

The information in this preliminary prospectus supplement is not complete and may be changed. This preliminary prospectus supplement and the accompanying prospectus are not an offer to sell these securities and they are not soliciting an offer to buy these securities in any jurisdiction where the offer or sale thereof is not permitted.

Subject to Completion July 25, 2019

PRELIMINARY PROSPECTUS SUPPLEMENT
(To Prospectus dated May 3, 2018)



Shares

Common Stock

We are offering _____ shares of our common stock in this offering.

We are an “emerging growth company” under applicable Securities and Exchange Commission rules and are subject to reduced public company reporting requirements.

Our common stock is listed on The Nasdaq Global Select Market under the symbol “CHMA.” On July 24, 2019, the last reported sale price of our common stock, as reported on The Nasdaq Global Select Market, was \$6.50 per share.

Investing in our common stock involves a high degree of risk. Please read the section entitled “**Risk Factors**” beginning on page S-13 of this prospectus supplement and in the related sections noted in the accompanying prospectus, and in the documents incorporated by reference herein and therein.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities, or determined if this prospectus supplement or the accompanying prospectus are truthful or complete. Any representation to the contrary is a criminal offense.

	Per Share	Total
Public offering price		
Underwriting discounts and commissions ⁽¹⁾		
Proceeds to us (before expenses)		

⁽¹⁾ See the section entitled “Underwriting” beginning on page S-23 for a description of the compensation payable to the underwriters.

We have granted the underwriters an option for 30 days after the date of this prospectus supplement to purchase up to an additional _____ shares of our common stock from us, at the price set forth above. If the underwriters exercise the option in full, the total proceeds to us, before expenses will be \$ _____.

We have suspended, and during the duration of this offering we are no longer offering, any securities pursuant to the prospectus supplement filed with the Securities and Exchange Commission on November 8, 2018, relating to the offer and sale of shares of our common stock pursuant to the Sales Agreement with Cowen and Company, LLC, dated November 8, 2018.

Delivery of the shares of common stock is expected to be made on or about _____, 2019.

Book Running Managers

Piper Jaffray

Cantor

, 2019

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Neither we nor the underwriters have authorized anyone to provide any information or make any representations other than those contained or incorporated by reference in this prospectus supplement, the accompanying prospectus or any free writing prospectus that we have authorized for use in connection with this offering. We take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. This prospectus supplement and the accompanying prospectus are an offer to sell only the shares offered hereby, but only under circumstances and in jurisdictions where it is lawful to do so. The information contained in this prospectus supplement, the accompanying prospectus and any free writing prospectus that we have authorized for use in connection with this offering is current only as of their respective dates. Our business, financial condition, results of operations and prospects may have changed since those dates. You should read this prospectus supplement, the accompanying prospectus, the documents incorporated by reference in this prospectus supplement and the accompanying prospectus and any free writing prospectus that we have authorized for use in connection with this offering when making your investment decision. You should also read and consider the information in the documents to which we have referred you in the section of this prospectus supplement entitled "Incorporation of Certain Information by Reference."

For investors outside the United States: We have not, and the underwriters have not, done anything that would permit this offering or possession or distribution of this prospectus supplement or the accompanying prospectus in any jurisdiction where action for that purpose is required, other than in the United States. Persons outside the United States who come into possession of this prospectus supplement or the accompanying prospectus must inform themselves about, and observe any restrictions relating to, this offering and the distribution of this prospectus supplement and the accompanying prospectus outside the United States.

ABOUT THIS PROSPECTUS SUPPLEMENT

This document is in two parts. The first part is this prospectus supplement, which describes the specific terms of this offering of common stock. The second part is the accompanying prospectus, which provides more general information, some of which may not apply to this offering. The information included or incorporated by reference in this prospectus supplement also adds to, updates and changes information contained or incorporated by reference in the accompanying prospectus. If information included or incorporated by reference in this prospectus supplement is inconsistent with the accompanying prospectus or the information incorporated by reference therein, then this prospectus supplement or the information incorporated by reference in this prospectus supplement will apply and will supersede the information in the accompanying prospectus and the documents incorporated by reference therein.

This prospectus supplement is part of a registration statement that we filed with the Securities and Exchange Commission, or SEC, using a “shelf” registration process. Under the shelf registration process, we may from time to time offer and sell any combination of the securities described in the accompanying prospectus up to a total dollar amount of \$100.00 million, of which this offering is a part.

You should rely only on the information contained or incorporated by reference in this prospectus supplement, the accompanying prospectus and any free writing prospectus prepared by us or on our behalf. We have not, and the underwriter has not, authorized any other person to provide you with information different from that contained in this prospectus supplement and the accompanying prospectus or incorporated by reference in this prospectus supplement and the accompanying prospectus. If anyone provides you with different or inconsistent information, you should not rely on it. We are not, and the underwriter is not, making an offer to sell or soliciting an offer to buy these securities under any circumstance in any jurisdiction where the offer or solicitation is not permitted. You should assume that the information contained in this prospectus supplement, the accompanying prospectus and any free writing prospectus prepared by us or on our behalf is accurate only as of the date of the respective document in which the information appears, and that any information in documents that we have incorporated by reference is accurate only as of the date of the document incorporated by reference, regardless of the time of delivery of this prospectus supplement or any sale of a security. Our business, financial condition, results of operations and prospects may have changed since those dates.

It is important for you to read and consider all of the information contained in this prospectus supplement and the accompanying prospectus in making your investment decision. We include cross-references in this prospectus supplement and the accompanying prospectus to captions in these materials where you can find additional related discussions. The table of contents in this prospectus supplement provides the pages on which these captions are located. You should read both this prospectus supplement and the accompanying prospectus, together with the additional information described in the sections entitled “Where You Can Find More Information” and “Incorporation by Reference” of this prospectus supplement, before investing in our common stock.

We are offering to sell, and seeking offers to buy, shares of common stock only in jurisdictions where offers and sales are permitted. The distribution of this prospectus supplement and the accompanying prospectus and the offering of the common stock in certain jurisdictions may be restricted by law. Persons outside the United States who come into possession of this prospectus supplement and the accompanying prospectus must inform themselves about, and observe any restrictions relating to, the offering of the common stock and the distribution of this prospectus supplement and the accompanying prospectus outside the United States. This prospectus supplement and the accompanying prospectus do not constitute, and may not be used in connection with, an offer to sell, or a solicitation of an offer to buy, any securities offered by this prospectus supplement and the accompanying prospectus by any person in any jurisdiction in which it is unlawful for such person to make such an offer or solicitation.

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Unless the context otherwise indicates, references in this prospectus to “Chiasma”, “we”, “our”, “us” and “the Company” refer, collectively, Chiasma, Inc. and its subsidiaries.

All references in this prospectus supplement to our consolidated financial statements include, unless the context indicates otherwise, the related notes thereto.

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

The industry and market data and other statistical information contained in the documents we incorporate by reference are based on management’s own estimates, independent publications, government publications, reports by market research firms or other published independent sources and, in each case, are believed by management to be reasonable estimates. Although we believe these sources are reliable, we have not independently verified the information.

CAUTIONARY STATEMENT REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement and the accompanying prospectus, including the documents that we incorporate by reference herein and therein, contain 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. Any statements about our expectations, beliefs, plans, objectives, assumptions or future events or performance are not historical facts and may be forward-looking. These statements are often, but are not always, made through the use of words or phrases such as “anticipate,” “believe,” “contemplate,” “continue,” “could,” “estimate,” “expect,” “intend,” “may,” “plan,” “potential,” “predict,” “project,” “seek,” “should,” “target,” “will,” “would,” and similar expressions, or the negative of these terms, or similar expressions. Accordingly, these statements involve estimates, assumptions and uncertainties which could cause actual results to differ materially from those expressed in them. Any forward-looking statements are qualified in their entirety by reference to the factors discussed throughout this prospectus supplement and the accompanying prospectus, and in particular those factors referenced in the sections entitled “Risk Factors.”

This prospectus supplement and the accompanying prospectus contain forward-looking statements that are based on our management’s belief and assumptions and on information currently available to our management. These statements relate to future events or our future financial performance, and involve known and unknown risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to be materially different from any future results, levels of activity, performance or achievements expressed or implied by these forward-looking statements. Forward-looking statements include, but are not limited to, statements about:

- our efforts to potentially obtain regulatory approval of octreotide capsules in the United States;
- the timing of regulatory filings, including our ability to resubmit our NDA for octreotide capsules by year-end 2019, anticipated six-month regulatory review process, if our resubmitted NDA is determined by FDA as a complete response to its April 2016 complete response letter, and expected commercial launch timing in the United States;
- our development of octreotide capsules, conditionally trade-named MYCAPSSA, 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 during the second half 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;

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- 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 manufacture sufficient amounts of octreotide capsules for clinical trials and commercialization activities;
- our ability to secure collaborators to license, manufacture, market and sell octreotide capsules or any products for which we receive regulatory approval in the future;
- our ability to protect our intellectual property and operate our business without infringing upon the intellectual property rights of others;
- our product development and operational plans generally;
- our expected use of proceeds from this offering; and
- our estimates and expectations regarding our capital requirements, cash and expense levels and liquidity sources.

We have included important factors in the cautionary statements included in this prospectus supplement and the accompanying prospectus and the documents we incorporate by reference herein and therein, particularly in the “Risk Factors” sections of these documents, that we believe could cause actual results or events to differ materially from the forward-looking statements that we make. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we may make. No forward-looking statement is a guarantee of future performance.

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

PROSPECTUS SUPPLEMENT SUMMARY

The following summary of our business highlights some of the information contained elsewhere in, or incorporated by reference into, this prospectus supplement. Because this is only a summary, however, it does not contain all of the information that may be important to you. You should carefully read this prospectus supplement and the accompanying prospectus, including the documents incorporated by reference, which are described under "Incorporation of Certain Information by Reference" in this prospectus supplement. You should also carefully consider the matters discussed in the section of this prospectus supplement entitled "Risk Factors" and under similar sections of the accompanying prospectus and other periodic reports incorporated herein and therein by reference.

Company Overview

We are a clinical-stage biopharmaceutical company focused on improving the lives of patients who face challenges associated with their existing treatments for rare and serious chronic disease. Employing our proprietary Transient Permeability Enhancer, or TPE, technology platform, we seek to develop oral medications that are currently available only as injections. We are developing oral octreotide capsules, conditionally trade-named MYCAPSSA, our sole TPE platform-based clinical product candidate, for the treatment of acromegaly. In July 2019, we announced positive top-line results from CHIASMA OPTIMAL, the second Phase 3 clinical trial we have completed of octreotide capsules for the maintenance therapy of adult patients with acromegaly. Based on the results from CHIASMA OPTIMAL, we plan to resubmit our New Drug Application, or NDA, by year-end 2019. We expect the United States Food and Drug Administration, or the FDA, will aim to complete its review of our anticipated NDA, if accepted for filing, within six months based on our expectation that the NDA will be designated a Class 2 resubmission by the FDA to address its April 2016 complete response letter, or CRL, to our original NDA.

Acromegaly is a rare and debilitating condition that results in the body's production of excess growth hormone, which in turn elevates insulin-like growth factor 1, or IGF-1, a byproduct of increased growth hormone. 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 \$2.7 billion annually, of which we estimate approximately \$810 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.

