease.

13. RULES. Subtenant agrees to comply with all reasonable rules and regulations that Sublandlord or Prime Landlord has made or may hereafter from time to time make for the Building and the Property. Sublandlord and Subtenant shall not be liable in any way for damage caused by the non-compliance by any of the other tenants of the Property of such rules and regulations. Sublandlord agrees to use commercially reasonable efforts to enforce the rules and regulations in a non-discriminatory manner, unless the context reasonably requires otherwise.

14. REPAIRS AND COMPLIANCE. Subtenant shall promptly pay for the costs incurred with respect to its obligations set forth in *Section 9* hereof and Subtenant shall, at Subtenant's own expense, comply with all laws and ordinances and all orders, rules and regulations of all public authorities and all requirements of all insurers at any time now or hereafter in effect and applicable to the Premises or to Subtenant's occupancy or particular use or manner of use (as opposed to business office use generally

where compliance would require any structural modification to the Premises) thereof and with all obligations imposed on Sublandlord under the Prime Lease applicable to the Premises or to Subtenant's occupancy during the Term of this Sublease, except that Subtenant shall not hereby be under any obligation to comply with any law, ordinance, rule or regulation requiring any structural alteration of or in connection with the Premises, unless such alteration is required by reason of Subtenant's particular use or manner of use of the Premises, or is a condition which has been created by or at the sufferance of Subtenant, or is required by reason of a breach of any of Subtenant's covenants and agreements hereunder. As used herein "structure" or "structural" shall have the definition ascribed to it in the Prime Lease or if no specific definition is given therein "structure" or "structural" shall mean that portion of the Building which is integral to the integrity of the Building as an existing enclosed unit and shall, in any event, include footings, foundation, outside walls, skeleton, bearing columns and interior bearing walls, floor slabs, roof and roofing system.

15. FIRE OR CASUALTY OR EMINENT DOMAIN. In the event Sublandlord is entitled under the Prime Lease to a rent abatement as a result of a fire or other casualty or as a result of a taking under the power of eminent domain, in each event to the extent affecting the Premises, the parties shall equitably adjust the abatement as between themselves, based on the relative impact, if any, of the fire or other casualty or taking, as the case may be, on the Premises and on other areas of the Building subject to the Prime Lease. If (a) the Premises or Building are substantially damaged by fire, or (b) all or part of the Premises or Building are taken and in either case (i) the Prime Lease is not terminated as a result thereof, (ii) such damage or taking shall materially interfere with Subtenant's use of or access to the Premises and (iii) such damage is not repaired within the applicable periods set forth in the Prime Lease, Subtenant may terminate this Sublease to the same extent as afforded to Sublandlord under the applicable provision of the Prime Lease. Further and without limitation, if the Premises or Building are substantially damaged by fire such that there is material interference with Tenant's use or of access to the Premises and the necessary repairs and restoration for which Sublandlord and Prime Landlord are responsible will not reasonably be completed within one year from the date of damage (as reasonably estimated by Sublandlord's professional architect or construction manager), or if the damage occurs within the last year of the Term of this Sublease and the anticipated repair time for repairs Sublandlord and/or Prime Landlord are obligated to make is greater than fifty percent (50.0%) of then then-remaining Term, then Subtenant may terminate this Sublease by written notice to Sublandlord within thirty (30) days following such fire or casualty (but not thereafter). To the extent that the Prime Lease requires that any damage be repaired or restored by the Tenant under the Prime Lease, such repairs shall be the responsibility of the Sublandlord hereunder (except as to Alterations or improvements made by Subtenant hereunder). Any notice to terminate shall be given no later than ten (10) business days after the date by which the damage was required to be repaired. If Subtenant shall give such notice, then this Sublease shall terminate on the date specified in the notice with the same force and effect as if such date were the date originally established as the expiration date hereof.

16. ALTERATIONS. Subtenant shall not make any alterations in or additions to the Premises or the Building (**"Alterations"**), unless expressly consented to in writing by Sublandlord and, where required under the Prime Lease, of the Prime Landlord. Sublandlord's consent shall not be unreasonably withheld, conditioned or delayed with respect to Alterations that are non-structural in nature, do not affect any Building systems, and cost, in the aggregate, less than $75,000.00, exclusive of painting and carpeting costs. Sublandlord also agrees that Sublandlord will not withhold its consent to first class improvements to the entry/reception area of the Premises or Subtenant's request to install interior window film within the area of the Premises Subtenant intends to use as its network operations or patient services center, subject in each case to the approval of the Prime Landlord for the same (if required). Sublandlord agrees to use commercially reasonable efforts to obtain such consent from the Prime Landlord, where such consent is required pursuant to the Prime Lease and where Sublandlord has provided its consent. If Alterations by Subtenant are permitted or consented to as aforesaid, Subtenant shall perform the same at its sole cost and expense and comply with all of the covenants and obligations of Sublandlord contained in the Prime Lease

pertaining to the performance of such Alterations. In the performance of any Alterations, Subtenant shall maintain harmonious labor relations. In addition to compliance with the requirements of the Prime Lease, whether or not Sublandlord's approval for such Alterations shall be required, Subtenant shall also (i) procure all necessary governmental permits, licenses and certificates, (ii) make all required filings of plans with governmental authorities before making any Alterations, (iii) obtain all required governmental approvals upon the completion thereof, and (iv) deliver copies to Sublandlord of all partial and final executed lien waivers from Subtenant's general contractor and subcontractors in standard AIA form satisfactory to Sublandlord, and upon completion of any Alterations, Subtenant shall deliver to Sublandlord (A) an architect's certificate from Subtenant's architect certifying that the Alterations have been completed substantially in accordance with the plans and specifications therefor and (B) three (3) complete "as built" or field marked sets of Subtenant's plans and specifications prepared on an AutoCAD Computer Assisted Drafting and Design System (or such other system or medium reasonably approved by Sublandlord and generally used in the industry).

17. SURRENDER; RESTORATION.

17.1 Upon the expiration of this Sublease, or upon the sooner termination of this Sublease or of the Subtenant's right to possession of the Premises, Subtenant will at once surrender and deliver up the Premises, together with all improvements thereon, (except as hereafter provided) to Sublandlord in good order, condition and repair, subject to ordinary wear and tear and damage by fire or other casualty. Such improvements shall include all plumbing, lighting, electrical, heating, cooling and ventilating fixtures and equipment used in the operation of the Premises (as distinguished from Subtenant's Trade Fixtures, as described in *Section 18* of this Sublease). Subtenant shall also surrender to Sublandlord all keys and keycards to the Premises and/or the Building. For purposes of clarification, Subtenant shall in no event be responsible for removal or restoration of any improvement or Alteration in place as of the Commencement Date or not made or installed by Subtenant or any assignee, sub-subtenant or other party claiming by, through or under Subtenant.

17.2

(a) If Subtenant is permitted, with consent of Sublandlord and (if required under the Prime Lease) the Prime Landlord, to construct or install any Alterations in the Premises, and unless Subtenant and Prime Landlord have entered into a Direct Lease and Prime Landlord shall have released Sublandlord in writing from any obligation to remove the same from the Prime Lease Premises, Subtenant shall, upon expiration or early termination of the Term of this Sublease, at its sole cost and expense, cause all such Alterations to be removed and all portions of the Premises restored substantially to their condition prior to the installation of such Alterations, but only if and to the extent that Sublandlord is required to remove or restore any such Alterations under the terms of the Prime Lease.

(b) Subtenant shall also at its expense remove, whether or not so designated at the time consent is given, all voice and data systems and related cabling and wiring and all security systems and devices installed by Subtenant at the Premises, unless and to the extent that the Prime Landlord otherwise agrees in writing. After any such removal in accordance with the foregoing, Subtenant shall repair any damage done to the Premises as a result of such removal, in a good and workmanlike manner.

(c) If the Prime Landlord requires removal of any Alterations installed or made by Subtenant, as provided in this *Section 17* and Subtenant does not cause such removal in accordance with this *Section 17*, Sublandlord may, at Subtenant's expense, remove the same (and repair any damage occasioned thereby) and dispose of the same, or at its election, deliver the same to any other place of business of Subtenant, or warehouse the same. Subtenant shall pay the actual and reasonable costs of such removal, repair, delivery and warehousing on demand and shall hold harmless and defend Sublandlord from any cost or expense it incurs due to Subtenant's breach of this *Section 17.2(c)*.

18. REMOVAL OF SUBTENANT'S PROPERTY. Upon the expiration or sooner termination of this Sublease, and unless Subtenant and Prime Landlord have entered into a Direct Lease, Subtenant shall remove all Subtenant's personal property, whether owned or leased, including, without limitation, Subtenant's furniture, business machines and equipment, signage, telecommunications equipment and other moveable installations not integral to operation of the Building (**"Trade Fixtures"**). Subtenant shall also (a) remove any cabling installed by Subtenant, and (b) repair any injury or damage to the Premises which may result from such removal of Trade Fixtures and cabling. Any property of Subtenant remaining after expiration or termination of this Sublease shall, without limiting any of Sublandlord's other rights or remedies under this Sublease, be conclusively deemed to have been abandoned by Subtenant and Sublandlord may, at its election, (i) retain the same or sell the same as its property, in either case without compensation to Subtenant or (ii) deliver the same, to any other place of business of Subtenant, or warehouse the same for the account and at the expense of Subtenant, or (iii) otherwise dispose of the same as Sublandlord shall see fit. Subtenant shall pay on demand all actual out-of-pocket costs reasonably incurred by Sublandlord in connection with the disposition of such property, including, without limitation, the reasonable cost of removal (and repair of damage to or the cost of restoration of the Premises caused by such removal) and all costs of delivery and warehousing, if applicable.

19. HOLDING OVER. Unless Subtenant and Prime Landlord have entered into a Direct Lease and provided written notice thereof to Sublandlord, Subtenant shall have no right to occupy the Premises or any portion thereof after the expiration of this Sublease or after termination of this Sublease for any reason or after termination of Subtenant's right to possession in consequence of an Event of Default hereunder. In the event Subtenant or any person claiming by, through or under Subtenant holds over or otherwise remains in possession after the expiration or sooner termination of the Term, Subtenant shall hold Sublandlord harmless and indemnify Sublandlord from and against any loss, cost, expense, claim or damage arising directly or indirectly therefrom; and Sublandlord may exercise any and all remedies available to it at law or in equity to recover possession of the Premises and to recover damages, including without limitation, any damages payable by Sublandlord to Prime Landlord by reason of such holdover. In addition to and without limitation of the foregoing, for each and every month or partial month that Subtenant or any party claiming by, through or under Subtenant remains in occupancy of all or any portion of the Premises after the expiration of this Sublease or after termination of this Sublease or Subtenant's right to possession, Subtenant shall pay, as minimum damages and not as a penalty, use and occupancy charges at a rate equal to two (2.0) times the rate of Annual Fixed Rent and 100% of the Additional Rent payable by Subtenant hereunder immediately prior to the expiration or other termination of this Sublease or of Subtenant's right to possession. The acceptance by Sublandlord of payment of such damages on account of a holdover shall not be construed as creating any new tenancy or recognizing any continued right to use and occupy the Premises after expiration or termination of the Term, except as a tenancy at sufferance, and acceptance of any lesser sum by Sublandlord shall not be construed to be in satisfaction of damages for such holding over, but only as a payment on account.