Our CHIASMA OPTIMAL trial was a randomized, double-blind, placebo-controlled, nine-month clinical trial of octreotide capsules that was conducted under a special protocol assessment, or SPA, agreement with the FDA. The trial enrolled 56 adult acromegaly patients whose disease was biochemically controlled by injectable somatostatin analogs (average IGF-1 $\leq 1.0 \times$ 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 $\square 1.3 \times$ ULN. Patients were randomized on a

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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. 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 and 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 $\leq 1.0 \times \text{ULN}$ (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 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 $> 1.0 \times \text{ULN}$; time to loss of response: IGF-1 of 2 consecutive visits is $\leq 1.3 \times \text{ULN}$; 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 vs. 30% of patients treated with placebo ($p = 0.001$).
 - Median time to loss of response (IGF-1 $> 1.0 \times \text{ULN}$) was not reached (> 36 weeks) for patients treated with octreotide capsules vs. 16 weeks for patients treated with placebo ($p < 0.001$).
 - Median time to loss of response (IGF-1 $\leq 1.3 \times \text{ULN}$) was not reached (> 36 weeks) for patients treated with octreotide capsules vs. 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 vs. 68% of patients treated with placebo ($p = 0.003$).

Additionally, in a pre-specified exploratory endpoint, mean IGF-1 values across all patients treated with octreotide capsules (including primary endpoint non-responders per protocol), remained within normal limits ($\leq 1.0 \times \text{ULN}$) up to the end of oral treatment. 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 and for those patients that required rescue medication, it was their last observed value prior to the use of rescue medication.

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In the CHIASMA OPTIMAL trial, octreotide capsules appeared safe and well tolerated. 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. 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 CHIASMA OPTIMAL:

	Octreotide Capsules		Placebo	
	n	%	n	%
Subjects with:				
At least one TEAE	28	100	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

We plan to submit an NDA by year-end 2019 for octreotide capsules for the maintenance treatment of adults with acromegaly. 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 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 both primary and 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 any NDA. We continue to believe that the data from the CHIASMA OPTIMAL trial alone is designed to address the efficacy concerns raised by the FDA in its CRL to our first NDA submission and that the FDA only expects to review safety data from our MPOWERED trial as part of its review of our planned NDA resubmission. We anticipate that our planned NDA resubmission will be classified by the FDA for a six-month review period. Any future requirement by the FDA to submit additional data, including the efficacy data from our MPOWERED clinical trial, as part of our planned NDA resubmission may delay or prevent the filing, review or approval of our NDA.

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 July 2018, we completed the enrollment of 135 adult acromegaly patients into the run-in phase of the trial. In October 2018, 80 patients were randomized following the six-month run-in phase in the MPOWERED trial. In October 2018, we also 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 the enrollment of 146 total patients in MPOWERED and expect to release top-line data from the MPOWERED trial in the second half of 2020.

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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 significant limitations and patient burdens, including suboptimal symptom control, pain, injection-site reactions and other injection-related side effects, inconvenience, lost work days and emotional issues. 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.

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 to explore the strategic merits of collaboration opportunities for commercializing octreotide capsules in the European Union and the rest of the world. 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. We are also pursuing additional patent applications relating to particular uses, dosages and packaging for octreotide capsules. On March 26, 2019, a United States patent which is directed to specific methods of using octreotide capsules was granted. This patent will expire in 2036.

Risks Affecting Us

- In light of our receipt of a CRL from the FDA in April 2016 regarding our NDA for octreotide capsules for the maintenance treatment of U.S. adult patients with acromegaly, our interactions with the FDA, and despite our receipt of a SPA for our Phase 3 CHIASMA OPTIMAL trial, 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.
- Even though our Phase 3 CHIASMA OPTIMAL trial is being conducted under a SPA agreed to with the FDA, we cannot guarantee that the design of, or data collected from, this trial or any of our clinical trials will be sufficient to support filing or approval of an NDA.
- We are substantially dependent on the regulatory approval and subsequent commercial success of octreotide capsules for the treatment of acromegaly in the United States, both of which may never occur.
- If we are not able to obtain required regulatory approvals for octreotide capsules, particularly in the United States, 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.
- Even if we receive regulatory approval of octreotide capsules for acromegaly, we may still face future development and regulatory challenges that could inhibit or preclude our ability to commercialize octreotide capsules for any indication.
- 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.

- 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.
- Even if we receive regulatory approval of octreotide capsules, it may not achieve an adequate level of acceptance by physicians, patients and third-party payors and government payors, and we may not generate sufficient revenue or be able to achieve or sustain profitability.
- We do not have a sales and marketing organization and, as a company, have not commercialized any products. If we are able to secure regulatory approval for octreotide capsules in acromegaly but are unable to establish effective sales and marketing capabilities in the United States and access them in the European Union and other international markets, we may not succeed in commercializing octreotide capsules.
- 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 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.
- 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.

Company Information

We were incorporated in 2001 and commenced active operations in the same year. Our operations to date have been limited to organizing and staffing our company, business planning, raising capital, developing our TPE technology, identifying potential drug candidates, undertaking nonclinical studies and, beginning in 2010, conducting clinical trials and preparing for regulatory submissions. To date, we have financed our operations primarily through private placements, funding received from a licensing agreement, a loan agreement and our initial and follow-on public offerings. We have no products approved for sale and all of our historical revenue has been related to one license agreement, which has been terminated.

Our principal executive offices are located at 460 Totten Pond Road, Suite 530, Waltham, MA 02451 and our telephone number is (617) 928-5300. Our website address is www.chiasmapharma.com. The reference to our website is intended to be an inactive textual reference and, except for the documents incorporated by reference as noted below, the information on, or accessible through, our website is not part of this prospectus supplement.

Implications of Being an Emerging Growth Company

As a company with less than \$1.07 billion in revenue during our most recently completed fiscal year, we qualify as an “emerging growth company” as defined in Section 2(a) of the Securities Act of 1933, as amended, or the Securities Act, as modified by the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. As an emerging growth company, we may take advantage of specified reduced disclosure and other requirements that are otherwise applicable, in general, to public companies that are not emerging growth companies. These provisions include:

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

We may take advantage of these exemptions for up to five years or such earlier time that we are no longer an emerging growth company. We would cease to be an emerging growth company if we have more than \$1.07 billion in annual revenues as of the end of a fiscal year, have more than \$700 million in market value of our capital stock held by non-affiliates as of any December 31 before that time or if we issue more than \$1.0 billion of non-convertible debt over a three-year-period. We may choose to take advantage of some, but not all, of the available exemptions.

The JOBS Act permits an emerging growth company to take advantage of an extended transition period to comply with new or revised accounting standards applicable to public companies. We have irrevocably elected not to avail ourselves of this extended transition period and, as a result, we will adopt new or revised accounting standards on the relevant dates on which adoption of such standards is required for non-emerging growth companies.

THE OFFERING

Issuer	Chiasma, Inc.
Common Stock Offered by Us	shares
Common Stock To Be Outstanding After This Offering	shares (or shares, if the underwriters exercise their option in full to purchase additional shares)
Underwriters' Option To Purchase Additional Shares	Up to an aggregate of shares
Use of Proceeds	We intend to use the net proceeds from this offering primarily for commercialization of MYCAPSSA in the United States, if approved, and for working capital and other general corporate purposes. See "Use of Proceeds" for additional information.
Risk Factors	Your investment involves a high degree of risk. See the information contained in or incorporated by reference under "Risk Factors" beginning on page S-13 of this prospectus supplement, and in the related sections of the accompanying prospectus and in the documents incorporated by reference herein and therein.
The NASDAQ Global Select Market Symbol	"CHMA"

The number of shares of our common stock that will be outstanding immediately after this offering as shown above is based on 31,777,227 shares outstanding as of June 30, 2019. The number of shares outstanding as of June 30, 2019 as used throughout this prospectus, unless otherwise indicated, excludes:

- 5,847,137 shares of common stock issuable upon the exercise of stock options outstanding as of June 30, 2019 at a weighted-average exercise price of \$4.86 per share;
- 3,567,015 shares of common stock issuable upon the exercise of warrants outstanding as of June 30, 2019 at exercise prices ranging from \$0.09 per share to \$9.13 per share;
- 1,798,425 shares of common stock reserved for future issuance under our 2015 Stock Option and Incentive Plan; and
- 260,000 shares of common stock reserved for the future issuance under our 2015 Employee Stock Purchase Plan.

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If the underwriters' option to purchase additional shares is exercised in full, we will issue and sell an additional _____ shares of our common stock and will have _____ shares outstanding after the offering.

Except as otherwise noted, all information in this prospectus supplement assumes no exercise of the underwriters' option to purchase additional shares.

RISK FACTORS

Your investment in our common stock involves a high degree of risk. Before deciding whether to invest in our common stock, you should carefully consider the risks discussed under the section captioned “Risk Factors” contained in our Annual Report on Form 10-K for the year ended December 31, 2018 which is incorporated by reference in this prospectus supplement and the accompanying prospectus in their entirety, together with other information in this prospectus supplement, the accompanying prospectus, the information and documents incorporated by reference herein and therein, and in any free writing prospectus that we have authorized for use in connection with this offering. If any of these risks actually occurs, our business, financial condition, results of operations or cash flow could be seriously harmed. This could cause the trading price of our common stock to decline, resulting in a loss of all or part of your investment.

Risks Related to this Offering

Our management team may invest or spend the proceeds of this offering in ways with which you may not agree or in ways which may not yield a significant return.

Our management will have broad discretion over the use of proceeds from this offering, including for any of the purposes described in the section entitled “Use of Proceeds,” as well as our existing cash and cash equivalents, and you will be relying on the judgment of our management regarding such application. Our management will have considerable discretion in the application of the net proceeds, and you will not have the opportunity, as part of your investment decision, to assess whether the proceeds are being used appropriately. The net proceeds may be used for corporate purposes that do not improve our operating results or enhance the value of our common stock.

You will experience immediate and substantial dilution.

The offering price per share in this offering may exceed the net tangible book value per share of our common stock outstanding prior to this offering. Based on the public offering price of \$ per share, and a net book value of \$26.0 million, or \$1.06 per share of common stock, as of March 31, 2019, if you purchase shares of common stock in this offering, you will suffer immediate and substantial dilution of \$ per share in the net tangible book value of the common stock you purchase. The exercise of outstanding stock options and warrants will result in further dilution of your investment. See the section titled “Dilution” below for a more detailed illustration of the dilution you would incur if you participate in this offering.

You may experience future dilution as a result of future equity offerings.

In order to raise additional capital, we may in the future offer additional shares of our common stock or other securities convertible into or exchangeable for our common stock at prices that may not be the same as the price per share in this offering. We may sell shares or other securities in any other offering at a price per share that is less than the price per share paid by investors in this offering, and investors purchasing shares or other securities in the future could have rights superior to those of existing stockholders. The price per share at which we sell additional shares of our common stock, or securities convertible or exchangeable into common stock, in future transactions may be higher or lower than the price per share paid by investors in this offering.

Sales of a substantial number of shares of our common stock in the public market after this offering could cause our stock price to fall.

Sales of a substantial number of shares of our common stock in the public market or the perception that these sales might occur could depress the market price of our common stock and could impair our ability to raise capital through the sale of additional equity securities. We are unable to predict the effect that sales may have on the prevailing market price of our common stock. In addition, the sale of substantial

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amounts of our common stock could adversely impact the price of our common stock. As of June 30, 2019, 31,777,227 shares of our common stock were outstanding. The sale, or the availability for sale, of a large number of shares of our common stock in the public market could cause the price of our common stock to decline.

The trading price of the shares of our common stock could be highly volatile, and purchasers of our common stock could incur substantial losses.

The market price for our common stock could be highly volatile and could continue to be subject to wide fluctuations in response to various factors. The market price for our common stock has varied between a high price of \$8.29 on June 7, 2019 and a low price of \$1.20 on August 10, 2018 in the twelve-month period ending on July 19, 2019. This volatility may affect the price at which you could sell the shares of our common stock, and the sale of substantial amounts of our common stock could adversely affect the price of our common stock. Our stock price is likely to continue to be volatile and subject to significant price and volume fluctuations in response to market and other factors, including those described, and incorporated by reference, in this “Risk Factors” section.

As a result, you may not be able to sell your shares of common stock at or above the price at which you purchase them. In addition, the stock market in general, and the Nasdaq Global Select Market and the stock of biotechnology and emerging pharmaceutical companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. Broad market and industry factors may negatively affect the market price of our common stock, regardless of our actual operating performance.

USE OF PROCEEDS

Based on the public offering price of \$ _____ per share of common stock, we estimate that the net proceeds to us from the sale of the shares of common stock that we are offering will be approximately \$ _____ million or approximately \$ _____ million, if the option to purchase additional shares is exercised in full by the underwriters, in each case, after deducting underwriting discounts, commissions and estimated offering expenses payable by us.

We expect to use the net proceeds received from this offering primarily for commercialization of MYCAPSSA in the United States, if approved, and for working capital and other general corporate purposes.

The expected use of the net proceeds from this offering represents our current intentions based upon our present plans and business conditions, which could change in the future as our plans and business conditions evolve. We cannot predict with certainty all of the particular uses for the net proceeds to be received upon the completion of this offering or the amounts that we will actually spend on the uses set forth above. The amount and timing of our actual expenditures will depend upon numerous factors, including the results of our development efforts, the timing of regulatory submissions and the feedback from regulatory authorities, the commercial success of our products, if regulatory approval is obtained, and the timing and success of our ongoing clinical trial, as well as any collaborations that we may enter into with third parties for octreotide capsules, and any unforeseen cash needs. We may also use a portion of the net proceeds to in-license, acquire or invest in additional businesses, technologies, products or assets, although currently we have no specific agreements, commitments or understandings in this regard. As a result, our management will have broad discretion over the use of the net proceeds from this offering.

The costs and timing of obtaining regulatory approval are highly uncertain, are subject to substantial risks and can often change. Accordingly, we may change the allocation of these proceeds as a result of contingencies such as the progress and results of our clinical trials and other development activities, the establishment of collaborations, our manufacturing requirements and regulatory or competitive developments.

Pending the application of the net proceeds as described above or otherwise, we may invest the proceeds in short-term, investment-grade, interest-bearing securities or guaranteed obligations of the U.S. government or other securities.

DILUTION

If you purchase our common stock in this offering, your ownership interest will be diluted to the extent of the difference between the price per share you pay in this offering and the net tangible book value per share of our common stock immediately after this offering. Our net tangible book value as of March 31, 2019 was approximately \$26.0 million, or approximately \$1.06 per share of common stock, based upon 24,489,959 shares outstanding as of that date. Net tangible book value per share is equal to our total tangible assets, less our total liabilities, divided by the total number of shares outstanding.

After giving effect to the sale of the shares of common stock in this offering at the public offering price of \$ _____ per share of common stock, excluding the exercise of the underwriters' option to purchase additional shares and after deducting underwriting discounts, commissions and other estimated offering expenses payable by us, our adjusted net tangible book value as of March 31, 2019 would have been approximately \$ _____ million, or approximately \$ _____ per share. This represents an immediate increase in net tangible book value of approximately \$ _____ per share to our existing stockholders, and an immediate dilution of \$ _____ per share to investors purchasing shares of common stock in the offering.

The following table illustrates the per share dilution to investors purchasing shares of common stock in the offering:

Public offering price per share of common stock	
Net tangible book value per share as of March 31, 2019	\$ 1.06
Increase per share attributable to sale of common stock to investors	_____
Adjusted net tangible book value per share after the offering	_____
Dilution per share to investors	_____

The above calculation is based on 24,489,959 shares of common stock outstanding as of March 31, 2019 and excludes as of that date:

- 4,831,464 shares of common stock issuable upon the exercise of stock options outstanding as of March 31, 2019 at a weighted-average exercise price of \$4.15 per share;
- 3,567,015 shares of common stock issuable upon the exercise of warrants outstanding as of March 31, 2019 at exercise prices ranging from \$0.09 per share to \$9.13 per share;
- 2,838,208 shares of common stock reserved for future issuance under our 2015 Stock Option and Incentive Plan; and
- 260,000 shares of common stock reserved for the future issuance under our 2015 Employee Stock Purchase Plan.

In addition, the amounts in the table above assume no exercise by the underwriters of their option to purchase additional shares.

If the underwriters exercise their option to purchase _____ shares of common stock in full, the as adjusted net tangible book value after this offering would be approximately \$ _____ per share, representing an increase in net tangible book value of approximately \$ _____ per share to existing stockholders and immediate dilution in net tangible book value of approximately \$ _____ per share to investors purchasing our common stock in this offering at the public offering price.

DIVIDEND POLICY

We have never declared or paid any dividends on our capital stock. We currently intend to retain all available funds and any future earnings, if any, to fund the development and expansion of our business and we do not anticipate paying any cash dividends in the foreseeable future. Moreover, any future indebtedness that we may incur could preclude us from paying dividends. Any future determination to pay dividends will be made at the discretion of our board of directors. Investors should not purchase our common stock with the expectation of receiving cash dividends.

MATERIAL U.S. FEDERAL INCOME TAX CONSIDERATIONS FOR NON-U.S. HOLDERS OF COMMON STOCK

The following discussion is a summary of the material U.S. federal income tax considerations applicable to non-U.S. holders (as defined below) with respect to their ownership and disposition of shares of our common stock issued pursuant to this offering. For purposes of this discussion, a non-U.S. holder means a beneficial owner of our common stock that is for U.S. federal income tax purposes:

- a non-resident alien individual;
- a foreign corporation or any other foreign organization taxable as a corporation for U.S. federal income tax purposes;
- a foreign estate, the income of which is not subject to U.S. federal income tax on a net income basis; or
- a trust, (A) that does not have a valid election in effect under applicable United States Treasury regulations to be treated as a United States Person, and (B) either (i) which is not subject to the primary supervision of a court within the United States, or (ii) for which one or more United States persons do not have the authority to control all substantial decisions.

This discussion does not address the tax treatment of partnerships or other entities that are pass-through entities for U.S. federal income tax purposes or persons that hold their common stock through partnerships or other pass-through entities. A partner in a partnership or other pass-through entity that will hold our common stock should consult his, her or its own tax advisor regarding the tax consequences of acquiring, holding and disposing of our common stock through a partnership or other pass-through entity, as applicable.

This discussion is based on current provisions of the U.S. Internal Revenue Code of 1986, as amended, which we refer to as the Code, existing and proposed U.S. Treasury Regulations promulgated thereunder, current administrative rulings and judicial decisions, all as in effect as of the date of this prospectus supplement and, all of which are subject to change or to differing interpretation, possibly with retroactive effect. Any such change or differing interpretation could alter the tax consequences to non-U.S. holders described in this prospectus supplement. There can be no assurance that the Internal Revenue Service, which we refer to as the IRS, will not challenge one or more of the tax consequences described herein. We assume in this discussion that a non-U.S. holder holds shares of our common stock as a capital asset, generally property held for investment.

This discussion does not address all aspects of U.S. federal income that may be relevant to a particular non-U.S. holder in light of that non-U.S. holder's individual circumstances nor does it address any aspects of any U.S. state, local or non-U.S. taxes, the alternative minimum tax, any tax considerations resulting from a non-U.S. holder having a functional currency other than the U.S. dollar, the Medicare tax on net investment income; or any other U.S. federal tax other than the income tax. This discussion also does not consider any specific facts or circumstances that may apply to a non-U.S. holder and does not address the special tax rules applicable to particular non-U.S. holders, such as:

- banks;
- insurance companies;
- tax exempt or governmental organizations;
- financial institutions;
- brokers or dealers in securities;
- regulated investment companies;

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- tax-qualified retirement plan;
- pension plans;
- “controlled foreign corporations,” “passive foreign investment companies,” and corporations that accumulate earnings to avoid U.S. federal income tax;
- “qualified foreign pension funds,” or entities wholly owned by a “qualified foreign pension fund”;
- persons deemed to sell our common stock under the constructive sale provisions of the Code;
- persons that elect to apply Section 1400Z-2 of the Code to gains recognized with respect to shares of our common stock;
- persons that hold our common stock as part of a straddle, hedge, conversion transaction, synthetic security or other integrated investment;
- persons who hold or receive our common stock pursuant to the exercise of any employee stock option or otherwise as compensation;
- persons who have elected to mark securities to market;
- persons for whom our stock constitutes “qualified small business stock” within the meaning of Section 1202 of the Code or as “Section 1244 stock” for purposes of Section 1244 of the Code; and
- certain U.S. expatriates.

This discussion is for general information only and is not tax advice. Accordingly, all prospective non-U.S. holders of our common stock should consult their own tax advisors with respect to the U.S. federal, state, local and non-U.S. tax consequences of the purchase, ownership and disposition of our common stock.

Distributions on Our Common Stock

Distributions, if any, on our common stock generally will constitute dividends for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. If a distribution exceeds our current and accumulated earnings and profits, the excess will be treated as a tax-free return of the non-U.S. holder’s investment, up to such holder’s tax basis in the common stock. Any remaining excess will be treated as capital gain, subject to the tax treatment described below in “Gain on sale, exchange or other disposition of our common stock.” Any such distributions will also be subject to the discussion below under the section titled “Withholding and Information Reporting Requirements—FATCA.”

Subject to the discussion in the following two paragraphs in this section, dividends paid to a non-U.S. holder generally will be subject to withholding of U.S. federal income tax at a 30% rate or such lower rate as may be specified by an applicable income tax treaty between the United States and such holder’s country of residence.

A non-U.S. holder of our common stock who claims the benefit of an applicable income tax treaty between the United States and such holder’s country of residence generally will be required to provide a properly executed IRS Form W-8BEN or W-8BEN-E (or successor form) and satisfy applicable certification and other requirements. Non-U.S. holders are urged to consult their tax advisors regarding their entitlement to benefits under a relevant income tax treaty. A non-U.S. holder that is eligible for a reduced rate of U.S. withholding tax under an income tax treaty may obtain a refund or credit of any excess amounts withheld by timely filing a U.S. tax return with the IRS.

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Dividends that are treated as effectively connected with a trade or business conducted by a non-U.S. holder within the United States and, if an applicable income tax treaty so provides, that are attributable to a permanent establishment or a fixed base maintained by the non-U.S. holder within the United States, are generally exempt from the 30% withholding tax if the non-U.S. holder satisfies applicable certification and disclosure requirements. To obtain this exemption, a non-U.S. holder must generally provide a properly executed original and unexpired IRS Form W-8ECI properly certifying such exemption. However, such U.S. effectively connected income, net of specified deductions and credits, is taxed at the same graduated U.S. federal income tax rates applicable to United States persons (as defined in the Code). Any U.S. effectively connected income received by a non-U.S. holder that is a corporation may also, under certain circumstances, be subject to an additional “branch profits tax” at a 30% rate or such lower rate as may be specified by an applicable income tax treaty between the United States and such holder’s country of residence.

Any documentation provided to an applicable withholding agent may need to be updated in certain circumstances. The certification requirements described above may also require a non-U.S. holder to provide its U.S. taxpayer identification number.