20. ENCUMBERING TITLE. Subtenant shall not do any act which shall in any way encumber or adversely affect the title of the Prime Landlord in and to the Building, the parcel or parcels of land upon which it is located, and any other buildings and/or improvements to such land (**"Property"**), nor shall the interest or estate of the Prime Landlord or Sublandlord be in any way subject to any claim by way of lien or encumbrance, whether by operation of law, by virtue of any express or implied contract by Subtenant, or by reason of any other act or omission of Subtenant. Any claim to, or lien upon, the Premises, the Building or the Property arising from any act or omission of Subtenant shall accrue only against the subleasehold estate of Subtenant and shall be subject and subordinate to the paramount title and rights of the Prime Landlord in and to the Building and the Property and the interest of Sublandlord in the Prime

Lease Premises. Without limiting the generality of the foregoing, Subtenant shall not permit the Premises, the Building or the Property to become subject to any lien of any mechanics, laborers or materialmen on account of labor or material furnished to Subtenant or claimed to have been furnished to Subtenant in connection with work of any character performed or claimed to have been performed on the Premises by, or at the direction or sufferance of Subtenant; provided, however, that if so permitted under the Prime Lease, and subject to any conditions imposed therein, Subtenant shall have the right to contest in good faith and with reasonable diligence, the validity of any such lien or claimed lien if Subtenant shall give to the Prime Landlord and Sublandlord such security as may be required under the Prime Lease, or if none is specified, such security as may be deemed satisfactory to them to assure payment thereof and to prevent any sale, foreclosure, or forfeiture of the Premises, the Building or the Property or a termination of the Prime Lease by reason of non-payment thereof and the existence of any lien or claim of lien; provided further, however, that on final determination of the lien or claim of lien, Subtenant shall within ten (10) days from notice thereof pay any judgment rendered, with all proper costs and charges, and shall have the lien released and any judgment satisfied.

21. INDEMNITY. Subject to the waivers of claims and rights of subrogation provisions in Section 11 hereof, Subtenant agrees to indemnify, defend and hold Sublandlord and its agents, officers, directors, members, shareholders, contractors and employees (**"Sublandlord Additional Indemnitees"**), or any of them, harmless from all costs, losses, damages, liabilities and expenses (including, without limitation, attorneys' fees and disbursements that they or any of them may incur) arising from the negligent or willful acts or omissions of Subtenant, its agents, employees, contractors or other persons for whose conduct Subtenant is responsible ("**Subtenant Responsible Parties**") that Sublandlord or any other person to be indemnified hereunder may incur, or for which Sublandlord may be liable to the Prime Landlord if and to the same extent such act or omission requires Sublandlord to indemnify, defend and hold harmless the Prime Landlord and other persons under the Prime Lease. Without limiting any of the foregoing, Subtenant further agrees to indemnify, defend and save harmless Sublandlord and the Sublandlord Additional Indemnitees, or any of them, from and against all claims of whatever nature arising from (a) the use or occupancy of the Premises or the conduct of any business thereon; (b) any work or thing whatsoever done, or any condition created (other than by the Prime Landlord, Sublandlord or the employees, agents or contractors of either or both of them) in or about the Premises, (c) any negligent or otherwise wrongful act or omission of Subtenant or Subtenant Responsible Parties, whether resulting in injury or death to persons or damage to property or otherwise; and (d) any failure of Subtenant to comply with the obligations, covenants and conditions required of Subtenant under this Sublease.

Subject to the waivers of claims and rights of subrogation provisions in Section 11 hereof, Sublandlord agrees to indemnify, defend and hold Subtenant and its agents, officers, directors, members, shareholders, contractors and employees harmless from all costs, losses, damages, liabilities and expenses (including, without limitation, attorneys' fees and disbursements) arising from the negligent or willful acts or omissions on or about the Premises or the Prime Lease Premises of Landlord, its agents, employees or contractors ("**Landlord Responsible Parties**") that Subtenant may incur.

22. SUBLANDLORD'S RESERVED RIGHTS. Supplementing the provisions of the Prime Lease that are incorporated herein by reference pursuant to *Section 32*, Sublandlord and the Prime Landlord shall have the right, on reasonable prior notice, to inspect the Premises, or to exhibit the Premises to persons having a legitimate interest (including, without limitation, those persons entitled to inspect or exhibit the Premises pursuant to the Prime Lease and prospective assignees of Sublandlord's leasehold interest under the Prime Lease) at any reasonable time during the Sublease Term. The foregoing access rights shall be subject to Subtenant's reasonable requirements and restrictions with respect to areas occupied by Subtenant's patient services group and containing confidential information or materials, but only in each case to the extent (i) required for Subtenant to comply with any applicable laws respecting patient privacy, and (ii) that Subtenant's requirements and restrictions are set forth in detailed written notice to Landlord

with reasonable prior notice. In addition to the foregoing, the Prime Landlord may, on reasonable prior notice, exhibit the Premises or have representatives of Sublandlord exhibit the Premises to prospective tenants, subtenants or occupants during the last year of the Term of the Sublease. Any inspection or exhibition of or entry upon the Premises (except in an emergency) shall be conducted at a time and in a manner that do not unreasonably interfere with Subtenant's use of the Premises.

23. DEFAULTS. Subtenant further agrees that any one or more of the following events shall be considered **"Events of Default"** by Subtenant:

(a) if the Subtenant neglects or fails to pay the Rent herein reserved or any part thereof, (including Annual Fixed Rent, Additional Rent and other charges) when due and payable, as herein provided, and such neglect or failure to pay Rent shall continue for five (5) days after the due date thereof, provided no Event of Default shall arise on the first instance of late payment by Subtenant in any period of twelve (12) consecutive months if Subtenant makes its late payment within five (5) business days following written notice from Sublandlord that Subtenant's payment was not made when due; or

(b) if the Subtenant neglects or fails to perform or observe or acts in derogation of any of the other covenants, agreements or provisions contained in this Sublease which, on the Subtenant's part, are to be performed or observed, and such neglect or failure or action with respect to the performance or observance of or compliance with such other covenants, agreements or provisions shall continue for thirty (30) days (or such additional time as may reasonably be required, provided a cure has been commenced within thirty (30) days and Subtenant thereafter diligently pursues such cure to completion with reasonable continuity) after written notice thereof given by the Sublandlord to the Subtenant; or

(c) if the leasehold interest hereby created shall be taken on execution, or by other process of law, or if any assignment shall be made of the property of Subtenant for the benefit of creditors; or

(d) if a receiver, trustee in bankruptcy or similar officer shall be appointed to take charge of all or any part of the property of Subtenant by a court of competent jurisdiction and such appointment shall not have been vacated or stayed or set aside or be dismissed within forty-five (45) days from the date upon which it is filed; or

(e) if a petition is filed by or against Subtenant seeking an adjudication as bankrupt or insolvent under the Federal bankruptcy laws as now in effect or hereafter amended or under any state insolvency or similar law or if any petition shall be filed or other judicial action taken by or against Subtenant to delay, reduce or modify its respective debts or obligations or to reorganize or modify its respective capital structure or indebtedness or to appoint a trustee, receiver or liquidator of Subtenant or of any property of Subtenant or Guarantor, or any proceeding or other action shall be commenced or taken by any governmental authority for the dissolution or liquidation of Subtenant and any of the same shall not have been vacated or stayed or set aside or be dismissed within forty-five (45) days from the date upon which it is filed; or

(f) if Subtenant shall admit in writing its inability to pay its debts as they become due; or

(g) if Subtenant shall do or permit to be done anything whereby a lien, security interest or other encumbrance (whether consensual or created by operation of law or otherwise) is created or filed against all or any part of the Premises, the Building, the Property or Subtenant's interest in this Sublease and is not discharged of record or bonded off within ten (10) days from the date of entry or granting thereof; or

(h) if Subtenant shall default in securing or maintaining insurance or in providing evidence of insurance as set forth in *Section 11* of this Sublease; or

(i) if Subtenant shall, by its failure to comply with any of its obligations in this Sublease cause a default of Sublandlord as tenant under the Prime Lease; or

(j) if Subtenant shall make an assignment, sublease or other transfer of its interest in this Sublease, whether by operation of law or otherwise, except in accordance with the provisions of this Sublease.

24. REMEDIES.

24.1 If an Event of Default by Subtenant has occurred in any of its obligations hereunder, then, in addition to Sublandlord's other rights and remedies herein, Sublandlord may perform the same for the account and at the expense of Subtenant immediately in the case of a default under *Section 23(h)* and as to other defaults, after first giving notice to Subtenant of such default and a reasonable time to cure the same (except that in the event of an emergency, notice shall be required only to the extent practicable under the circumstances). Sublandlord may make any repairs which are essential for the protection and maintenance of the Premises or any portion thereof or to protect its leasehold interest under the Prime Lease, if Subtenant fails to commence any such repairs that are Subtenant's responsibility hereunder within ten (10) days after receipt of notice from Sublandlord, or immediately, if emergency conditions occur. In the event of a default or threatened default by Subtenant, Sublandlord shall also, in addition to its other rights and remedies herein, have the right to seek injunctive relief.

24.2 Upon the occurrence of any one or more Events of Default, Sublandlord may exercise any remedy against Subtenant that the Prime Landlord may exercise for default by Sublandlord under the Prime Lease or this Sublease.

24.3 If Sublandlord incurs any expense by reason of the failure of Subtenant to comply with any of its obligations under this Sublease, or if Sublandlord incurs any expense, including, without limitation, attorneys fees and disbursements, in successfully instituting, prosecuting or defending any action or proceeding instituted by reason of a default of Subtenant, including, without limitation, expenses incurred to avoid an Event of Default under the Prime Lease, then, whether or not the Sublease is terminated by reason of such default, Subtenant shall pay or reimburse Sublandlord for the expenses so incurred by Sublandlord within thirty (30) days following the submission of an invoice or invoices for the same.

25. NOTICES AND CONSENTS. All notices, demands, requests, consents or approvals (each, a "**Notice**") which may or are required to be given by either party to the other shall be in writing and shall be deemed given when received or refused if sent by United States registered or certified mail, postage prepaid, return receipt requested or if sent by a recognized national overnight commercial courier service (i) if to Subtenant, and prior to the Subtenant's occupancy of the Premises for the conduct of Subtenant's business, addressed to Subtenant at the addresses specified in *Section 1(B)* , and thereafter to the Premises, or in either case at such other place as Subtenant may from time to time designate by notice in writing to Sublandlord or (ii) if for Sublandlord, addressed to Sublandlord at the address specified in *Section 1(C)*, or at such other place as Sublandlord may from time to time designate in writing to Subtenant. Subtenant agrees promptly to deliver a copy of each Notice sent from Subtenant to the Prime Landlord and promptly to deliver to Sublandlord a copy of any Notice received from the Prime Landlord. Each party may rely upon any Notice given in writing by the attorney for the other.