Gain on Sale or Other Taxable Disposition of Our Common Stock

Subject to the discussion below under “Backup Withholding and Information Reporting” and “Withholding and Information Reporting Requirements—FATCA,” a non-U.S. holder generally will not be subject to any U.S. federal income or withholding tax on any gain realized upon such holder’s sale or other taxable disposition of shares of our common stock unless:

- the gain is effectively connected with the non-U.S. holder’s conduct of a U.S. trade or business and, if an applicable income tax treaty so provides, is attributable to a permanent establishment or a fixed-base maintained by such non-U.S. holder in the United States, in which case the non-U.S. holder generally will be taxed on a net income basis at the graduated U.S. federal income tax rates applicable to United States persons (as defined in the Code) and, if the non-U.S. holder is a foreign corporation, the branch profits tax described above in “Distributions on Our Common Stock” also may apply;
- the non-U.S. holder is a nonresident alien individual who is present in the United States for 183 days or more in the taxable year of the disposition and certain other conditions are met, in which case the non-U.S. holder will be subject to a 30% tax (or such lower rate as may be specified by an applicable income tax treaty between the United States and such holder’s country of residence) on the net gain derived from the disposition, which may be offset by certain U.S. source capital losses of the non-U.S. holder, if any (even though the individual is not considered a resident of the United States), provided that the non-U.S. holder has timely filed U.S. federal income tax returns with respect to such losses; or
- we are, or have been, at any time during the five-year period preceding such sale or other taxable disposition (or the non-U.S. holder’s holding period, if shorter) a “U.S. real property holding corporation,” unless our common stock is regularly traded on an established securities market, as defined by applicable Treasury Regulations, and the non-U.S. holder holds no more than 5% of our outstanding common stock, directly or indirectly, actually or constructively, during the shorter of the 5-year period ending on the date of the disposition or the period that the non-U.S. holder held our common stock. If we are determined to be a U.S. real property holding corporation and the foregoing exception does not apply, then a purchaser may generally withhold 15% of the proceeds payable to a non-U.S. holder from a sale of our common stock and the non-U.S. holder generally will be taxed on its net gain derived from the disposition at the graduated U.S. federal income tax rates applicable to United States persons (as defined in the Code). Generally, a corporation is a U.S. real property holding corporation only if the fair market value of its U.S. real property interests

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equals or exceeds 50% of the sum of the fair market value of its worldwide real property interests plus its other assets used or held for use in a trade or business. Although there can be no assurance, we do not believe that we are, or have been, a U.S. real property holding corporation, or that we are likely to become one in the future. No assurance can be provided that our common stock will be regularly traded on an established securities market for purposes of the rules described above.

Backup Withholding and Information Reporting

We must report annually to the IRS and to each non-U.S. holder the gross amount of the distributions on our common stock paid to such holder and the tax withheld, if any, with respect to such distributions. Non-U.S. holders may have to comply with specific certification procedures to establish that the holder is not a United States person (as defined in the Code) in order to avoid backup withholding at the applicable rate, currently 24%, with respect to dividends on our common stock. Dividends paid to non-U.S. holders subject to withholding of U.S. federal income tax, as described above in “Distributions on Our Common Stock,” generally will be exempt from U.S. backup withholding.

Information reporting and backup withholding will generally apply to the proceeds of a disposition of our common stock by a non-U.S. holder effected by or through the U.S. office of any broker, U.S. or foreign, unless the holder certifies its status as a non-U.S. holder and satisfies certain other requirements, or otherwise establishes an exemption. Generally, information reporting and backup withholding will not apply to a payment of disposition proceeds to a non-U.S. holder where the transaction is effected outside the United States through a non-U.S. office of a broker. However, for information reporting purposes, dispositions effected through a non-U.S. office of a broker with substantial U.S. ownership or operations generally will be treated in a manner similar to dispositions effected through a U.S. office of a broker. Non-U.S. holders should consult their own tax advisors regarding the application of the information reporting and backup withholding rules to them. Copies of information returns may be made available to the tax authorities of the country in which the non-U.S. holder resides or is incorporated under the provisions of a specific treaty or agreement. Backup withholding is not an additional tax. Any amounts withheld under the backup withholding rules from a payment to a non-U.S. holder can be refunded or credited against the non-U.S. holder’s U.S. federal income tax liability, if any, provided that an appropriate claim is filed with the IRS in a timely manner.

Withholding and Information Reporting Requirements – FATCA

The Foreign Account Tax Compliance Act, or FATCA, generally imposes a U.S. federal withholding tax at a rate of 30% on payments of dividends on, or gross proceeds from the sale or other disposition of, our common stock paid to a foreign entity unless (i) if the foreign entity is a “foreign financial institution,” such foreign entity undertakes certain due diligence, reporting, withholding, and certification obligations, (ii) if the foreign entity is not a “foreign financial institution,” such foreign entity identifies certain of its U.S. investors, if any, or (iii) the foreign entity is otherwise exempt under FATCA. Under applicable U.S. Treasury regulations, withholding under FATCA currently applies to payments of dividends on our common stock. Currently proposed U.S. Treasury Regulations provide that FATCA withholding does not apply to gross proceeds from the disposition of property of a type that can produce U.S. source dividends or interest; however, prior versions of the rules would have made such gross proceeds subject to FATCA withholding. Taxpayers (including withholding agents) can currently rely on the proposed Treasury Regulations. Under certain circumstances, a non-U.S. holder may be eligible for refunds or credits of this withholding tax. An intergovernmental agreement between the United States and an applicable foreign country may modify the requirements described in this paragraph. Non-U.S. holders should consult their tax advisors regarding the possible implications of this legislation on their investment in our common stock and the entities through which they hold our common stock, including, without limitation, the process and deadlines for meeting the applicable requirements to prevent the imposition of the 30% withholding tax under FATCA.

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The preceding discussion of material U.S. federal tax considerations is for general information only. It is not tax advice. Prospective investors should consult their own tax advisors regarding the particular U.S. federal, state, local and non-U.S. tax consequences of purchasing, holding and disposing of our common stock, including the consequences of any proposed changes in applicable laws.

UNDERWRITING

Subject to the terms and conditions set forth in the underwriting agreement, dated July , 2019 between us, Piper Jaffrey & Co., 345 Park Avenue, 12th Floor, New York, NY 10154, and Cantor Fitzgerald & Co., 499 Park Avenue, New York, New York 10022, as representatives of the underwriters named below (the “Representatives”) and the book-running managers of this offering, we have agreed to sell to the underwriters, and each of the underwriters has agreed, severally and not jointly, to purchase from us, the shares of common stock shown opposite its name below:

<u>Underwriter</u>	<u>Number of Shares</u>
Piper Jaffrey & Co.	
Cantor Fitzgerald & Co.	
Total	

The underwriting agreement provides that the obligations of the several underwriters are subject to certain conditions precedent such as the receipt by the underwriters of officers’ certificates and legal opinions and approval of certain legal matters by their counsel. The underwriting agreement provides that the underwriters will purchase all of the shares of common stock if any of them are purchased. We have agreed to indemnify the underwriters and certain of their controlling persons against certain liabilities, including liabilities under the Securities Act, and to contribute to payments that the underwriters may be required to make in respect of those liabilities.

The underwriters are offering the shares of common stock subject to their acceptance of the shares of common stock from us and subject to prior sale. The underwriters reserve the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part.

Option to Purchase Additional Shares

We have granted to the underwriters an option, exercisable 30 days from the date of this prospectus supplement, to purchase, from time to time, in whole or in part, up to an aggregate of shares from us at the public offering price set forth on the cover page of this prospectus supplement, less underwriting discounts and commissions. If the underwriters exercise this option, each underwriter will be obligated, subject to certain conditions, to purchase a number of additional shares approximately proportionate to that underwriter’s initial purchase commitment as indicated in the table above.

Commission and Expenses

The underwriters have advised us that they propose to offer the shares of common stock to the public at the public offering price set forth on the cover page of this prospectus supplement and to certain dealers, which may include the underwriters, at that price less a concession not in excess of \$ per share of common stock. The underwriters may allow, and certain dealers may reallow, a discount from the concession not in excess of \$ per share of common stock to certain brokers and dealers. After the initial offering, the Representatives may change the offering price and other selling terms.

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The following table shows the public offering price, the underwriting discounts and commissions that we are to pay the underwriters and the proceeds, before expenses, to us in connection with this offering. Such amounts are shown assuming both no exercise and full exercise of the underwriters' option to purchase additional shares.

	Without Option to Purchase Additional Shares	With Option to Purchase Additional Shares	Without Option to Purchase Additional Shares	With Option to Purchase Additional Shares
Public offering price				
Underwriting discounts and commissions				
Proceeds to us, before expenses				

We estimate expenses payable by us in connection with this offering, other than the underwriting discounts and commissions referred to above, will be approximately \$. We have also agreed to reimburse the underwriters for certain fees and expenses, which reimbursed fee is deemed underwriting compensation for this offering by FINRA.

Listing

Our common stock is listed on NASDAQ Global Stock Market under the trading symbol "CHMA."

No Sales of Similar Securities

We, our officers and our directors, and affiliates of MPM Capital, our largest stockholder, have agreed, subject to certain specified exceptions, not to directly or indirectly, for a period of 60 days after the date of the underwriting agreement:

- sell, offer, contract or grant any option to sell (including any short sale), pledge, transfer, establish an open "put equivalent position" within the meaning of Rule 16a-1(h) under the Securities Exchange Act of 1934, as amended, or otherwise dispose of, any shares of common stock, options or warrants to acquire shares of common stock, or securities exchangeable or exercisable for or convertible into shares of common stock currently or hereafter owned either of record or beneficially,
- enter into any swap, hedge or other agreement or transaction that transfers, in whole or in part, the economic consequence of ownership of common stock, or securities exchangeable or exercisable for or convertible into shares of common stock, or
- publicly announce an intention to do any of the foregoing for a period of 60 days after the date of this prospectus supplement without the prior written consent of the Representatives.

In addition, we and each such person agrees that, without the prior written consent of the Representatives, we or such other person will not, during the restricted period, make any demand for, or exercise any right with respect to, the registration of any shares of common stock or any security convertible into or exercisable or exchangeable for common stock.

The Representatives may, in their sole discretion and at any time or from time to time before the termination of the 60-day period release all or any portion of the securities subject to lock-up agreements.

Market Making, Stabilization and Other Transactions

The underwriters may make a market in the common stock as permitted by applicable laws and regulations. However, the underwriters are not obligated to do so, and the underwriters may discontinue any market-making activities at any time without notice in their sole discretion. Accordingly, no

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assurance can be given as to the liquidity of the trading market for the common stock, that you will be able to sell any of the common stock held by you at a particular time or that the prices that you receive when you sell will be favorable.

The underwriters have advised us that they, pursuant to Regulation M under the Securities Exchange Act of 1934, as amended, and certain persons participating in the offering, may engage in short sale transactions, stabilizing transactions, syndicate covering transactions or the imposition of penalty bids in connection with this offering. These activities may have the effect of stabilizing or maintaining the market price of the common stock at a level above that which might otherwise prevail in the open market. Establishing short sales positions may involve either “covered” short sales or “naked” short sales.

“Covered” short sales are sales made in an amount not greater than the underwriters’ option to purchase additional shares of our common stock in this offering. The underwriters may close out any covered short position by either exercising their option to purchase additional shares of our common stock or purchasing shares of our common stock in the open market. In determining the source of shares to close out the covered short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which they may purchase shares through the option to purchase additional shares.

“Naked” short sales are sales in excess of the option to purchase additional shares of our common stock. The underwriters must close out any naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the shares of our common stock in the open market after pricing that could adversely affect investors who purchase in this offering.

A stabilizing bid is a bid for the purchase of shares of common stock on behalf of the underwriters for the purpose of fixing or maintaining the price of the common stock. A syndicate covering transaction is the bid for or the purchase of shares of common stock on behalf of the underwriters to reduce a short position incurred by the underwriters in connection with the offering. Similar to other purchase transactions, the underwriters’ purchases to cover the syndicate short sales may have the effect of raising or maintaining the market price of our common stock or preventing or retarding a decline in the market price of our common stock. As a result, the price of our common stock may be higher than the price that might otherwise exist in the open market. A penalty bid is an arrangement permitting the underwriters to reclaim the selling concession otherwise accruing to a syndicate member in connection with the offering if the common stock originally sold by such syndicate member are purchased in a syndicate covering transaction and therefore have not been effectively placed by such syndicate member.

Neither we, nor any of the underwriters make any representation or prediction as to the direction or magnitude of any effect that the transactions described above may have on the price of our common stock. The underwriters are not obligated to engage in these activities and, if commenced, may end any of these activities at any time.

Passive Market Making

The underwriters may also engage in passive market making transactions in our common stock on the NASDAQ in accordance with Rule 103 of Regulation M during a period before the commencement of offers or sales of shares of our common stock in this offering and extending through the completion of distribution. A passive market maker must display its bid at a price not in excess of the highest independent bid of that security. However, if all independent bids are lowered below the passive market maker’s bid, that bid must then be lowered when specified purchase limits are exceeded. Passive market making may cause the price of our common stock to be higher than the price that otherwise would exist in the open market in the absence of those transactions. The underwriters are not required to engage in passive market making and, if commenced, may end passive market making activities at any time.

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Electronic Distribution

A prospectus in electronic format may be made available by e-mail or on the web sites or through online services maintained by one or more of the underwriters, selling group members (if any) or their affiliates. The underwriters may agree with us to allocate a specific number of shares of common stock for sale to online brokerage account holders. Any such allocation for online distributions will be made by the underwriters on the same basis as other allocations. Other than the prospectus in electronic format, the information on the underwriters' web sites and any information contained in any other web site maintained by any of the underwriters is not part of this prospectus supplement, has not been approved and/or endorsed by us or the underwriters and should not be relied upon by investors.

Other Activities and Relationships

The underwriters and certain of their respective affiliates are full service financial institutions engaged in a wide range of activities for their own accounts and the accounts of customers, which may include, among other things, corporate finance, mergers and acquisitions, merchant banking, equity and fixed income sales, trading and research, derivatives, foreign exchange, futures, asset management, custody, clearance and securities lending. The underwriters and certain of their affiliates have, from time to time, performed, and may in the future perform, various investment banking and financial advisory services for us and our affiliates, for which they received or will receive customary fees and expenses.

In addition, in the ordinary course of its business, the underwriters and their respective affiliates may, directly or indirectly, hold long or short positions, trade and otherwise conduct such activities in or with respect to debt or equity securities and/or bank debt of, and/or derivative products. Such investment and securities activities may involve our securities and instruments. The underwriters and their respective affiliates may also make investment recommendations or publish or express independent research views in respect of such securities or instruments and may at any time hold, or recommend to clients that they acquire, long or short positions in such securities and instruments.

Stamp Taxes

If you purchase shares of common stock offered in this prospectus supplement, you may be required to pay stamp taxes and other charges under the laws and practices of the country of purchase, in addition to the offering price listed on the cover page of this prospectus supplement.

NOTICE TO INVESTORS

Canada

This prospectus supplement constitutes an “exempt offering document” as defined in and for the purposes of applicable Canadian securities laws. No prospectus has been filed with any securities commission or similar regulatory authority in Canada in connection with the offer and sale of the common stock. No securities commission or similar regulatory authority in Canada has reviewed or in any way passed upon this prospectus supplement or on the merits of the common stock and any representation to the contrary is an offence.

Canadian investors are advised that this prospectus supplement has been prepared in reliance on section 3A.3 of National Instrument 33-105 *Underwriting Conflicts* (“NI 33-105”). Pursuant to section 3A.3 of NI 33-105, this prospectus supplement is exempt from the requirement that the Company and the underwriter(s) provide investors with certain conflicts of interest disclosure pertaining to “connected issuer” and/or “related issuer” relationships that may exist between the Company and the underwriter(s) as would otherwise be required pursuant to subsection 2.1(1) of NI 33-105.

Resale Restrictions

The offer and sale of the common stock in Canada is being made on a private placement basis only and is exempt from the requirement that the Company prepares and files a prospectus under applicable Canadian securities laws. Any resale of the common stock acquired by a Canadian investor in this offering must be made in accordance with applicable Canadian securities laws, which may vary depending on the relevant jurisdiction, and which may require resales to be made in accordance with Canadian prospectus requirements, pursuant to a statutory exemption from the prospectus requirements, in a transaction exempt from the prospectus requirements or otherwise under a discretionary exemption from the prospectus requirements granted by the applicable local Canadian securities regulatory authority. These resale restrictions may under certain circumstances apply to resales of the common stock outside of Canada.

Representations of Purchasers

Each Canadian investor who purchases the common stock will be deemed to have represented to the Company and the underwriter(s) that the investor (i) is purchasing the common stock as principal, or is deemed to be purchasing as principal in accordance with applicable Canadian securities laws, for investment only and not with a view to resale or redistribution; (ii) is an “accredited investor” as such term is defined in section 1.1 of National Instrument 45-106 *Prospectus Exemptions* (“NI 45-106”) or, in Ontario, as such term is defined in section 73.3(1) of the *Securities Act* (Ontario); and (iii) is a “permitted client” as such term is defined in section 1.1 of National Instrument 31-103 *Registration Requirements, Exemptions and Ongoing Registrant Obligations*.

Taxation and Eligibility for Investment

Any discussion of taxation and related matters contained in this prospectus supplement does not purport to be a comprehensive description of all of the tax considerations that may be relevant to a Canadian investor when deciding to purchase the common stock and, in particular, does not address any Canadian tax considerations. No representation or warranty is hereby made as to the tax consequences to a resident, or deemed resident, of Canada of an investment in the common stock or with respect to the eligibility of the common stock for investment by such investor under relevant Canadian federal and provincial legislation and regulations.

Rights of Action for Damages or Rescission

Securities legislation in certain of the Canadian jurisdictions provides certain purchasers of securities pursuant to an offering memorandum (such as this prospectus supplement), including where the

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distribution involves an “eligible foreign security” as such term is defined in Ontario Securities Commission Rule 45-501 *Ontario Prospectus and Registration Exemptions* and in Multilateral Instrument 45-107 *Listing Representation and Statutory Rights of Action Disclosure Exemptions*, as applicable, with a remedy for damages or rescission, or both, in addition to any other rights they may have at law, where the offering memorandum, or other offering document that constitutes an offering memorandum, and any amendment thereto, contains a “misrepresentation” as defined under applicable Canadian securities laws. These remedies, or notice with respect to these remedies, must be exercised or delivered, as the case may be, by the purchaser within the time limits prescribed under, and are subject to limitations and defences under, applicable Canadian securities legislation. In addition, these remedies are in addition to and without derogation from any other right or remedy available at law to the investor.

Language of Documents

Upon receipt of this document, each Canadian investor hereby confirms that it has expressly requested that all documents evidencing or relating in any way to the sale of the securities described herein (including for greater certainty any purchase confirmation or any notice) be drawn up in the English language only. *Par la réception de ce document, chaque investisseur Canadien confirme par les présentes qu’il a expressément exigé que tous les documents faisant foi ou se rapportant de quelque manière que ce soit à la vente des valeurs mobilières décrites aux présentes (incluant, pour plus de certitude, toute confirmation d’achat ou tout avis) soient rédigés en anglais seulement.*

Australia

This prospectus is not a disclosure document for the purposes of Australia’s Corporations Act 2001 (Cth) of Australia, or Corporations Act, has not been lodged with the Australian Securities & Investments Commission and is only directed to the categories of exempt persons set out below. Accordingly, if you receive this prospectus in Australia:

You confirm and warrant that you are either:

- a “sophisticated investor” under section 708(8)(a) or (b) of the Corporations Act;
- a “sophisticated investor” under section 708(8)(c) or (d) of the Corporations Act and that you have provided an accountant’s certificate to the company which complies with the requirements of section 708(8)(c)(i) or (ii) of the Corporations Act and related regulations before the offer has been made; or
- a “professional investor” within the meaning of section 708(11)(a) or (b) of the Corporations Act.

To the extent that you are unable to confirm or warrant that you are an exempt sophisticated investor or professional investor under the Corporations Act any offer made to you under this prospectus is void and incapable of acceptance.

You warrant and agree that you will not offer any of the shares issued to you pursuant to this prospectus for resale in Australia within 12 months of those securities being issued unless any such resale offer is exempt from the requirement to issue a disclosure document under section 708 of the Corporations Act.

European Economic Area

In relation to each Member State of the European Economic Area, no offer of any securities which are the subject of the offering contemplated by this prospectus has been or will be made to the public in that Member State other than any offer where a prospectus has been or will be published in relation to such securities that has been approved by the competent authority in that Member State or, where appropriate, approved in another Member State and notified to the relevant competent authority in that

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Member State in accordance with the Prospectus Directive, except that an offer of such securities may be made to the public in that Member State:

- to any legal entity which is a “qualified investor” as defined in the Prospectus Directive;
- to fewer than 150, natural or legal persons (other than qualified investors as defined in the Prospectus Directive), as permitted under the Prospectus Directive, subject to obtaining the prior consent of the representatives of the underwriters for any such offer; or
- in any other circumstances falling within Article 3(2) of the Prospectus Directive,

provided that no such offer of securities shall require the Company or any of the underwriters to publish a prospectus pursuant to Article 3 of the Prospectus Directive or supplement a prospectus pursuant to Article 16 of the Prospectus Directive.

For the purposes of this provision, the expression an “offer to the public” in relation to any securities in any Member State means the communication in any form and by any means of sufficient information on the terms of the offer and the securities to be offered so as to enable an investor to decide to purchase or subscribe the securities, as the same may be varied in that Member State by any measure implementing the Prospectus Directive in that Member State and the expression “Prospectus Directive” means Directive 2003/71/EC (and amendments thereto, including the 2010 PD Amending Directive), and includes any relevant implementing measure in the Member State and the expression “2010 PD Amending Directive” means Directive 2010/73/EU.

Hong Kong

No securities have been offered or sold, and no securities may be offered or sold, in Hong Kong, by means of any document, other than to persons whose ordinary business is to buy or sell shares or debentures, whether as principal or agent; or to “professional investors” as defined in the Securities and Futures Ordinance (Cap. 571) of Hong Kong and any rules made under that Ordinance; or in other circumstances which do not result in the document being a “prospectus” as defined in the Companies Ordinance (Cap. 32) of Hong Kong or which do not constitute an offer to the public within the meaning of the Companies Ordinance (Cap.32) of Hong Kong. No document, invitation or advertisement relating to the securities has been issued or may be issued or may be in the possession of any person for the purpose of issue (in each case whether in Hong Kong or elsewhere), which is directed at, or the contents of which are likely to be accessed or read by, the public of Hong Kong (except if permitted under the securities laws of Hong Kong) other than with respect to securities which are or are intended to be disposed of only to persons outside Hong Kong or only to “professional investors” as defined in the Securities and Futures Ordinance (Cap. 571) of Hong Kong and any rules made under that Ordinance.

This prospectus has not been registered with the Registrar of Companies in Hong Kong. Accordingly, this prospectus may not be issued, circulated or distributed in Hong Kong, and the securities may not be offered for subscription to members of the public in Hong Kong. Each person acquiring the securities will be required, and is deemed by the acquisition of the securities, to confirm that he is aware of the restriction on offers of the securities described in this prospectus and the relevant offering documents and that he is not acquiring, and has not been offered any securities in circumstances that contravene any such restrictions.

Japan

The offering has not been and will not be registered under the Financial Instruments and Exchange Law of Japan (Law No. 25 of 1948 of Japan, as amended), or FIEL, and the Initial Purchaser will not offer or sell any securities, directly or indirectly, in Japan or to, or for the benefit of, any resident of Japan (which term as used herein means, unless otherwise provided herein, any person resident in Japan, including any

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corporation or other entity organized under the laws of Japan), or to others for re-offering or resale, directly or indirectly, in Japan or to a resident of Japan, except pursuant to an exemption from the registration requirements of, and otherwise in compliance with, the FIEL and any other applicable laws, regulations and ministerial guidelines of Japan.

Singapore

This prospectus has not been and will not be lodged or registered with the Monetary Authority of Singapore. Accordingly, this prospectus and any other document or material in connection with the offer or sale, or the invitation for subscription or purchase of the securities may not be issued, circulated or distributed, nor may the securities be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to the public or any member of the public in Singapore other than (i) to an institutional investor under Section 274 of the Securities and Futures Act, Chapter 289 of Singapore, or the SFA, (ii) to a relevant person as defined under Section 275(2), or any person pursuant to Section 275(1A) of the SFA, and in accordance with the conditions, specified in Section 275 of the SFA, or (iii) otherwise pursuant to, and in accordance with the conditions of any other applicable provision of the SFA.