26. PROVISIONS REGARDING SUBLEASE. This Sublease and all the rights of parties hereunder are subject and subordinate to the Prime Lease and to the matters to which the Prime Lease is or shall be subject. Subtenant agrees that it will not, by its act or omission to act, cause a default or an Event of Default under the Prime Lease. In furtherance of the foregoing, the parties hereby confirm, each to the other, that it is not practical in this Sublease to enumerate all of the rights and obligations of the various parties under the Prime Lease and, except as otherwise expressly provided herein, to specifically allocate those rights and obligations in this Sublease. Accordingly, in order to afford to Subtenant the benefits of this Sublease and of those provisions of the Prime Lease which by their nature are intended to benefit the person in possession of the Premises, and in order to provide the benefits to Sublandlord of this Sublease and to protect Sublandlord against a default by Subtenant which might cause a default or Event of Default by Sublandlord under the Prime Lease, Subtenant and Sublandlord agree that:

(a) Sublandlord shall pay, when and as due, all Fixed Rent, Additional Rent and other charges payable by Sublandlord to Prime Landlord under the Prime Lease so long as the same remains in effect;

(b) Sublandlord shall perform its covenants and obligations under the Prime Lease (so long as the same remains in effect) which do not require for their performance possession of the Premises and which are not otherwise to be performed hereunder by Subtenant on behalf of Sublandlord;

(c) Subtenant shall perform all affirmative covenants of the Prime Lease relative to the Premises and the Term (and except for any such covenants that are by their nature personal to Sublandlord) and shall refrain from performing any act that is prohibited by the negative covenants of the Prime Lease, where, in each case, the obligation to perform or refrain from performing is specifically (or can reasonably be construed to be) imposed upon the person in possession of the Premises or is otherwise applicable to all occupants of the Building. In all events, Subtenant shall perform affirmative covenants which are also covenants of Sublandlord under the Prime Lease no later than three (3) business days prior to the date when Sublandlord's performance is required under the Prime Lease, or by such earlier date as will afford a reasonable time for Sublandlord to effect a cure (if the obligation is not timely performed by Subtenant) so as to prevent a default under the Prime Lease, but in no event shall Subtenant's performance be required in less than three (3) business days. Sublandlord shall have the right to enter the Premises to confirm compliance and, if necessary, to cure any breach of this Sublease by Subtenant giving rise to risk of bodily injury, death or substantial damage to property of Sublandlord, the Prime Landlord or a third party, or any Event of Default;

(d) Sublandlord shall not agree to an amendment to the Prime Lease or enter into any agreement with the Prime Landlord which would result in (i) a material reduction of essential building services and amenities appurtenant to the Premises to the extent provided in the Prime Lease or in this Sublease, (ii) a material adverse effect upon access and egress to the Premises, (iii) a material increase in obligations of Subtenant under this Sublease or a material adverse effect on Subtenant's rights under this Sublease, or (iv) a reduction in the length of the Term or in a termination of this Sublease prior to its expiration, unless consented to by Subtenant in its sole discretion or arising from fire, casualty or eminent domain; and

(e) If Prime Landlord shall default in any of its obligations to Sublandlord with respect to the Premises or any other area or facility that Subtenant has the right to use hereunder, Subtenant shall be entitled to request in writing that Sublandlord endeavor to enforce Sublandlord's rights against Prime Landlord with respect thereto. In the event Subtenant makes such a request, Sublandlord agrees to issue a written request to Prime Landlord that it fulfill its unperformed obligation(s) under the Prime Lease and in the event that the Prime Landlord continues to not perform its required obligation under the Prime Lease within a reasonable time, Sublandlord agrees that it will make demand upon the Prime Landlord to perform its obligations under the Prime Lease and shall use commercially reasonable efforts to cause the Prime Landlord to cure such default or failure, but in no event shall Sublandlord be obligated to threaten or initiate any legal proceeding, or exercise any offset, deduction or similar right under the Prime Lease respecting the same, or take other legal action to enforce the Prime Lease.

Sublandlord shall promptly deliver to Subtenant a copy of any written notice received by Sublandlord from Prime Landlord or any governmental agency which could reasonably be expected to result in a material adverse effect on Subtenant's rights to use or occupy the Premises in accordance with and subject to the provisions of this Sublease.

(f) Sublandlord hereby grants to Subtenant the right to receive all of the services and benefits with respect to the Premises that are to be provided by the Prime Landlord under the Prime Lease with respect to the Premises; provided, however, that Sublandlord shall have no duty to perform any obligations of the Prime Landlord that the Prime Landlord is required to provide under the Prime Lease. Except for its limited obligations set forth in Section 26(e) hereof, Sublandlord shall have no responsibility for or be liable to Subtenant for any default, failure or delay on the part of the Prime Landlord in the performance or observance by the Prime Landlord of any of its obligations under the Prime Lease, nor shall such default by the Prime Landlord affect this Sublease or waive or defer the performance of any of Subtenant's obligations hereunder. Sublandlord shall not be liable to Subtenant for money damages on account of any failure of the Prime Landlord to perform nor shall any such failure constitute a constructive eviction of Subtenant unless Sublandlord would be entitled under the Prime Lease to claim constructive eviction on account of such failure. If, by reason of the failure of the Prime Landlord to observe or perform its obligations, Sublandlord is entitled to receive and actually receives any rent abatement under the Prime Lease attributable to the Premises during the Term, then Subtenant shall be entitled to its equitable share of the same, net of reasonable collection costs. Any such abatement shall be equitably adjusted by Sublandlord in its commercially reasonable judgment, based on the relative impact, if any, of such failure of the Prime Landlord on the Premises and on other areas of the Building.

27. ADDITIONAL SERVICES PROVIDED TO SUBTENANT. If Subtenant requests additional services not provided by the Prime Landlord under the Prime Lease, or to be provided by the Prime Landlord but at additional cost, Subtenant shall pay for such services to Sublandlord (or at Sublandlord's written request, directly to the Prime Landlord) within such time as the Prime Landlord requires or, if the Prime Landlord has billed the same to Sublandlord, shall pay or reimburse Sublandlord within thirty (30) days after an invoice has been submitted to Subtenant setting forth the amount owed (with reasonable supporting documentation thereof to be provided to Subtenant upon its written request). Sublandlord agrees to pass through to Subtenant (without fee, mark-up or profit) any costs billed by the Prime Landlord or otherwise incurred by Sublandlord for services furnished to Subtenant (and not provided under the Prime Lease at no additional cost) at Subtenant's request (or as reasonably required due to Subtenant's failure to perform its obligations under this Sublease), including, without limitation, any after-hours utility charges incurred by Subtenant following its request for such service. If at any time a charge for such additional services is attributable to the use of such services both by Sublandlord and by Subtenant, the cost thereof shall be equitably divided between Sublandlord and Subtenant, and Subtenant shall be entitled to commercially reasonable back-up documentation therefor promptly upon its written request.

28. PRIME LANDLORD'S CONSENT.

This Sublease is being entered into pursuant to Section 12.3 of the Prime Lease, and therefore no Landlord consent for this Sublease is required. However, simultaneously with the execution and delivery hereof, Sublandlord, Prime Landlord and Subtenant are each executing and delivering an agreement confirming the Prime Landlord's consent is not required for this Sublease, and as contemplated by the provisions of Section 12.7 of the Prime Lease in connection herewith, such agreement being in the form attached hereto as **Exhibit E**. Sublandlord will be responsible for the payment of any costs and expenses charged by Prime Landlord in connection with such agreement.

29. BROKERAGE. Each party warrants to the other that it has had no dealings with any broker or agent in connection with this Sublease other than the Broker(s) as specified in *Section 1(T)*, whose commissions shall be paid by Sublandlord pursuant to separate written agreements between Sublandlord and one or more of such Broker(s). Each party covenants to pay, hold harmless and indemnify the other party from and against any and all costs (including reasonable attorneys' fees), expense or liability for any compensation, commissions and charges claimed by any other broker or other agent with respect to this Sublease or the negotiation thereof on behalf of such party. Sublandlord shall be solely responsible for payment of any commission or fee to the Broker(s), subject to and in accordance with the above-described agreements.

30. FORCE MAJEURE. Neither Sublandlord nor Subtenant shall be deemed in default with respect to any of the terms, covenants and conditions of this Sublease if such party's failure to timely perform is due in whole or in part to any strike, lockout, labor trouble (whether legal or illegal,), civil disorder, failure of power, restrictive governmental laws, orders and regulations, riots, insurrections, acts of terrorism or war, shortages, accidents, fire, other casualties, acts of God, unusual scarcity or inability to obtain labor or material or delays caused directly by the other party or its agents, employees and invitees, or any other cause beyond the reasonable control of the party seeking to be excused (any such event individually or collectively, "**Force Majeure**") (except that no such event of Force Majeure shall excuse the monetary or insurance obligations of either party hereunder).

31. RISER USAGE/SIGNAGE/OFFICE CLEANING AND OTHER SERVICES.

(a) Riser Usage. Sublandlord shall provide to Subtenant or cause the Prime Landlord to provide to Subtenant, at no cost to Subtenant, adequate riser space in connection with Subtenant's cabling between the IDF room located within the Premises and the utility and communication demarcation points in the Building, and Sublandlord shall not unreasonably withhold its consent to Subtenant's Alterations consisting of one or more telecommunications devices to be installed for Subtenant's use in connection with its business conducted at the Premises, provided the same is at Subtenant's sole cost and expense, any required consent of the Prime Landlord is obtained, and Subtenant complies with all provisions of this Sublease and the Prime Lease Applicable thereto. Any such equipment and related connections shall be considered Trade Fixtures for purposes of this Sublease.

(b) Signage. Sublandlord shall provide Building-standard signage for Subtenant in the main lobby of the Building, subject to Prime Landlord's approval. Sublandlord will also not unreasonably withhold, condition or delay its consent to Subtenant's improving the signage in the main lobby of the Building, provided the same is approved by the Prime landlord and is at no cost, expense or liability to Sublandlord.

(c) Cleaning and Other Services. Subject to the terms of this Sublease, Sublandlord shall cause the Prime Landlord to provide office cleaning and other services to the Premises as described in Exhibit C to the Prime Lease, but in each case subject to and in accordance with the provisions of the Prime Lease. The cost thereof shall be included in Operating Expenses.

32. INCORPORATION OF PRIME LEASE; CERTAIN EXCLUSIONS. Except as otherwise expressly provided in, or otherwise inconsistent with, this Sublease, or to the extent not applicable to the Premises, the terms, provisions, covenants, stipulations, conditions, rights, obligations, remedies and agreements contained in the Prime Lease are incorporated in this Sublease by reference, and are made a part hereof as if herein set forth at length, Sublandlord being substituted for the "Landlord" under the Prime Lease, Subtenant being substituted for the "Tenant" under the Prime Lease, and the Premises being substituted for the "Premises" under the Prime Lease. Notwithstanding the foregoing, in the event of any conflict or inconsistency between the provisions of the Prime Lease and this Sublease, the terms and provisions of this Sublease shall govern and control. Further, in no event will Subtenant be bound by any provision of the Prime Lease that has been redacted. In addition:

(a) Subtenant shall have no extension rights, development rights or rights of first offer, first refusal or other preferential right to purchase or lease the Property or any part thereof (including, without limitation, under Section 16.31 of the Prime Lease);

(b) Subtenant shall have no set-off or abatement rights other than as expressly set forth in this Sublease.

(c) Subtenant shall not have any measurement rights set forth in the Prime Lease.

(d) Article 4 of the Prime Lease (Construction) shall not be applicable.

(e) Section 6.4 (Effect of Multiple Rent Commencement Dates) of the Prime Lease shall not be applicable.

(f) Section 9.1.1 (Certain Alterations Which Do Not Require Landlord's Approval) of the Prime Lease shall not be applicable.

(g) Section 12.2 (Exceptions for Mergers and Affiliate Transactions) and Section 12.3 (Exception for Certain Subleases) of the Prime Lease shall not be applicable.

(h) Sublandlord shall not be required to provide the insurance described in Section 13.6 (Landlord's Insurance) of the Prime Lease.

(i) Section 15.6 (Self-Help) of the Prime Lease shall not be applicable.

(j) Section 16.8 (Recording) of the Prime Lease shall not be applicable.

(k) Section 16.15 (Landlord's Financing; Tenant's Shadow Rating) of the Prime Lease shall be inapplicable.

(l) Section 16.16 (Status Reports and Financial Statements) is inapplicable and the applicable provisions of this Sublease shall govern.

(m) Section 16.18 (Holding Over) of the Prime Lease is inapplicable and the provisions of *Section 19* of this Sublease shall govern.

(n) Section 16.21 (Late Payment) of the Prime Lease is inapplicable and the provisions of *Section 7* of this Sublease shall govern.

(o) Section 16.24 (Limitations on Landlord's Liability) of the Prime Lease is inapplicable to Sublandlord hereunder.

(p) Section 16.26 (Letters of Credit) of the Prime Lease is inapplicable and the provisions of *Section 38* of this Sublease shall govern.

(q) Section 16.30 (Letters of Credit) of the Prime Lease is inapplicable and the provisions of this Sublease shall govern.

(r) Section 16.32 (Arbitration) of the Prime Lease.

(s) The provisions in the First Amendment, the Second Amendment, July 2006 Letter Agreement, the Acknowledgment of Merger, the Third Amendment, the Fourth Amendment, and the June 2014 Letter Agreement shall all be inapplicable.