Where the securities are subscribed or purchased under Section 275 of the SFA by a relevant person which is:

- a corporation (which is not an accredited investor as defined under Section 4A of the SFA) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or
- a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary is an accredited investor,

shares, debentures and units of shares and debentures of that corporation or the beneficiaries' rights and interest in that trust shall not be transferable for six months after that corporation or that trust has acquired the Offer Shares under Section 275 of the SFA except:

- to an institutional investor under Section 274 of the SFA or to a relevant person defined in Section 275(2) of the SFA, or to any person pursuant to an offer that is made on terms that such shares, debentures and units of shares and debentures of that corporation or such rights and interest in that trust are acquired at a consideration of not less than \$200,000 (or its equivalent in a foreign currency) for each transaction, whether such amount is to be paid for in cash or by exchange of securities or other assets, and further for corporations, in accordance with the conditions, specified in Section 275 of the SFA;
- where no consideration is given for the transfer; or
- where the transfer is by operation of law.

Switzerland

The securities may not be publicly offered in Switzerland and will not be listed on the SIX Swiss Exchange, or SIX, or on any other stock exchange or regulated trading facility in Switzerland. This prospectus has been prepared without regard to the disclosure standards for issuance prospectuses under art. 652a or art. 1156 of the Swiss Code of Obligations or the disclosure standards for listing prospectuses under art. 27 ff. of the SIX Listing Rules or the listing rules of any other stock exchange or regulated trading facility in Switzerland. Neither this prospectus nor any other offering or marketing material relating to the securities or the offering may be publicly distributed or otherwise made publicly available in Switzerland.

Neither this prospectus nor any other offering or marketing material relating to the offering, the Company or the securities have been or will be filed with or approved by any Swiss regulatory authority.

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In particular, this prospectus will not be filed with, and the offer of securities will not be supervised by, the Swiss Financial Market Supervisory Authority FINMA, or FINMA, and the offer of securities has not been and will not be authorized under the Swiss Federal Act on Collective Investment Schemes, or CISA. The investor protection afforded to acquirers of interests in collective investment schemes under the CISA does not extend to acquirers of securities.

Israel

This document does not constitute a prospectus under the Israeli Securities Law, 5728-1968, or the Securities Law, and has not been filed with or approved by the Israel Securities Authority. In the State of Israel, this document is being distributed only to, and is directed only at, and any offer of the shares is directed only at, investors listed in the first addendum, or the Addendum, to the Israeli Securities Law, consisting primarily of joint investment in trust funds, provident funds, insurance companies, banks, portfolio managers, investment advisors, members of the Tel Aviv Stock Exchange, underwriters, venture capital funds, entities with equity in excess of NIS 50 million and “qualified individuals”, each as defined in the Addendum (as it may be amended from time to time), collectively referred to as qualified investors (in each case purchasing for their own account or, where permitted under the Addendum, for the accounts of their clients who are investors listed in the Addendum). Qualified investors will be required to submit written confirmation that they fall within the scope of the Addendum, are aware of the meaning of same and agree to it.

United Kingdom

This prospectus is only being distributed to, and is only directed at, persons in the United Kingdom that are qualified investors (as defined in the Prospectus Directive) that are also (i) investment professionals falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005, as amended, referred to herein as the “Order”, and/or (ii) high net worth entities falling within Article 49(2)(a) to (d) of the Order and other persons to whom it may lawfully be communicated or caused to be communicated. Each such person is referred to herein as a “Relevant Person”.

This prospectus and its contents are confidential and should not be distributed, published or reproduced (in whole or in part) or disclosed by recipients to any other persons in the United Kingdom. Any person in the United Kingdom that is not a Relevant Person should not act or rely on this document or any of its contents.

Any invitation or inducement to engage in investment activity (within the meaning of Section 21 of the Financial Services and Markets Act 2000 (the “FSMA”) may only be communicated or caused to be communicated in connection with the issue or sale of the securities in circumstances in which Section 21(1) of the FSMA does not apply. All applicable provisions of the FSMA must be complied with in respect of anything done by any person in relation to the securities in, from or otherwise involving the United Kingdom.

LEGAL MATTERS

The validity of the shares of common stock offered hereby will be passed upon for us by Goodwin Procter LLP, Boston, Massachusetts. Certain legal matters relating to this offering will be passed upon for the underwriters by Duane Morris LLP, New York, New York.

EXPERTS

The financial statements incorporated in this prospectus supplement by reference from our Annual Report on Form 10-K have been audited by Deloitte & Touche LLP, an independent registered public accounting firm, as stated in their report, which is incorporated herein by reference. Such financial statements have been so incorporated in reliance upon the report of such firm given upon their authority as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

This prospectus supplement is part of a registration statement that we have filed with the SEC. Certain information in the registration statement has been omitted from this prospectus in accordance with the rules of the SEC. We are subject to the information requirements of the Exchange Act and, in accordance therewith, file annual, quarterly and special reports, proxy statements and other information with the SEC. These documents also may be accessed through the SEC's electronic data gathering, analysis and retrieval system, or EDGAR, via electronic means, including the SEC's home page on the Internet (www.sec.gov). You may also inspect the registration statement and this prospectus on this website.

We have the authority to designate and issue more than one class or series of stock having various preferences, conversion and other rights, voting powers, restrictions, limitations as to dividends, qualifications, and terms and conditions of redemption. We will furnish a full statement of the relative rights and preferences of each class or series of our stock which has been so designated and any restrictions on the ownership or transfer of our stock to any shareholder upon request and without charge. Written requests for such copies should be directed to Chiasma, Inc., 460 Totten Pond Road, Suite 530, Waltham, MA 02451, Attention: Secretary, or by telephoning us at (617) 928-5300. Our website is located at www.chiasmapharma.com. Information contained on our website is not incorporated by reference into this prospectus, and, except for the documents incorporated by reference as noted below, you should not consider any information on, or that can be accessed from, our website as part of this prospectus or any accompanying prospectus supplement.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to incorporate by reference into this prospectus supplement the information contained in other documents we file with the SEC, which means that we can disclose important information to you by referring you to those documents. Any statement contained in any document incorporated or deemed to be, incorporated by reference herein shall be deemed to be modified or superseded, for purposes of this prospectus supplement, to the extent that a statement contained in or omitted from this prospectus supplement, or in any other subsequently filed document that also is, or is deemed to be, incorporated by reference herein, modifies or supersedes such statement. Any such statement so modified or superseded shall not be deemed, except as so modified or superseded, to constitute a part of this prospectus supplement. We incorporate by reference the documents listed below, which have been filed by us:

- our Annual Report on [Form 10-K](#) for the year ended December 31, 2018, filed with the SEC on March 8, 2019;
- our Quarterly Report on [Form 10-Q](#) for the quarter ended March 31, 2019, filed with the SEC on May 9, 2019;
- our Current Reports on Form 8-K filed with the SEC on [March 29, 2019](#), [June 5, 2019](#), [June 17, 2019](#) and [July 23, 2019](#) (other than the portions of the filing that are furnished rather than filed pursuant to Items 2.02 and 7.01 of a Current Report on Form 8-K)
- our [Definitive Proxy Statement](#) on Schedule 14A filed with the SEC on April 29, 2019 (with respect to those portions incorporated by reference into our Annual Report on [Form 10-K](#) for the year ended December 31, 2018); and
- the description of our common stock contained in our registration statement on [Form 8-A](#) filed with the SEC on July 14, 2015, including any amendments or reports filed for the purposes of updating this description.

Additionally, all documents filed by us with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act (other than any portions of filings that are furnished rather than filed pursuant to Items 2.02 and 7.01 of a Current Report on Form 8-K), after the date of this prospectus supplement and before the termination or completion of this offering shall be deemed to be incorporated by reference into this prospectus supplement from the respective dates of filing of such documents. Any information that we subsequently file with the SEC that is incorporated by reference as described above will automatically update and supersede any previous information that is part of this prospectus supplement.

Upon written or oral request, we will provide you without charge, a copy of any or all of the documents incorporated by reference, other than exhibits to those documents unless the exhibits are specifically incorporated by reference in the documents. You may request a copy of any or all of these filings by writing to us at: Chiasma, Inc., 460 Totten Pond Road, Suite 530, Waltham, MA 02451, Attention: Secretary, or by telephoning us at (617) 928-5300.

PROSPECTUS

\$100,000,000

CHIASMA, INC.

**Common Stock
Preferred Stock
Debt Securities
Warrants
Units**

We may from time to time issue, in one or more series or classes, up to \$100,000,000 in aggregate principal amount of our common stock, preferred stock, debt securities, warrants and/or units. We may offer these securities separately or together in units. We will specify in the accompanying prospectus supplement the terms of the securities being offered. We may sell these securities to or through underwriters and also to other purchasers or through agents. We will set forth the names of any underwriters or agents, and any fees, conversions, or discount arrangements, in the accompanying prospectus supplement. We may not sell any securities under this prospectus without delivery of the applicable prospectus supplement.

You should read this document and any prospectus supplement or amendment carefully before you invest in our securities.

Our common stock is listed on The NASDAQ Global Select Market under the symbol "CHMA." On March 20, 2018, the closing price for our common stock, as reported on The NASDAQ Global Select Market, was \$1.55 per share. Our principal executive offices are located at 460 Totten Pond Road, Suite 530, Waltham, MA 02451.

Investing in our securities involves a high degree of risk. You should review carefully the risks and uncertainties described under the heading "[Risk Factors](#)" contained in this prospectus beginning on page 2 and any applicable prospectus supplement, and under similar headings in the other documents that are incorporated by reference into this prospectus.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

The date of this Prospectus is May 3, 2018.

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the Securities and Exchange Commission, or the SEC, using a “shelf” registration process. Under this shelf registration process, we may from time to time sell any combination of the securities described in this prospectus in one or more offerings for an aggregate initial offering price of up to \$100,000,000.

This prospectus provides you with a general description of the securities we may offer. Each time we sell securities, we will provide one or more prospectus supplements that will contain specific information about the terms of the offering. The prospectus supplement may also add, update or change information contained in this prospectus. You should read both this prospectus and the accompanying prospectus supplement together with the additional information described under the heading “Where You Can Find More Information”.

You should rely only on the information contained in or incorporated by reference in this prospectus, any accompanying prospectus supplement or in any related free writing prospectus filed by us with the SEC. We have not authorized anyone to provide you with different information. This prospectus and the accompanying prospectus supplement do not constitute an offer to sell or the solicitation of an offer to buy any securities other than the securities described in the accompanying prospectus supplement or an offer to sell or the solicitation of an offer to buy such securities in any circumstances in which such offer or solicitation is unlawful. You should assume that the information appearing in this prospectus, any prospectus supplement, the documents incorporated by reference and any related free writing prospectus is accurate only as of their respective dates. Our business, financial condition, results of operations and prospects may have changed materially since those dates.

Unless the context otherwise indicates, references in this prospectus to “Chiasma”, “we”, “our”, “us” and “the Company” refer, collectively, to Chiasma, Inc. and its subsidiaries.

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 logo” and our corporate logo. “CHIASMA”, “MYCAPSSA” and “TPE” are registered U.S. federal trademarks. All trademarks or trade names referred to in this prospectus are the property of their respective owners. Solely for convenience, the trademarks and trade names in this prospectus may be referred to without the ® and ™ symbols, but such references should not be construed as any indicator that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto.