33. PARKING.

33.1 During the Term, and beginning on the Commencement Date, Subtenant (or its employees) shall be entitled to the use of (but shall not be obligated to use) up to sixty-three (63) parking spaces in the garage and surface parking facilities on the Property (the **"Parking Spaces"**), for no additional cost or expense other than as provided in this Sublease. Sublandlord and Subtenant agree that all such Parking Spaces shall be unreserved spaces, available on a "self-park, first-come, first served" basis, with no specific allocation to Subtenant of any number of garage or exterior parking spaces. If the Premises is reduced by the exercise of Sublandlord's right of recapture under *Section 12.4* or otherwise, the number of parking spaces to which Subtenant is entitled shall be reduced proportionally.

33.2 Sublandlord's failure or inability to provide any such parking spaces because of casualty, taking, or for any other reason beyond Sublandlord's control shall, in no event, entitle Subtenant to terminate this Sublease or receive any abatement in Rent, provided that the foregoing shall not limit Subtenant's other rights and remedies set forth in this Sublease, including without limitation Section 15. Subtenant and all partners and employees of Subtenant that use the Parking Spaces agree to comply with all reasonable rules and regulations applicable to the use of the parking spaces as Sublandlord or the Prime Landlord, or both, may impose from time to time, and in the event such partners or employees of Subtenant fail to so comply with such rules and regulations on an ongoing basis after notice of such failure and if such pattern of failure to comply has not been cured, then Sublandlord shall have no continuing obligation to make any such Parking Spaces available for use by persons who have so failed to comply with such rules and regulations.

34. FURNITURE.

All furniture (including modular furniture) and existing cabling and equipment located in the Premises on the Commencement Date shall remain in the Premises during the Term, and shall, effective as of the expiration of sooner termination of this Lease, become Tenant's sole and exclusive personal property (free and clear of all liens and encumbrances) unless, at least thirty (30) days prior to such time, Subtenant delivers written notice to Sublandlord stating that it does not desire to retain any of such furniture, cabling and equipment (it being understood that Tenant may not elect to keep only certain items thereof). At Subtenant's request, Sublandlord will deliver a commercially reasonable bill of sale conveying the furniture to Subtenant, in then-existing "as is, where" is condition, and without any representation or warranty of any kind (and expressly disclaiming any implied warranties of fitness or merchantability), other than that Sublandlord is the owner thereof and may lawfully convey the same to Subtenant free of all liens, equipment leases or other financing arrangements. Unless Subtenant timely so elects, all such furniture, cabling and equipment shall immediately become Trade Fixtures, as defined in *Section 18*, and shall be subject to the provisions of *Section 18*. No representations or warranties are made herein by Sublandlord (other than as to Sublandlord's ownership and right to convey), including, without limitation, as to the condition of such furniture, cabling or equipment, the suitability thereof for Subtenant's use, or any compliance of the same with applicable law. As a part of Sublandlord's Work, Sublandlord will remove from the Premises those items of furniture listed on Exhibit D.

35. SUBTENANT'S FINANCIAL STATEMENTS.

35.1 Subtenant acknowledges that the financial capability of Subtenant to perform its obligations hereunder is material to Sublandlord and that Sublandlord would not enter into this Sublease but for its belief, based on its review of Subtenant's financial statements, that Subtenant is capable of performing such financial obligations. Subtenant hereby represents, warrants and certifies to Sublandlord that its financial statements previously furnished to Sublandlord were at the time given true and correct in all material respects. Unless such information is generally available to the public, at any time during the Term (but not more than twice in any calendar year), Subtenant shall provide Sublandlord, upon ten (10) business days' prior written notice from Sublandlord, its then-most recent annual financial statements for Subtenant. Such statements shall be prepared in accordance with generally accepted accounting principles and (if such is the practice of Subtenant) audited by an independent certified public accountant. The terms of this *Section 35.1* requiring delivery of financial statements shall not be applicable to any Guarantor so long as such Guarantor is a publicly-traded corporation.

36. ESTOPPEL CERTIFICATE. Subtenant hereto agrees at any time and from time to time within ten (10) business days after a written request therefor by Sublandlord, to execute, acknowledge and deliver to Sublandlord a statement in writing certifying that this Sublease is unmodified and in full force and effect (or if there shall have been modifications, which modifications shall be identified, that this Sublease, as modified, is in full force and effect) and stating, to the actual knowledge of Subtenant, whether or not Sublandlord is in default in performance of any covenant, agreement or condition contained in this Sublease and, if so, specifying each such default of which Subtenant may have knowledge and certifying as to the status of any other matter relating to this Sublease as may be reasonably requested by the requesting party. Such certificate may also be relied upon, as to a certificate executed by Subtenant, by any of the Prime Landlord, a mortgagee of the Prime Landlord, a prospective purchaser or ground lessor of the Building or land upon which it is located and any prospective assignees of Sublandlord. No such certificate shall have the effect of amending express provisions of this Sublease, and in the event of any conflict between the express terms and conditions of this Sublease and any such certificate, the express terms and conditions of this Sublease shall control.

37. DEFINITIONS. Capitalized terms not otherwise specifically defined herein shall have the meaning ascribed to them in the Prime Lease as though such definitions are set forth and incorporated herein, and provisions of the Prime Lease to which reference is made hereunder shall also be deemed incorporated by reference herein.

38. LETTER OF CREDIT.

(a) To secure the full and prompt payment by Subtenant of all amounts due under this Sublease and the performance of all obligations of Subtenant hereunder, Subtenant shall, simultaneously with the execution and delivery of this Sublease, provide Sublandlord with a letter of credit (the "**Letter of Credit**") in the initial amount equal to Eighty Five Thousand One Hundred Thirty-Four and 34/100 Dollars ($85,134.34). The Letter of Credit shall be in a form reasonably satisfactory to Sublandlord and issued by a banking corporation reasonably satisfactory to Sublandlord. It shall have an expiration date no earlier than the first anniversary of the date of issuance thereof and shall be automatically renewed from year to year through December 31, 2022 unless the issuer thereof provides notice to Sublandlord of its intent not to renew the subject letter of credit at least forty-five (45) days prior to the expiration thereof. Subtenant shall, throughout the term of this Sublease, deliver to Sublandlord, in the event of the termination or non-renewal of any such letter of credit, replacement letters of credit in lieu thereof (each such letter of credit and such extensions or replacements thereof, as the case may be, shall constitute the Letter of Credit hereunder) no later than ten (10) days prior to the expiration date of the preceding Letter of Credit. If Subtenant shall fail to obtain any replacement of or amendment to a Letter of Credit within any of the

applicable time limits set forth in this Section 38, such failure shall, at the option of Sublandlord constitute an Event of Default; and Sublandlord shall have the right (but not the obligation), at its option, to draw down the full amount of the existing Letter of Credit and retain the same as a cash security hereunder, and notwithstanding such draw by Sublandlord, Sublandlord shall retain all other rights and remedies that are available to Sublandlord under this Sublease.

(b) If (i) an Event of Default occurs, (ii) the Letter of Credit is not replenished or replaced when required hereunder, or (iii) the credit rating of the long-term debt of the issuer of the Letter of Credit (according to Moody's, Standard & Poor's or similar national rating agency reasonably identified by Sublandlord) is downgraded to a grade below the prevailing minimum standards for major leases by landlords of comparable office buildings in the MetroWest area; or the issuer of the Letter of Credit enters into any supervisory agreement with any governmental authority; or the issuer of the Letter of Credit fails to meet any capital requirements imposed by applicable laws (unless Subtenant delivers to Sublandlord a replacement Letter of Credit complying with the terms of this Sublease within twenty-one (21) days after demand therefor from Sublandlord), then, in any of such events, Sublandlord may, at its election, (but shall not be obligated to) draw down the entire Letter of Credit or any portion thereof and use, apply or retain the whole or any part thereof to the extent required for the payment of: (a) any sum or expense which Subtenant has failed to pay timely in accordance with requirements of this Sublease, (b) any sum which Sublandlord may expend or may be required to expend by reason of an Event of Default, including, without limitation, any reletting costs or expenses (including, market leasing commission and reasonable attorneys' fees relating to the reletting of all or any portion of the Subleased Premises), (c) any damages or deficiency actually incurred in the reletting of the Subleased Premises following an Event of Default, whether such damages or deficiency accrued before or after summary proceedings or other re-entry by Sublandlord, or (d) any damages awarded to Sublandlord in accordance with the terms and conditions of this Sublease. To insure that Sublandlord may utilize the proceeds of the Letter of Credit in the manner, for the purpose, and to the extent provided herein, each Letter of Credit shall provide that the full amount or any portion thereof may be drawn down by Sublandlord upon the presentation to the issuing bank (or the advising bank, if applicable) of Sublandlord's draft drawn on the issuing bank with an accompanying memoranda or statement of beneficiary certifying that it is entitled to make such draw. In no event shall the Letter of Credit require Sublandlord to submit evidence to the issuing (or advising) bank of the truth or accuracy of any such written statement (exclusive of any requirements of the issuing or advising bank that the beneficiary submit a signature verification document) and in no event shall the issuing bank or Subtenant have the right to dispute the truth or accuracy of any such statement nor shall the issuing (or advising) bank have the right to review the applicable provisions of this Sublease. In no event and under no circumstance shall the draw down on or use of any amounts under the Letter of Credit or utilization or retention of all or any portion of the proceeds thereof by Sublandlord constitute a basis or defense to the exercise of any other of Sublandlord's rights and remedies under this Sublease or under any Law, including, without limitation, Sublandlord's right to assert a claim against Subtenant under Title 11 U.S.C. §502(b)(6) or any other provision of Title 11 of the United States Code.

(c) If an Event of Default occurs and Sublandlord utilizes all or any part of the security represented by the Letter of Credit but does not terminate this Sublease as provided herein Sublandlord may, in addition to exercising its other rights and remedies, retain the unapplied and unused balance of the portion of the Letter of Credit drawn down by Sublandlord as cash security for the faithful performance and observance by Subtenant thereafter (within any applicable notice or cure periods) of the terms, provisions, and conditions of this Sublease, and may use, apply, or retain the whole or any part of said cash security to the extent required for payment of Rent or any other sum or expense which Subtenant has failed to pay timely in accordance with requirements of this Sublease, or for any sum which Sublandlord may expend or be required to expend by reason of an Event of Default. In the event Sublandlord uses or applies any portion or all of the proceeds of the Letter of, Subtenant shall forthwith restore the amount so used or applied by the provision of a replacement Letter of Credit) so that at all times the amount represented by the Letter of Credit shall be not less than the initial amount required hereunder.

(d) Provided no Event of Default then exists and Subtenant has no outstanding monetary obligations to Sublandlord under this Sublease, the Letter of Credit or any remaining cash security shall be returned to Subtenant within thirty (30) days after both (i) the expiration or early termination of this Sublease and (ii) the delivery to Sublandlord of possession of the entirety of the Subleased Premises. In the event of any assignment of the Prime Lease by Sublandlord, Sublandlord shall transfer the Letter of Credit or the proceeds therefrom (as applicable) to the transferee, with contemporaneous written notice thereof to Subtenant. The costs and expenses of the first such transfer of the Letter of Credit shall be paid by Subtenant, but any and all costs charged to Subtenant by the Letter of Credit issuer in connection with any subsequent transfer shall be reimbursed to Subtenant by Sublandlord within thirty (30) days following Subtenant's written request therefor. Upon such transfer of the Letter of Credit (or proceeds thereof. if any), Sublandlord shall thereupon be released by Subtenant from all liability for the return thereof, and Subtenant shall look solely to the new landlord or transferee for the return of the same. The provisions of the preceding sentence shall apply to every subsequent assignment of the Prime Lease by Sublandlord, and any successor of Sublandlord shall, upon any such assignment, transfer the Letter of Credit (or proceeds, if any) to any transferee and shall thereupon be relieved of all liability with respect thereto. Subtenant shall not assign or encumber or attempt to assign or encumber the security represented by the Letter of Credit or proceeds thereof, and neither Sublandlord nor its successors or assigns shall be bound by any such assignment, encumbrance, attempted assignment or attempted encumbrance.

(e) Neither the Letter of Credit, nor any proceeds therefrom, if any, shall be deemed an advance rent deposit or an advance payment of any other kind, or a measure or limitation of Sublandlord's damages or constitute a bar or defense to any of the Sublandlord's other remedies under this Sublease or at law or in equity upon an Event of Default.

(f) As a material inducement to Sublandlord to enter into this Sublease, Subtenant hereby acknowledges and agrees that the Letter of Credit and the proceeds thereof (including, without limitation, any cash security created by the drawdown of all or any portion of the Letter of Credit) and the obligation to make available or pay to Sublandlord all or a portion thereof in satisfaction of any obligation of Subtenant under this Sublease, shall be deemed third-party obligations and not the obligation of Subtenant hereunder and, accordingly, (a) shall not be subject to any limitation on damages contained in Section 502(b)(6) of Title 11 of the United States Code or any other limitation on damages that may apply under any Law in connection with a bankruptcy, insolvency or other similar proceeding by, against or on behalf of Subtenant, (b) shall not diminish or be offset against any amounts that Sublandlord would be able to claim against Subtenant pursuant to Title 11 U.S.C. §502(b)(6) as if no Letter of Credit existed, and (c) may be relied on by Sublandlord in the event of an assignment of this Sublease that is not expressly in accordance with the terms of this Sublease even if such assignment has been authorized and approved by a court exercising jurisdiction in connection with a bankruptcy, insolvency or other similar proceeding by, against or on behalf of Subtenant

39. SUBTENANT'S REPRESENTATIONS, WARRANTIES AND COVENANTS.

39.1 Subtenant represents, warrants and covenants that:

(a) It is a corporation duly organized, validly formed and in good standing under the laws of the State of Delaware and qualified to do business in the Commonwealth of Massachusetts.

(b) During the Term and for a period of one year after the Expiration Date, it shall at all times maintain a registered agent for service of process in the Commonwealth of Massachusetts. The name and address of such registered agent as of the date hereof is: CT Corporation, 155 Federal Street, Boston, MA 02110.

(c) (i) Subtenant is not, nor is it owned or controlled directly or indirectly by, any person, group, entity or nation named on the Specially Designated Nationals and Blocked Persons List maintained by the Office of Foreign Assets Control of the United States Treasury ("**OFAC**") (any such person, group, entity or nation being hereinafter referred to as a "**Prohibited Person**"); (ii) Subtenant is not (nor is it owned or controlled, directly or indirectly, by any person, group, entity or nation which is) acting directly or indirectly for or on behalf of any Prohibited Person; and (iii) Subtenant (and any person, group, or entity which Subtenant controls, directly or indirectly) has not conducted nor will conduct business nor has engaged nor will engage in any transaction or dealing with any Prohibited Person that either may cause or causes Sublandlord to be in violation of any OFAC rule or regulation, including without limitation any assignment of this Sublease or any sub-subletting of all or any portion of the Premises. In connection with the foregoing, it is expressly understood and agreed that (x) any breach by Subtenant of the foregoing representations and warranties shall be deemed a default by Subtenant under this Sublease and shall be covered by the indemnity provisions of *Section 21* of this Sublease, and (y) the representations and warranties contained in this *Section 39.1(c)* shall be continuing in nature and shall survive the expiration or earlier termination of this Sublease.

40. BUILDING SECURITY. Access for the Premises and the Property shall be via a card reader system or similar device, and in the event that such system fails to operate on any occasion Sublandlord shall provide access to the Premises through a reasonable alternative means. Subtenant acknowledges and agrees that access to the Building (and other portions of the Property) and access to and use of the Premises are subject at all times to security procedures that the Prime Landlord or Sublandlord, or both, may impose from time to time following prior written notice to Subtenant. Sublandlord agrees to act reasonably with respect to establishment and application of its security procedures, including reasonable prior notice of changes in any such procedures to the extent practicable. If Sublandlord requires, Subtenant agrees to furnish to the Prime Landlord and Sublandlord a personnel list and identification photographs for its employees who are permitted access to the Premises and such other information as the Prime Landlord or Sublandlord may reasonably request, which information shall be updated from time to time by Subtenant to enable any Building or Property security service to identify those personnel of Subtenant who are entitled to access; provided, however, that neither Sublandlord nor Prime Landlord shall be responsible for the denial of access to those persons not reasonably identifiable as approved personnel or invitees of Subtenant. Subtenant acknowledges and agrees that access to the Building, appurtenant areas, and the Premises is subject at all times to such security procedures, including, without limitation, required evacuation in the event of an emergency and in such event, Subtenant shall not be entitled to an abatement of Rent nor shall Subtenant have any claim for constructive eviction. Sublandlord may from time to time provide additional security services to the Building and the Prime Lease Premises, including, without limitation, one or more manned or unmanned security stations, security patrols, security cameras and video-monitoring, all as Sublandlord may deem necessary or proper in its commercially reasonable discretion. Sublandlord shall provide to Subtenant up to one hundred (100) access cards to the Building and Premises at no cost to Subtenant, provided the same are requested by Subtenant (with applicable employee names) not later than June 30, 2020. Thereafter, Subtenant shall pay to Sublandlord the actual cost incurred by Sublandlord to provide key cards or access cards to Subtenant for its employees (and any replacements thereof), together with Subtenant's Share of all other costs and expenses incurred by Landlord during the Term in connection with the security measures, services and equipment described in this Section 40. Sublandlord represents to Subtenant that the costs and expenses associated with the security services and system management is currently estimated to be not greater than fifty cents ($0.50) per rentable square foot of Premise area per annum. Such amounts shall be payable within thirty (30) days following Sublandlord's monthly written invoices to Subtenant for the same, or at Sublandlord's option Sublandlord may require Subtenant to pay estimated installments on account of such security costs, subject to annual reconciliation at the same time and in the same manner as Additional Rent is determined under *Section 8* hereof.

41. SHUTTLE SERVICE. Reference is hereby made to Section 11.10 of the Original Lease and the Special Permit described therein relating to, inter alia, the implementation and funding of a shuttle service to the Property. If and to the extent any of Subtenant's employees utilize the shuttle service described therein, Subtenant shall be responsible for Subtenant's Share of all costs and expenses incurred by Landlord during the Term in connection with such shuttle service. Such amounts shall be payable within thirty (30) days following Sublandlord's monthly written invoices to Subtenant for the same, or at Sublandlord's option Sublandlord may require Subtenant to pay estimated installments on account of such shuttle service, subject to annual reconciliation at the same time and in the same manner as Additional Rent is determined under *Section 8* hereof

42. MISCELLANEOUS.

42.1 This Sublease shall be binding upon Sublandlord and its successors and assigns, and upon Subtenant and its successors and permitted assigns, and shall be governed by and construed in accordance with the laws of the Commonwealth of Massachusetts (without reference to conflicts of laws principles).

42.2 If any provision of this Sublease or portion of such provision or the application thereof to any person or circumstance is for any reason held invalid or unenforceable, the remainder of this Sublease (or the remainder of such provision) and the application thereof to other persons or circumstances shall not be affected thereby.

42.3 The captions are inserted only as a matter of convenience and for reference, and in no way define, limit or describe the scope of this Sublease or the intent of any provisions thereof.

42.4 This Sublease and the Exhibits attached hereto and incorporated herein contain the entire and only agreement between the parties and any and all statements and representations, written and oral, including previous correspondence and agreements between the parties hereto, are merged herein. Subtenant and Sublandlord acknowledge that all representations and statements upon which they relied in executing this Sublease are contained herein and that they in no way relied upon any other statements or representations, written or oral. This Sublease may not be modified orally or in any manner other than by written agreement signed by the parties hereto.

42.5 Each of Subtenant and Sublandlord represents to the other that each of the signatories on its behalf is duly authorized to execute this Sublease on behalf of such party. Upon Sublandlord's request, Subtenant shall provide Sublandlord with evidence that any requisite resolution, corporate authority and any other necessary consents have been duly adopted and obtained.

42.6 Without limiting any other obligation of Subtenant which may survive the expiration or prior termination of the Term, all obligations on the part of Subtenant to indemnify, defend, or hold Sublandlord harmless, as set forth in this Sublease, shall survive the expiration or prior termination of the Term.

42.7 Notwithstanding anything in this Sublease to the contrary, (i) Subtenant specifically agrees that in no event shall any officer, director, trustee, employee or representative of Prime Landlord or Sublandlord or any of the Sublandlord Additional Indemnitees ever be personally liable for any obligation under this Sublease, nor shall Sublandlord or any of the Sublandlord Additional Indemnitees be liable for consequential or incidental damages or for lost profits whatsoever in connection with this Sublease, and (ii) Sublandlord specifically agrees that in no event shall any officer, director, trustee, employee or representative of Subtenant ever be personally liable for any obligation under this Sublease, nor shall Subtenant ever be liable for consequential, punitive, multiple or incidental damages or for lost profits whatsoever in connection with this Sublease.

42.8 Subtenant shall not grant any security interest whatsoever in any Trade Fixtures without the prior written consent of Sublandlord, except that Subtenant may grant a security interest over its unattached personal property to the extent the granting of such a security interest is not prohibited under the Prime Lease.

42.9 No rights to any view or to light or air over any property, whether belonging to Prime Landlord, Sublandlord or any other person, are granted to subtenant by this Sublease. If at any time any windows of the Premises are temporarily darkened or the light therefrom is obstructed by reason of any repairs, improvements, maintenance or cleaning in or about the Property, the same shall be without liability to Sublandlord and without any reduction or diminution of Subtenant's obligations under this Sublease.

[Remainder of page is intentionally blank]

IN WITNESS WHEREOF, the parties have caused this Sublease to be executed under seal by their respective officers or other persons hereunto duly authorized as of the day and year first above written.

SUBLANDLORD:

PTC INC.,
a Delaware corporation

By: /s/ *Aaron von Staats*
Name: *Aaron von Staats*
Title: *Executive Vice President, General Counsel*

SUBTENANT:

CHIASMA, INC.,
a Delaware corporation

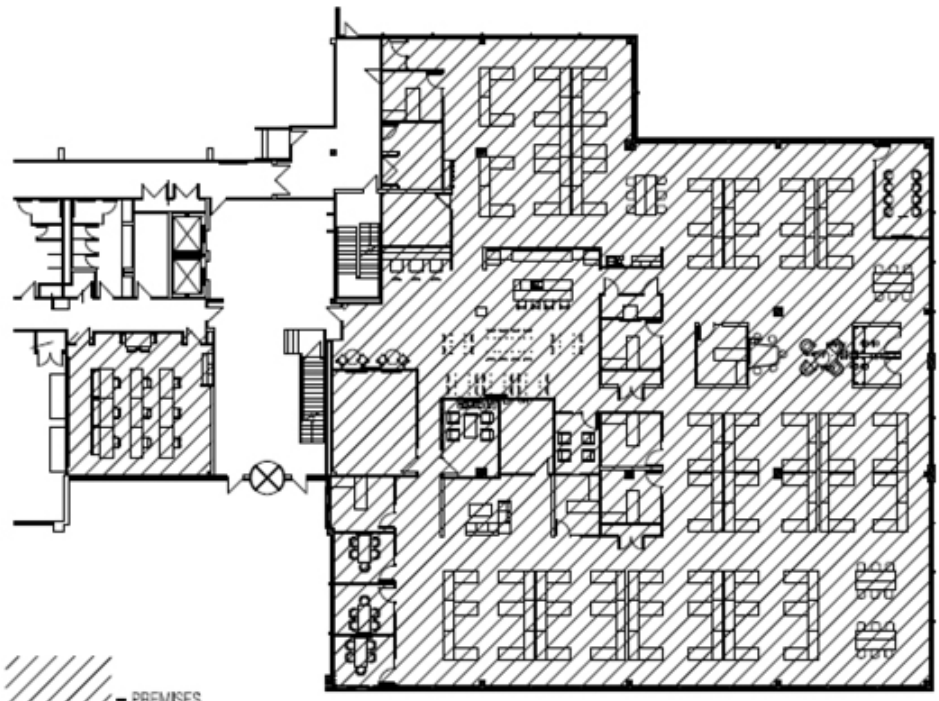
By: /s/ *Raj Kannan*
Name: Raj Kannan
Title: *Chief Executive Officer*