RISK FACTORS

Investing in our securities involves a high degree of risk. You should carefully consider the risks described below and in the documents incorporated by reference in this prospectus and any prospectus supplement, as well as other information we include or incorporate by reference into this prospectus and any applicable prospectus supplement, before making an investment decision. Our business, financial condition or results of operations could be materially adversely affected by the materialization of any of these risks. The trading price of our securities could decline due to the materialization of any of these risks, and you may lose all or part of your investment. This prospectus and the documents incorporated herein by reference also contain forward-looking statements that involve risks and uncertainties. Actual results could differ materially from those anticipated in these forward-looking statements as a result of certain factors, including the risks described below and in the documents incorporated herein by reference, including (i) our annual report on Form 10-K for the fiscal year ended December 31, 2017, which is on file with the SEC and is incorporated herein by reference, and (ii) other documents we file with the SEC that are deemed incorporated by reference into this prospectus.

CAUTIONARY STATEMENT REGARDING FORWARD-LOOKING STATEMENTS

This prospectus, including the documents that we incorporate by reference, 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. Any statements about our expectations, beliefs, plans, objectives, assumptions or future events or performance are not historical facts and may be forward-looking. These statements are often, but are not always, made through the use of words or phrases such as “anticipate,” “believe,” “contemplate,” “continue,” “could,” “estimate,” “expect,” “intend,” “may,” “plan,” “potential,” “predict,” “project,” “seek,” “should,” “target,” “will,” “would,” and similar expressions, or the negative of these terms, or similar expressions. Accordingly, these statements involve estimates, assumptions and uncertainties which could cause actual results to differ materially from those expressed in them. Any forward-looking statements are qualified in their entirety by reference to the factors discussed throughout this report, and in particular those factors referenced in the section “Risk Factors.”

This prospectus contains forward-looking statements that are based on our management’s belief and assumptions and on information currently available to our management. These statements relate to future events or our future financial performance, and involve known and unknown risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to be materially different from any future results, levels of activity, performance or achievements expressed or implied by these forward-looking statements. Forward-looking statements include, but are not limited to, statements about:

- the U.S. regulatory review process of our New Drug Application, or NDA, for octreotide capsules in acromegaly, and our efforts to conduct and complete a new Phase 3 clinical trial of octreotide capsules in adult acromegaly patients per our agreement with the U.S. Food and Drug Administration, or the FDA, under a Special Protocol Assessment, or SPA, to potentially enable us to resubmit our NDA to the FDA in order to secure regulatory approval of octreotide capsules in acromegaly;
- our ability to preserve patients, sites and other resources necessary to enable us to simultaneously conduct two Phase 3 clinical trials in adult patients with acromegaly; one addressing the FDA’s concerns raised in the FDA’s April 2016 Complete Response Letter, and agreed to in a SPA, and the other to seek regulatory approval from the European Medicines Agency, or EMA; and to produce data packages from each trial that could be suitable for submission in both the United States and Europe;
- any regulatory approvals that may be issued or denied by the FDA, the EMA or other regulatory agencies for octreotide capsules in acromegaly or other indications;
- the therapeutic benefits, effectiveness and safety of octreotide capsules;
- our estimates of the size and characteristics of the markets that may be addressed by octreotide capsules;
- the commercial success and market acceptance of octreotide capsules or any future product candidates that are approved for marketing in the United States or other countries;
- our ability to generate future revenue;
- the number, designs, results and timing of our clinical trials of octreotide capsules and the timing of the commencement and availability of data from these trials;
- the safety and efficacy of therapeutics marketed by our competitors that are targeted to indications which octreotide capsules have been developed to treat;
- our ability to leverage our Transient Permeability Enhancer, or TPE, platform to develop and commercialize novel oral product candidates incorporating peptides that are currently only available in injectable or other non-absorbable forms;
- the possibility that competing products or technologies may make octreotide capsules, other product candidates we may develop and successfully commercialize or our TPE technology obsolete;

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- our ability to manufacture sufficient amounts of octreotide capsules for clinical trials and commercialization activities;
- our ability to secure collaborators to license, manufacture, market and sell octreotide capsules or any products for which we receive regulatory approval in the future;
- our ability to protect our intellectual property and operate our business without infringing upon the intellectual property rights of others;
- our product development and operational plans generally; and
- our estimates and expectations regarding our capital requirements, cash and expense levels and liquidity sources.

THE COMPANY

We are a clinical-stage biopharmaceutical company focused on improving the lives of patients who face challenges associated with their existing treatments for rare and serious chronic disease. Employing our proprietary Transient Permeability Enhancer, or TPE, technology platform, we seek to develop oral medications that are currently available only as injections. We are currently developing oral octreotide capsules, conditionally trade-named “MYCAPSSA”, our sole TPE platform-based clinical product candidate, in two Phase 3 clinical trials in adult patients for the treatment of acromegaly to potentially support regulatory approval in the United States and Europe. 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. 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 \$2.5 billion annually, of which we estimate approximately \$775 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 United States Food and Drug Administration, or the FDA, on the design of the trial, reached through a Special Protocol Assessment, or SPA, in August 2017. The trial, referred to as CHIASMA OPTIMAL, is 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. We expect to release top-line data from this trial by the end of 2019. 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 Europe. The MPOWERED trial is a global, randomized, open-label and active-controlled 15-month trial expected to enroll approximately 130 adult acromegaly patients, of which we expect to randomize at least 80 patients who are responders to octreotide capsules following a six-month run-in to either octreotide capsules or injectable somatostatin receptor ligands (octreotide or lanreotide), and then followed for an additional nine months. We currently expect to release top-line data from the MPOWERED trial in 2020.

Octreotide capsules is the first somatostatin analog formulated for oral administration to complete a Phase 3 clinical trial. In November 2014, we completed a multinational open-label Phase 3 clinical trial of oral octreotide capsules for the treatment of acromegaly. Our original New Drug Application, or NDA, for octreotide capsules was submitted in June 2015 and accepted for filing by the FDA in August 2015. In April 2016, the FDA issued a complete response letter, or CRL, which indicated that the review of our application was complete and that our NDA was not ready for approval in its present form. In June 2016, we participated in an End of Review meeting with the FDA to discuss the concerns the FDA raised in the CRL. In its CRL, the FDA advised us that it did not believe our NDA had provided substantial evidence of efficacy to warrant approval, and advised us that we would need to conduct another clinical trial in order to overcome this deficiency. The FDA expressed concerns regarding certain aspects of our single-arm, open-label Phase 3 clinical trial and strongly recommended that we conduct a randomized, double-blind and controlled trial that enrolls patients from the United States and is of sufficiently long duration to ensure that control of disease activity is stable at the time point selected for the primary efficacy assessment. In addition, the FDA advised that, during a site inspection, certain deficiencies were conveyed to the representative of one of our suppliers that would need to be resolved before approval. While the FDA did not note any safety concerns related to octreotide capsules in the CRL, it subsequently indicated in the June 2016 End of Review meeting minutes that the size, duration, dropout rate and absence of a control group in our 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.

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,

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to potentially enable us to resubmit the NDA in order to secure regulatory approval of octreotide capsules in acromegaly. The trial, referred to as CHIASMA OPTIMAL (Octreotide capsules vs. Placebo Treatment In Multinational centers), which we initiated in September 2017, is a randomized, double-blind, placebo-controlled, nine-month clinical trial in 50 adult acromegaly patients (at least 20% of whom must be recruited from the United States) whose disease is biochemically controlled, based upon levels of insulin-like growth factor 1, or IGF-1, a byproduct of increased growth hormone, or GH, levels caused by acromegaly, on injectable somatostatin analogs at baseline (average $IGF-1 \leq 1.0 \times$ upper limit of normal (ULN)). The patients must also have confirmed active acromegaly following their last surgical intervention based upon an elevated IGF-1 at that time of $\leq 1.3 \times$ ULN. The trial will be randomized on a 1:1 basis to octreotide capsules or placebo. Patients will be 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. Patients meeting predefined biochemical failure withdrawal criteria in either treatment arm during the course of the trial will be considered treatment failures and revert to their original treatment of injections and will be monitored for the remainder of the trial. The primary endpoint of the study is the proportion of patients who maintain their biochemical response compared to placebo at the end of the nine-month double-blind, placebo controlled period as measured using the average of the last two IGF-1 levels $\leq 1.0 \times$ ULN.

The hierarchical secondary endpoints that will be considered by the FDA in evaluating the totality of evidence for octreotide capsules treatment effect include:

- Proportion of patients who maintain GH response at week 36 compared to screening;
- Time to loss of response: $IGF-1 > 1.0 \times ULN$;
- Time to loss of response: $IGF-1 > 1.3 \times ULN$;
- Change from screening to end of treatment in mean GH; and
- Change in IGF-1 from baseline to end of treatment.

The FDA required that the last two secondary endpoints be analyzed by comparing the octreotide capsules treatment arm to the placebo treatment arm at the end of the nine month, double-blind placebo controlled phase, including those patients that have been rescued by injectable somatostatin analogs. We estimate that as many as 90% or more, of the placebo-treated patients may require rescue therapy. As such, we have agreed to analyze the octreotide capsules treatment arm versus the placebo arm at the end of the study. We expect in particular the placebo arm will be highly populated with patients on injectable somatostatin analog rescue therapy. This analysis is referred to in statistical parlance as an ITT estimand. While we do not believe that superiority of Mycapssa will be demonstrated in these last two endpoints, we do believe that if we statistically achieve the primary efficacy endpoint, that is, the proportion of patients who maintain their biochemical response compared to placebo at the end of the nine-month double-blind placebo controlled period, and successfully achieve superiority in the higher-priority secondary endpoints, the totality of evidence supporting a robust treatment effect of octreotide capsules should be clear from the OPTIMAL trial. We anticipate that the FDA will review the totality of the data collected from the CHIASMA OPTIMAL trial, including both primary and secondary endpoints and whether the data collected are sufficiently robust to support the interpretability of these analyses, in determining whether to approve our NDA, if submitted, for the marketing and sale of octreotide capsules. There can be no assurance that the data collected from the CHIASMA OPTIMAL trial will be sufficient to support approval of our NDA, if submitted, for the marketing and sale of octreotide capsules. An open-label extension phase is planned following the nine-month study, which could enable patients who completed the randomized phase to continue receiving octreotide capsules and for us to collect long-term safety information. The results of the extension phase are not required as the basis for an efficacy claim.

In March 2016, in support of potential approval in Europe, we initiated an additional international Phase 3 clinical trial of octreotide capsules in acromegaly — MPOWERED — designed to show parallel comparative safety and effectiveness as required by the European Medicines Agency, or EMA. Assuming we receive

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favorable results from this second Phase 3 clinical trial in octreotide capsules, we expect to submit a Marketing Authorization Application, or MAA, to the EMA. Following the FDA's position that the MPOWERED clinical trial will not be sufficient to address the concerns in the CRL, in late 2016, we modified certain elements of the MPOWERED trial in an effort to preserve patients, sites and other resources necessary to conduct the CHIASMA OPTIMAL Phase 3 trial addressing the FDA's concerns and produce data packages suitable for submission in both the United States and the European Union. We now believe that approximately 130 patients will be required to enter the 6-month run-in phase of the trial in order to achieve the target 80 octreotide capsules responders randomized to the 9-month comparator phase of the 15-month trial, the number requested by the EMA. Based upon our first completed Phase 3 trial experience with octreotide capsules, we had estimated approximately 150 patients would be required to enter the run-in phase. Thus far, the aggregate number of patients withdrawing or not responding to octreotide capsules during the run-in phase is lower than originally expected. In September 2017, we announced that we had surpassed 50% patients randomized in the MPOWERED trial.

Importantly, we expect that the safety and efficacy data generated in all of our clinical trials of octreotide capsules, including our completed phase 3 clinical trial, the CHIASMA OPTIMAL clinical trial and the MPOWERED clinical trial, to the extent such data is available at the time of filing, will be integrated into our planned NDA, if resubmitted, and planned MAA filing. While CHIASMA OPTIMAL has been 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 each planned application for marketing approval could be impacted by the trial results from any of our clinical trials.

Acromegaly is a condition caused by a benign tumor of the pituitary gland that releases excess GH, which in turn elevates 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.