[Signature Page]

EXHIBIT A

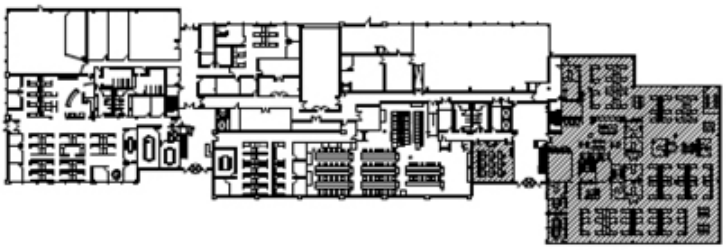
Description of Premises

[SEE ATTACHED]



– PREMISES

PREMISES PLAN



KEY PLAN

300 Summer Street | 1st Floor | Boston, MA 02210
Tel: 617 737 3768 | Fax: 617 426 3799

CLIENT
CRESA

ADDRESS
140 KENDRICK STREET
BUILDING C, FLOOR 2
NEEDHAM, MA

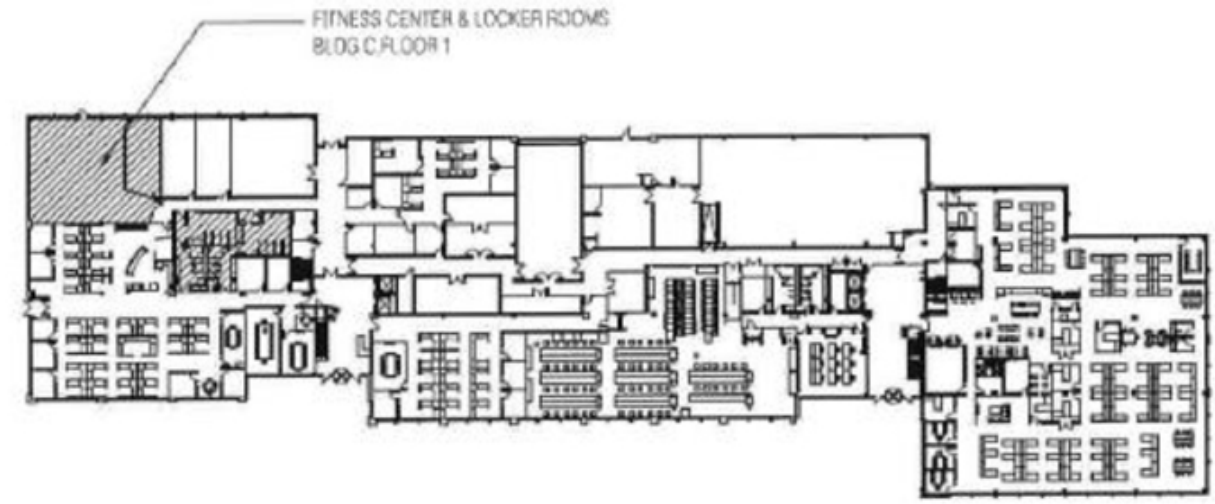
DRAWING TITLE
LEASE EXHIBIT

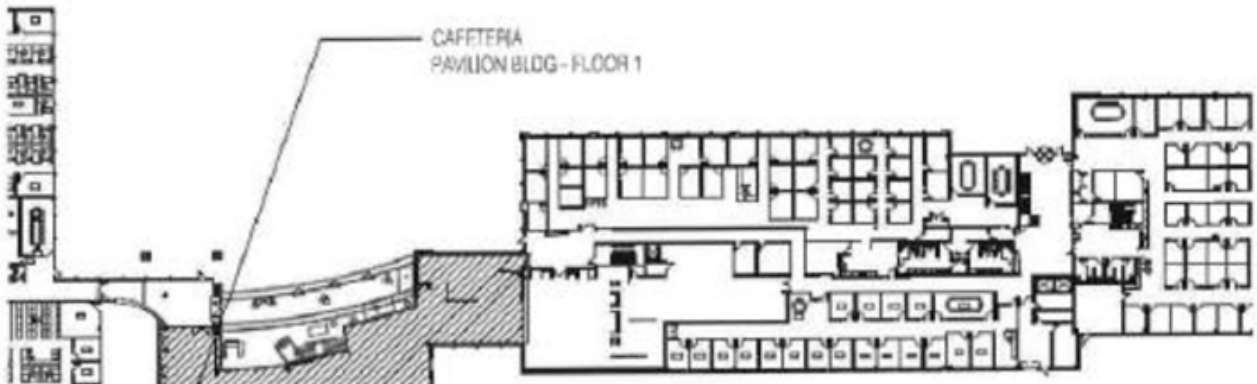
PROJECT NUMBER	DATE
19,006	07.15.19
SCALE	DRAWN BY / CHECKED BY
NTS	- / -

SHEET NUMBER
EXH-01

EXHIBIT B

Plans for Fitness Center, Common Conference Facility, and Cafeteria





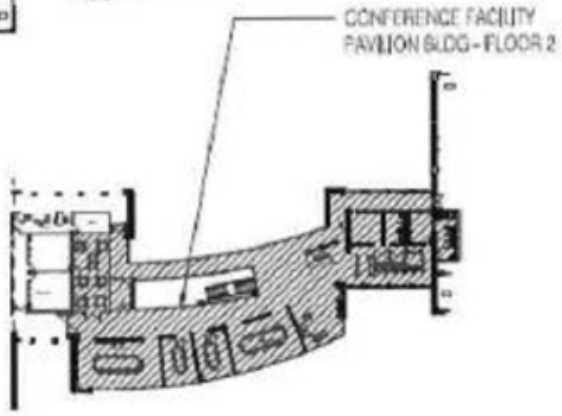


EXHIBIT C

INTENTIONALLY OMITTED

EXHIBIT D

Description of Sublandlord's Work

1. **Touch-up painting of first floor bathroom doors and first floor bathroom hallway.**
2. **Patch holes in Premises walls and touch-up paint where needed, as indicated on Attachment 1 hereto.**
3. **Repair and replace carpet, as needed, as indicated on Attachment 1 hereto.**
4. **The Premises' window blinds to be delivered in good working order.**
5. **Sublandlord to remove all tables and chairs that are in the 1,027 SF section of the Premises (except the TV's and refrigerator, which shall remain). All furniture in the remaining 16,587 SF portion of the Premises to remain.**
6. **Removal of all toxic or hazardous materials or substances, excluding (a) any building materials, or (b) other toxic or hazardous substances currently existing in compliance with all applicable laws and codes, and not in any reportable concentration thereunder.**

ATTACHMENT 1

See Attached Plan Depicting Carpet Replacement Areas

Chasma paint

- paint
- carpet

BUILDING C- FIRST FLOOR KEY PLAN

fusion
design consultants

CRESA

PTC CAMPUS
BUILDING C
NEEDHAM, MASSACHUSETTS

FIRST FLOOR PLAN
EXISTING SUITE
16,587 RSF

BLDG C- 1C

EXHIBIT E

FORM OF AGREEMENT WITH PRIME LANDLORD

SEE ATTACHED

AGREEMENT

AGREEMENT dated as of the 11th day of October, 2019, by and between BP 140 KENDRICK STREET PROPERTY LCC (as successor to BP 140 Kendrick Street LLC, as successor to Boston Properties Limited Partnership, "Landlord"), PTC, Inc. ("Tenant"), and Chiasma, Inc. ("Subtenant").

RECITALS

By Indenture of Lease dated December 14, 1999, as amended and affected to date (the "Lease"), Landlord did lease to Tenant and Tenant did lease from Landlord certain premises located at 140 Kendrick Street, Needham, Massachusetts consisting of approximately 320,655 rentable square feet (89,758 rentable square feet in Building A, 122,797 rentable square feet in Building B, and 108,100 rentable square feet in Building C (Building A, Building B and Building C each as defined in the Lease)), which premises are more particularly described in the Lease (the "Premises").

Tenant desires to sublease to Subtenant 17,614 square feet of rentable floor area of the Premises (the "Subleased Premises") upon the terms and conditions contained in a sublease between Tenant and Subtenant dated October 11, 2019 (the "Sublease").

Tenant and Subtenant desire to have Landlord consent to the Sublease upon the terms set forth hereinbelow.

NOW, THEREFORE, in consideration of One Dollar ($1.00) and other good and valuable consideration, paid by each of the parties hereto to the other, the receipt and sufficiency of which is hereby acknowledged, and in further consideration of the provisions herein, Landlord, Tenant and Subtenant hereby agree as follows:

1. Intentionally Omitted.

2. Compliance by Subtenant; Enforcement.

(a) Subtenant (i) shall comply with and perform the terms of the Sublease to be complied with or performed on the part of the subtenant under the Sublease, (ii) shall not violate any of the applicable terms of the Lease and (iii) assumes, during the term of the Sublease, the performance of the terms of the Lease to be performed on the part of the tenant under the Lease to the extent that such terms are applicable to the Subleased Premises (including, without limitation, the indemnity, insurance and waiver of subrogation provisions of the Lease, which shall be applicable to the Subleased Premises as if such Subleased Premises were the Premises for the purposes of said provisions) and provided that Subtenant's liability for the payment of rent and other amounts shall be limited to amounts set forth in the Sublease. Subject to the limitations of subsection (iii) of the immediately preceding sentence with respect to Subtenant, Tenant and Subtenant shall be jointly and severally liable to Landlord for compliance with and performance of all of the terms, covenants, agreements, provisions, obligations and conditions to be performed or observed by the tenant under the Lease.

(b) Tenant shall enforce the terms of the Sublease against Subtenant. Without limiting the foregoing, Landlord shall have the right, but not the obligation, to proceed directly against Subtenant (in Landlord's name or in Tenant's name, as determined by Landlord in Landlord's sole discretion) in order to (i) enforce compliance with and performance of all of the terms, covenants, agreements, provisions, obligations and conditions to be performed or observed by Subtenant under the Sublease, the Lease (to the extent applicable to the Subleased Premises) or under this Agreement or (ii) terminate the Sublease if any action or omission of Subtenant (continuing beyond the expiration of applicable notice and cure periods) constitutes a default under the Lease. Tenant shall cooperate with Landlord in connection with any such action or proceeding, and Tenant and Subtenant hereby jointly and severally indemnify and hold Landlord harmless from and against all costs and expenses including, without limitation, reasonable attorneys' fees, incurred by Landlord in connection with any such action or proceeding.

3. Subordination; Attornment. The Sublease shall be subject and subordinate at all times to the Lease and all amendments thereof, this Agreement and all other instruments to which the Lease is or may hereafter be subject and subordinate. The provisions of this Agreement and the execution and delivery of the Sublease shall not constitute a recognition of the Sublease or the Subtenant thereunder; it being agreed that in the event of termination (whether voluntary or involuntary), rejection (pursuant to 11 U.S.C. §365) or expiration of the Lease, unless otherwise elected by Landlord as hereinafter set forth, the Sublease shall be deemed terminated and Subtenant shall have no further rights (including, without limitation, rights, if any, under 11 U.S.C. §365(h)) with respect to the Subleased Premises. If (a) the Lease is (or both the Lease and the Sublease are) terminated for any reason whatsoever or rejected (pursuant to 11 U.S.C. §365) by Tenant prior to its (or their) scheduled expiration date(s) or (b) if Landlord shall succeed to Tenant's estate in the Subleased Premises, and provided that Landlord and Subtenant have not entered into a direct lease pursuant to which Subtenant would continue to occupy the Premises after the expiration of the Sublease, then in any such event, Subtenant shall have no right to use or occupy any portion of the Premises (or other space in the Building occupied or controlled by Tenant) which is not part of the Subleased Premises, and at Landlord's election, Subtenant shall either attorn to and recognize Landlord as Subtenant's landlord under the Sublease or enter into a new direct lease with Landlord upon the then executory terms of the Sublease (and if Landlord so elects as aforesaid Subtenant hereby waives its right to treat the Sublease as terminated under 11 U.S.C. §365(h)), provided that, in any such event, Landlord shall not be (i) liable for any previous act or omission of Tenant; (ii) subject to any offset or defense which theretofore accrued to Subtenant (including, without limitation, any rights under 11 U.S.C. §365(h)); (iii) bound by any rent or other sums paid by Subtenant more than one month in advance; (iv) liable for any security deposit not actually received by Landlord; (v) liable for any work or payments on account of improvements to the Subleased Premises; or (vi) bound by any amendment of the Sublease not consented to in writing by Landlord (but only to the extent such consent is required by the terms and provisions of the Lease). Subtenant shall promptly execute and deliver any instrument Landlord may reasonably request to evidence such

attornment or direct lease. In the event of such attornment or direct lease, Tenant shall transfer to Landlord any security deposit under the Sublease (such obligation to include, without limitation, the transfer and modification of any letter of credit posted as security). Subtenant shall reimburse Landlord for any costs and expenses that may be incurred by Landlord in connection with such attornment or direct lease including, without limitation, reasonable attorneys' fees. Notwithstanding the foregoing, if Landlord does not elect to have Subtenant attorn to Landlord or enter into a new direct lease as described above, the Sublease and all rights of Subtenant to the Subleased Premises shall terminate upon the date of expiration or termination of the Lease or Tenant's right to possession thereunder. The terms of this Section 3 supersede any contrary provisions in the Sublease.

4. Representations and Warranties. Tenant and Subtenant represent, warrant and covenant to Landlord that (a) no rent, fees or other consideration has been or will be paid to Tenant by Subtenant for the right to use or occupy the Subleased Premises or for the use, sale or rental of Tenant's fixtures, leasehold improvements, equipment, furniture or other personal property other than as set forth in the Sublease, and (b) attached hereto as Exhibit A is a true, correct and complete copy of the Sublease that embodies the complete and entire agreement between Tenant and Subtenant.

5. Amendment or Termination of Sublease. Tenant and Subtenant agree that they shall not change, modify, amend, cancel or terminate the Sublease or enter into any additional agreements relating to or affecting the use or occupancy of the Subleased Premises or the use, sale or rental of Tenant's fixtures, leasehold improvements, equipment, furniture or other personal property, without first obtaining Landlord's prior written consent thereto (but only to the extent such consent is required by the terms and provisions of the Lease).

6. No Waiver or Release. Neither this Agreement, the Sublease, nor any acceptance of rent or other consideration from Subtenant by Landlord (whether before or after the occurrence of any default by Tenant under the Lease) shall operate to waive, modify, impair, release or in any manner affect any of the covenants, agreements, terms, provisions, obligations or conditions contained in the Lease, or to waive any breach thereof, or any rights of Landlord against any person, firm, association or corporation liable or responsible for the performance thereof, or to increase the obligations or diminish the rights of Landlord under the Lease, or to increase the rights or diminish the obligations of Tenant thereunder, or to, in any way, be construed as giving Subtenant any greater rights than those to which the original tenant named in the Lease would be entitled or any longer time period to perform than is provided to the original tenant under the Lease. Tenant hereby agrees that the obligations of Tenant as tenant under the Lease and this Agreement shall not be discharged or otherwise affected by reason of the giving or withholding of any consent or approval for which provision is made in the Lease. All terms, covenants, agreements, provisions and conditions of the Lease are hereby ratified and declared by Tenant to be in full force and effect, and Tenant hereby unconditionally reaffirms its primary, direct and ongoing liability to Landlord for the performance of all obligations to be performed by the Tenant as tenant under the Lease, including, without limitation, the obligations to pay all rent and all other charges in the full amount, in the manner and at the times provided for in the Lease.

7. No Further Assignment or Subletting. Tenant and Subtenant hereby agree that the terms, conditions, restrictions and prohibitions set forth in the Lease regarding subletting and assignment shall, notwithstanding this Agreement, (a) apply to the Sublease and the Subleased Premises, (b) continue to be binding upon Tenant and Subtenant with respect to all future assignments and transfers of the Lease or the Sublease, and all future sublettings of the Premises or the Subleased Premises, and (c) apply to Subtenant with the same effect as if Subtenant had been the original tenant named in the Lease. The giving of this Agreement shall not be construed either as a consent by Landlord to, or as permitting, any other or further assignment or transfer of the Lease or the Sublease, whether in whole or in part, or any subletting or licensing of the Premises or the Subleased Premises or any part thereof, or as a waiver of the restrictions and prohibitions set forth in the Lease regarding subletting, assignment or other transfer of any interest in the Lease or the Premises. Subtenant shall not assign the Sublease or sublet or license all or any part of the Subleased Premises, voluntarily or by operation of law, or permit the use or occupancy thereof by others, without the prior written consent of Landlord in accordance with the terms of the Lease.

8. No Ratification of Sublease. Tenant and Subtenant acknowledge that Landlord is not a party to the Sublease and is not bound by the provisions thereof, and recognize that, accordingly, Landlord has not, and will not, review or pass upon any of the provisions of the Sublease. Nothing contained herein shall be construed as an approval of, or ratification by Landlord of, any of the particular provisions of the Sublease or a modification or waiver of any of the terms, covenants and conditions of the Lease or as a representation or warranty by Landlord.

9. Default; Remedies. Any breach or violation of any provisions of the Lease by Subtenant (continuing beyond the expiration of applicable notice and cure periods in the Lease) shall be deemed to be and shall constitute a default by Tenant under the Lease. In the event (a) of any default by Tenant or Subtenant in the full performance and observance of any of their respective obligations under this Agreement, which default shall not be cured within thirty (30) days after notice to the party in default (with a copy of such notice delivered to the other party at the same time), or (b) any representation or warranty of Tenant or Subtenant made herein shall prove to be false or misleading in any material respect, then (i) such event may, at Landlord's option, be deemed an Event of Default by Tenant under the Lease and (ii) Landlord may give written notice of such default to the party in violation (with a copy of such notice delivered to the other party at the same time), and if such violation shall not be discontinued or corrected within thirty (30) days after the giving of such notice, Landlord may, in addition to Landlord's other remedies, revoke this Agreement and, as between Subtenant and Landlord, Subtenant shall have no further rights with respect to the Subleased Premises. Subject to Landlord's right to require Subtenant to attorn or enter into a direct lease under Paragraph 3 hereof, if Subtenant shall fail to vacate and surrender the Subleased Premises upon the expiration, rejection or earlier termination (whether voluntary or involuntary) of the Lease, Landlord shall be entitled to all of the rights and remedies which are available to a landlord against a tenant holding over after the expiration of a term. Subtenant expressly waives for itself and for any person claiming through or under Subtenant, any rights which Subtenant or any such person may have under 11 U.S.C. §365(h), including, without limitation, any right to remain in possession of the Premises under §365(h)(1)(A)(ii) and any right of offset under §365(h)(1)(B) against any amounts due and owing to Landlord.

10. Notices.

(a) Any notices given under this Agreement shall be effective only if in writing and given in the manner notices are required to be given under the Lease, addressed to the Tenant at the address set forth in the Lease with respect to the Tenant, addressed to the Landlord at the following address, with a copy to Landlord, Attention: Regional General Counsel:

c/o Boston Properties Limited Partnership
Prudential Center
800 Boylston Street, Suite 1900
Boston, Massachusetts 02199-8103

with respect to the Landlord, and at the Subleased Premises with respect to Subtenant, or at such other address for such purpose designated by notice in accordance with the provisions hereof.

(b) Tenant and Subtenant shall promptly deliver to Landlord a copy of any default or termination notice sent or received by either party with respect to the Sublease.

(c) Except as otherwise provided herein, all such notices shall be effective when received; provided, that (i) if receipt is refused, notice shall be effective upon the first occasion that such receipt is refused, or (ii) if the notice is unable to be delivered due to a change of address of which no notice was given, notice shall be effective upon the date such delivery was attempted.

11. Brokerage.

(a) Tenant represents, warrants and covenants to Landlord that Tenant has dealt with no broker in connection with the Sublease other than Cresa Partners and Colliers International (together, the “Broker”). In the event any claim is made against Landlord relative to dealings by Tenant with any broker in connection with the Sublease, Tenant shall defend the claim against Landlord with counsel of Tenant’s selection first approved by Landlord and save harmless and indemnify Landlord on account of loss, cost or damage which may arise by reason of such claim. Tenant agrees that it shall be solely responsible for the payment of brokerage commissions to the Broker.

(b) Subtenant represents, warrants and covenants to Landlord that Subtenant has dealt with no broker in connection with the Sublease other than the Broker. In the event any claim is made against Landlord relative to dealings by Subtenant with any other broker in connection with the Sublease, Subtenant shall defend the claim against Landlord with counsel of Subtenant’s selection first approved by Landlord and save harmless and indemnify Landlord on account of loss, cost or damage which may arise by reason of such claim.

12. Assignment of Sublease Rents.

(a) Subject to the license granted in this paragraph, Tenant hereby unconditionally and irrevocably grants, transfers, assigns and sets over to Landlord all of Tenant's interest in the rents, issues and profits of the Sublease (collectively, the "**Sublease Rents**"), together with full power and authority, in the name of Tenant, or otherwise, to demand, receive, enforce, collect or receipt for any or all of the foregoing, to endorse or execute any checks or other instruments or orders, to file any claims and to take any other action which Landlord may deem necessary or advisable in connection therewith; provided, that no exercise of such rights by Landlord shall release Tenant from any of its obligations under the Lease or the Sublease. Tenant intends that the assignment described in this Paragraph 12 shall be a present, actual, absolute and unconditional assignment; provided, however, that except to the extent specified by Landlord in a notice or demand given to Tenant and Subtenant exercising Landlord's right to collect the Sublease Rents directly from Subtenant, Tenant shall have a license to collect the Sublease Rents, but neither prior to accrual nor more than one month in advance (except for security deposits and escalations provided for in the Sublease). Tenant hereby irrevocably authorizes Subtenant to rely upon and comply with any such notice or demand by Landlord for the payment to Landlord of any Sublease Rents due or to become due, and Subtenant will have no obligation to inquire as to the propriety of any such notice or demand, or to see to the application of any amounts so paid. Landlord shall be accountable only for the Sublease Rents actually collected hereunder and not for the rental value of the Subleased Premises.

(b) Neither this Agreement nor the assignment described in this Paragraph 12 nor any action or inaction on the part of Landlord shall constitute an assumption on the part of Landlord of any duty or obligation under the Sublease, nor shall Landlord have any duty or obligation to make any payment to be made by Tenant under the Sublease or the Lease, or to present or file any claim, or to take any other action to collect or enforce the payment of any amounts which have been assigned to Landlord or to which it may be entitled hereunder at any time or times. The collection and application of the Sublease Rents or other charges, or any other action taken by Landlord in connection therewith, shall not (i) cure or waive any default under the Lease, (ii) waive or modify any notice thereof theretofore given by Landlord, (iii) create any direct tenancy between Landlord and Subtenant, or (iv) otherwise limit in any way the rights of Landlord hereunder or under the Lease.

(c) Tenant, at its expense, will execute and deliver all such instruments and take all such action as Landlord, from time to time, may reasonably request in order to obtain the full benefits of the assignment provided for in this Paragraph 12.

(d) All Sublease Rents collected by Landlord (less the cost of collection reasonably incurred, including, without limitation, reasonable attorneys' fees) under this Paragraph 12 will be applied against Tenant's obligations under the Lease.

13. Miscellaneous.

(a) Remedies Cumulative. Each right and remedy of Landlord provided for in this Agreement or in the Lease shall be cumulative and shall be in addition to every other right and remedy provided for herein and therein or now or hereafter existing at law or in equity or by statute or otherwise, and the exercise by Landlord of any one or more of the rights or remedies so provided for or existing shall not preclude the simultaneous or subsequent exercise by Landlord of any or all other rights or remedies so provided for or so existing.

(b) Landlord's Liability. Landlord's liability under this Agreement shall be limited to the same extent Landlord's liability is limited under the Lease.

(c) Successors and Assigns. The terms and provisions of this Agreement shall bind and inure to the benefit of the parties hereto and their respective successors and assigns, except that no violation of the provisions of this Agreement shall operate to vest any rights in any successor or assignee of Tenant or Subtenant.

(d) Captions. The captions contained in this Agreement are for convenience only and shall in no way define, limit or extend the scope or intent of this Agreement, nor shall such captions affect the construction hereof.

(e) Counterparts. This Agreement may be executed in one or more counterparts, and by different parties hereto on separate counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument.

(f) No Privity of Estate. It is expressly understood and agreed that, except with respect to Landlord's election to have Subtenant attorn to or enter into a direct lease with Landlord pursuant to Section 3 above, neither this Agreement nor any direct dealings between Landlord and Subtenant during the term of the Sublease (including, without limitation, the direct billing by Landlord to Subtenant of work order, or other charges relating to Subtenant's occupancy) shall create or constitute, or shall be deemed to create or constitute, privity of estate, any landlord-tenant relationship, or occupancy or tenancy agreement between Landlord and Subtenant.

(g) Binding Effect. This Agreement is offered to Tenant and Subtenant for signature and it is understood that this Agreement shall be of no force and effect and shall not be binding upon Landlord unless and until Landlord shall have executed and delivered a copy of this Agreement to both Tenant and Subtenant.

(h) Review of Sublease. To the extent permitted by the terms of the Lease, Tenant shall reimburse Landlord for any fees which may be charged by Landlord and for any costs incurred by Landlord in connection with the Sublease, including, without limitation, the costs of making investigations as to the acceptability of the proposed subtenant and legal costs incurred in connection with the granting of this Agreement. Such amounts, if any, shall be due and payable concurrently with the execution and delivery of this Agreement by Tenant.

(i) Compliance with Laws. Without limiting the obligations under the Lease, Tenant shall be responsible in connection with the Sublease, at its sole cost and expense, for performing all work necessary to comply with all applicable laws, ordinances, rules, regulations, statutes, by-laws, court decisions and orders and requirements of all public authorities and insurers of the Building and other requirements of the Lease with respect to insurance obligations of Tenant.

(j) Conflict. If there shall be any conflict or inconsistency between the terms, covenants and conditions of this Agreement or the Lease and the terms, covenants and conditions of the Sublease, then the terms, covenants and conditions of this Agreement and the Lease shall prevail. In the event that there shall be any conflict or inconsistency between this Agreement and the Lease, such conflict or inconsistency shall be determined for the benefit of Landlord.

(k) Agreement Limited. This Agreement shall be deemed limited solely to the Sublease, and Landlord reserves the right to consent or withhold consent and all other rights as set forth in and in accordance with the Lease with respect to any other matters.

(l) Alterations. Tenant and Subtenant acknowledge that any additions, alterations, demolitions or improvements to be performed in connection with the Sublease shall be first approved by Landlord in accordance with the Lease and subject to all of the terms and conditions of the Lease. Without limitation, Landlord acknowledges that Subtenant plans to enhance the main entry to the Premises with additional glass walls in place of drywall and to construct a new reception area, subject to Landlord's timely review and approval. Within thirty (30) days after receipt of an invoice from Landlord, Tenant shall pay to Landlord as a fee for Landlord's review of any work or plans in connection with the Sublease, as Additional Rent, an amount equal to the sum of: (i) $150.00 per hour for senior staff and $100.00 per hour for junior staff, plus (ii) third party expenses incurred by Landlord to review such plans and work. Upon the expiration or earlier termination of the Sublease, at Landlord's option, Tenant and Subtenant shall at their expense remove all such additions, alterations and improvements and restore the Subleased Premises to its original condition. All contractors, vendors and service providers requiring access to the Subleased Premises or the Building shall be subject to Landlord's prior and continuing review and approval with respect to insurance, security and operational matters, if and as provided in the Lease.

(m) Terms. Terms defined in the Lease and used, but not defined, herein shall have the meanings ascribed to them in the Lease.

(n) Entire Agreement. This Agreement contains the entire agreement of the parties with respect to the matters contained herein and may not be modified, amended or otherwise changed except by written instrument signed by the parties sought to be bound.

(o) Partial Invalidity. If any term, provision or condition contained in this Agreement shall, to any extent, be invalid or unenforceable, the remainder of this Agreement, or the application of such term, provision or condition to persons or circumstances other than those with respect to which it is invalid or unenforceable, shall not be affected thereby, and each and every other term, provision and condition of this Agreement shall be valid and enforceable to the fullest extent possible permitted by law.

(p) Attorneys' Fees. If any party commences litigation for the specific performance of this Agreement, for damages for the breach hereof or otherwise for enforcement of any remedy hereunder, the parties hereto agree to and hereby do waive any right to a trial by jury and, in the event of any such commencement of litigation, the prevailing party shall be entitled to recover from the other party such costs and reasonable attorneys' fees as may have been incurred.

(q) Authority. Tenant and Subtenant each respectively represent, warrant and covenant to Landlord that (i) each is a duly formed and existing entity qualified to do business in the jurisdiction in which the Building is located and (ii) each has full right, power and authority to enter into this Agreement and that the persons or person executing this Agreement on behalf of Tenant and Subtenant, as the case may be, are duly authorized to do so.

(r) Governing Law. This Agreement shall for all purposes be construed in accordance with, and governed by, the laws of the jurisdiction in which the Building is located.

(s) OFAC. As an inducement to Landlord to enter into this Agreement, Subtenant hereby represents, warrants and covenants to Landlord that: (i) Subtenant is not, nor is it controlled nor is more than 10% of it owned, directly or indirectly by, any person, group, entity or nation named on any list issued by the Office of Foreign Assets Control of the United States Department of the Treasury ("OFAC") pursuant to Executive Order 13224 or any similar list or any law, order, rule or regulation or any Executive Order of the President of the United States as a terrorist, "Specially Designated National and Blocked Person" or other banned or blocked person (any such person, group, entity or nation being hereinafter referred to as a "Prohibited Person"); (ii) Subtenant is not (nor is it controlled nor is more than 10% of it owned, directly or indirectly, by any person, group, entity or nation which is) acting directly or indirectly for or on behalf of any Prohibited Person; and (iii) from and after the effective date of the above-referenced Executive Order, Subtenant (and any person, group, or entity which Subtenant controls, directly or indirectly) has not conducted nor will conduct business nor has engaged nor will engage in any transaction or dealing with any Prohibited Person that may cause or causes Landlord to be in violation of the U.S. Patriot Act or any OFAC rule or regulation, including, without limitation, any assignment of this Consent or any further subletting, if, and to the extent, permitted hereunder, of all or any portion of the Subleased Premises or the making or receiving of any contribution of funds, goods or services to or for the benefit of a Prohibited Person in violation of the U.S. Patriot Act or any OFAC rule or regulation. In connection with the foregoing, it is expressly understood and agreed that (x) any breach by Subtenant of the foregoing shall be deemed a default by Subtenant under Paragraph 9 above, and shall be covered by the indemnity provisions of the Lease, and (y) the representations, warranties and covenants contained in this subsection shall be continuing in nature and shall survive the expiration or earlier termination of the Sublease.

(t) Profits. Landlord and Tenant acknowledge and agree that any "Assignment/Sublease Profits" (as such term is defined in the Lease) associated with the Sublease shall be paid to Landlord as determined by Landlord in accordance with the terms of the Lease.

(u) Subrogation. Any insurance policy carried by Landlord with respect to its property shall include a clause or endorsement denying to the insurer rights of subrogation against the Subtenant to the extent rights have been waived by Landlord prior to the occurrence of injury or loss. Landlord hereby waives any rights of recovery against Subtenant or its employees, agents, officers and directors for injury or loss due to hazards covered by such insurance (or, if greater, the insurance required under the Lease to be carried by Landlord) to the extent of the indemnification received thereunder.

[Signatures on next page.]

EXECUTED under seal as of the date and year first above written.

WITNESS:

/s/ Casey Torto

LANDLORD:

BP 140 KENDRICK STREET PROPERTY LLC, a Delaware limited liability company

BY: BP 140 KENDRICK STREET LLC, a Delaware limited liability company, its managing member

BY: BOSTON PROPERTIES LIMITED PARTNERSHIP, a Delaware limited partnership, its managing member

BY: BOSTON PROPERTIES, INC., a Delaware corporation, its general partner

By: */s/ Patrick Mulvihill*
Name: Patrick Mulvihill
Title: Vice President, Leasing

WITNESS:

/s/ Christopher MacKrell

TENANT:

PTC INC., a Delaware corporation

By: */s/ Aaron Von Staats*
Name: Aaron Von Staats
Title: Executive Vice President, General Counsel

WITNESS:

/s/ Kelley Wharff

SUBTENANT:

CHIASMA, INC.

By: */s/ Raj Kannan*
Name: Raj Kannan
Title: *Chief Executive Officer*

Exhibit 21.1

SUBSIDIARIES OF THE REGISTRANT

The following is a list of our subsidiaries:

Name	State or Other Jurisdiction of Incorporation	Name Under Which Does Business
Chiasma (Israel) Ltd.	Israel	Same
Chiasma Securities Corp	United States	Same

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the incorporation by reference in Registration Statement Nos. 333-233654 and 333-223850 on Form S-3 and Nos. 330-230162, 333-210259 and 333-205773 on Form S-8 of our report dated March 16, 2020, relating to the consolidated financial statements of Chiasma, Inc. appearing in this Annual Report on Form 10-K for the year ended December 31, 2019.

/s/ Deloitte & Touche LLP

Boston, MA
March 16, 2020

Exhibit 31.1

CERTIFICATION PURSUANT TO
SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Raj Kannan, certify that:

(1) I have reviewed this annual report on Form 10-K for the year ended December 31, 2019 of Chiasma, Inc.;

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

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

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

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

(b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

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

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

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

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

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

Dated: March 16, 2020

/s/ Raj Kannan
Raj Kannan
Chief Executive Officer and Director
(*Principal Executive Officer*)

Exhibit 31.2

CERTIFICATION PURSUANT TO
SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Mark J. Fitzpatrick, certify that:

(1) I have reviewed this annual report on Form 10-K for the year ended December 31, 2019 of Chiasma, Inc.;

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

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

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

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

(b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

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

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

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

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

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

Dated: March 16, 2020

/s/ Mark J. Fitzpatrick
Mark J. Fitzpatrick
President
(*Principal Financial Officer*)

Exhibit 32.1

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

In connection with the annual report on Form 10-K of Chiasma, Inc. (the "Company") for the fiscal year ended December 31, 2019, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), each of the undersigned officers herby certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that, to my knowledge:

(1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company at the dates and for the periods indicated in the Report.

Date: March 16, 2020

/s/ Raj Kannan
Raj Kannan
Chief Executive Officer and Director
(Principal Executive Officer)

Date: March 16, 2020

/s/ Mark J. Fitzpatrick
Mark J. Fitzpatrick
President
(Principal Financial Officer)