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 significant limitations and patient burdens, including suboptimal symptom control, pain, injection-site reactions and other injection-related side effects, inconvenience, lost work days and emotional issues. Based on data reviewed in early 2016, 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 accounts. Patients with acromegaly undergoing treatment in the United States are 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.

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

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We were incorporated in 2001 and commenced active operations in the same year. Our operations to date have been limited to organizing and staffing our company, business planning, raising capital, developing our TPE technology, identifying potential drug candidates, undertaking nonclinical studies and, beginning in 2010, conducting clinical trials and preparing for regulatory submissions. To date, we have financed our operations primarily through private placements, funding received from a licensing agreement, a loan agreement and our initial public offering. We have no products approved for sale and all of our historical revenue has been related to one license agreement, which has been terminated.

Our principal executive offices are located at 460 Totten Pond Road, Suite 530, Waltham, MA 02451 and our telephone number is (617) 928-5300.

RATIO OF EARNINGS TO FIXED CHARGES

The following table sets forth our ratio of earnings to fixed charges for the periods shown. You should read this table in conjunction with the financial statements and notes incorporated by reference in this prospectus. We have no preferred shares outstanding and paid no dividends on preferred shares during the periods indicated. Therefore, the ratios of earnings to combined fixed charges and preferred dividends are the same as the ratios of earnings to fixed charges presented below.

	Years Ended December 31,				
	2017	2016	2015	2014	2013
Ratio of Earnings to Fixed Charges	<u>N/A</u>	<u>N/A</u>	<u>N/A</u>	<u>N/A</u>	<u>35.22</u>

For purposes of calculating the ratios in the table above, earnings consist of net loss before income taxes. Fixed charges include interest expense on indebtedness and an estimate of the interest expense within rental expense.

Due to our net losses for the years ended December 31, 2017, 2016, 2015 and 2014, earnings were insufficient to cover fixed charges for such periods and we are unable to disclose a ratio of earnings to fixed charges for such periods. The dollar amount of the deficiency in earnings available for fixed charges for the years ended December 31, 2017, 2016, 2015, and 2014 was approximately \$27.4 million, \$60.8 million, \$35.7 million and \$1.8 million, respectively.

USE OF PROCEEDS

We intend to use the net proceeds from the sale of any securities offered under this prospectus for general corporate purposes unless otherwise indicated in the applicable prospectus supplement. General corporate purposes may include research and development costs, including the conduct of one or more clinical trials, potential strategic acquisitions of complementary businesses, services or technologies, expansion of our technology infrastructure and capabilities, working capital, capital expenditures and general corporate purposes. We may temporarily invest the net proceeds in a variety of capital preservation instruments, including investment grade, interest bearing instruments and U.S. government securities, until they are used for their stated purpose. We have not determined the amount of net proceeds to be used specifically for such purposes. As a result, management will retain broad discretion over the allocation of net proceeds.

SECURITIES WE MAY OFFER

This prospectus contains summary descriptions of the securities we may offer from time to time. These summary descriptions are not meant to be complete descriptions of each security. The particular terms of any security will be described in the applicable prospectus supplement.

DESCRIPTION OF CAPITAL STOCK

The following description of our common stock and preferred stock, together with the additional information we include in any applicable prospectus supplements, summarizes the material terms and provisions of the common stock and preferred stock that we may offer under this prospectus. The following description of our capital stock does not purport to be complete and is subject to, and qualified in its entirety by, our Amended and Restated Certificate of Incorporation and our Amended and Restated Bylaws, which are exhibits to the registration statement of which this prospectus forms a part, and by applicable law. We refer in this section to our Amended and Restated Certificate of Incorporation as our “certificate of incorporation”, and we refer to our Amended and Restated Bylaws as our “bylaws.” The terms of our common stock and preferred stock may also be affected by Delaware law.

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. As of March 20, 2018, we had 24,383,994 shares of common stock outstanding and no shares of preferred stock outstanding.

Common Stock

Holders of our common stock are entitled to one vote for each share held of record on all matters submitted to a vote of shareholders and 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. All outstanding shares are fully-paid and non-assessable.

Listing

Our common stock is listed on The NASDAQ Global Select Market under the symbol “CHMA.” On March 20, 2018, the closing price for our common stock, as reported on The NASDAQ Global Select Market, was \$1.55 per share.

Transfer Agent and Registrar

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

Preferred Stock

Our board of directors is authorized to issue up to 5,000,000 shares of preferred stock in one or more series without shareholder approval. Our board of directors may determine the rights, preferences, privileges and restrictions, including voting rights, dividend rights, conversion rights, redemption privileges and liquidation preferences, of each series of preferred stock.

The purpose of authorizing our board of directors to issue preferred stock in one or more series and determine the number of shares in the series and its rights and preferences is to eliminate delays associated with a shareholder vote on specific issuances. Examples of rights and preferences that the board of directors may fix are:

- dividend rights;

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- dividend rates;
- conversion rights;
- voting rights;
- terms of redemption; and
- liquidation preferences.

The existence of authorized but unissued shares of preferred stock may enable our board of directors to render more difficult or to discourage an attempt to obtain control of us by means of a merger, tender offer, proxy contest or otherwise. For example, if in the due exercise of its fiduciary obligations, our board of directors were to determine that a takeover proposal is not in the best interests of us or our stockholders, our board of directors could cause shares of preferred stock to be issued without stockholder approval in one or more private offerings or other transactions that might dilute the voting or other rights of the proposed acquirer, stockholder or stockholder group. The rights of holders of our common stock described above will be subject to, and may be adversely affected by, the rights of any preferred stock that we may designate and issue in the future. The issuance of shares of preferred stock could decrease the amount of earnings and assets available for distribution to holders of shares of common stock. The issuance may also adversely affect the rights and powers, including voting rights, of these holders and may have the effect of delaying, deterring or preventing a change in control of us.

We will incorporate by reference as an exhibit to the registration statement, which includes this prospectus, the form of any certificate of designation that describes the terms of the series of preferred stock we are offering. This description and the applicable prospectus supplement will include:

- the title and stated value;
- the number of shares authorized;
- the liquidation preference per share;
- the purchase price;
- the dividend rate, period and payment date, and method of calculation for dividends;
- whether dividends will be cumulative or non-cumulative and, if cumulative, the date from which dividends will accumulate;
- the procedures for any auction and remarketing, if any;
- the provisions for a sinking fund, if any;
- the provisions for redemption or repurchase, if applicable, and any restrictions on our ability to exercise those redemption and repurchase rights;
- any listing of the preferred stock on any securities exchange or market;
- whether the preferred stock will be convertible into our common stock, and, if applicable, the conversion price, or how it will be calculated, and the conversion period;
- whether the preferred stock will be exchangeable into debt securities, and, if applicable, the exchange price, or how it will be calculated, and the exchange period;
- voting rights, if any, of the preferred stock;
- preemptive rights, if any;
- restrictions on transfer, sale or other assignment, if any;
- whether interests in the preferred stock will be represented by depositary shares;

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- a discussion of any material United States federal income tax considerations applicable to the preferred stock;
- the relative ranking and preferences of the preferred stock as to dividend rights and rights if we liquidate, dissolve or wind up our affairs;
- any limitations on issuance of any class or series of preferred stock ranking senior to or on a parity with the series of preferred stock as to dividend rights and rights if we liquidate, dissolve or wind up our affairs; and
- any other specific terms, preferences, rights or limitations of, or restrictions on, the preferred stock.

When we issue shares of preferred stock under this prospectus, the shares will fully be paid and nonassessable and will not have, or be subject to, any preemptive or similar rights.

Provisions of our Certificate of Incorporation and Bylaws and Delaware Anti-Takeover Law

Certain provisions of the Delaware General Corporation Law and of our certificate of incorporation and bylaws could have the effect of delaying, deferring or discouraging another party from acquiring control of us. These provisions, which are summarized below, are expected to discourage certain types of coercive takeover practices and inadequate takeover bids and, as a consequence, they might also inhibit temporary fluctuations in the market price of our common stock that often result from actual or rumored hostile takeover attempts. These provisions are also designed in part to encourage anyone seeking to acquire control of us or considering unsolicited tender offers or other unilateral takeover proposals to first negotiate with our board of directors rather than pursue non-negotiated takeover attempts. These provisions might also have the effect of preventing changes in our management. It is possible that these provisions could make it more difficult to accomplish transactions that stockholders might otherwise deem to be in their best interests. However, we believe that the advantages gained by protecting our ability to negotiate with any unsolicited and potentially unfriendly acquirer outweigh the disadvantages of discouraging such proposals, including those priced above the then-current market value of our common stock, because, among other reasons, the negotiation of such proposals could improve their terms.

Board Composition and Filling Vacancies.

Our certificate of incorporation provides for a classified board of directors consisting of three classes of directors, each of which shall consist, as nearly as may be possible, of one-third of the total number of directors. Each class serves for a staggered three-year term. Our certificate of incorporation also provides that directors may be removed only with cause and only by the affirmative vote of the holders of 75% or more of the voting power of the outstanding shares of capital stock entitled to vote thereon. Furthermore, any vacancy on our board of directors, however occurring, including a vacancy resulting from an increase in the size of our board, may only be filled by the affirmative vote of a majority of our directors then in office even if less than a quorum.

No Written Consent of Stockholders.

Our certificate of incorporation provides that all stockholder actions are required to be taken by a vote of the stockholders at an annual or special meeting, and that stockholders may not take any action by written consent in lieu of a meeting.

Meetings of Stockholders.

Our certificate of incorporation and bylaws provide that only a majority of the members of our board of directors then in office may call special meetings of stockholders and only those matters set forth in the notice of the special meeting may be considered or acted upon at a special meeting of stockholders. Our bylaws limit the business that may be conducted at an annual meeting of stockholders to those matters properly brought before the meeting.

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Advance Notice Requirements.

Our bylaws establish advance notice procedures with regard to stockholder proposals relating to the nomination of candidates for election as directors or new business to be brought before meetings of our stockholders. These procedures provide that notice of stockholder proposals must be timely given in writing to our corporate secretary prior to the meeting at which the action is to be taken. Generally, to be timely, notice must be received at our principal executive offices not less than 90 days nor more than 120 days prior to the first anniversary date of the annual meeting for the preceding year. Our bylaws specify the requirements as to form and content of all stockholders' notices.

Amendment to Certificate of Incorporation and Bylaws. As required by the Delaware General Corporation Law, any amendment of our certificate of incorporation must first be approved by a majority of our board of directors, and if required by law or our certificate of incorporation, must thereafter be approved by a majority of the outstanding shares entitled to vote on the amendment and a majority of the outstanding shares of each class entitled to vote thereon as a class, except that the amendment of the provisions relating to stockholder action, board composition, limitation of liability and the amendment of our certificate of incorporation must be approved by not less than 75% of the outstanding shares entitled to vote on the amendment, and not less than 75% of the outstanding shares of each class entitled to vote thereon as a class. Our bylaws may be amended by the affirmative vote of a majority of the directors then in office, subject to any limitations set forth in the bylaws; and may also be amended by the affirmative vote of at least 75% of the outstanding shares entitled to vote on the amendment, or, if our board of directors recommends that the stockholders approve the amendment, by the affirmative vote of the majority of the outstanding shares entitled to vote on the amendment, in each case voting together as a single class.

Delaware Anti-Takeover 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. A "business combination" includes, among other things, a merger, asset or stock sale or other transaction resulting in a financial benefit to the interested stockholder. An "interested stockholder" is a person who, together with affiliates and associates, owns, or did own within three years prior to the determination of interested stockholder status, 15% or more of the corporation's voting stock. Under Section 203, a business combination between a corporation and an interested stockholder is prohibited unless it satisfies one of the following conditions:

- before the stockholder became interested, the board of directors approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder;
- upon consummation of the transaction which resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 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; or
- at or after the time the stockholder became interested, the business combination was approved by the board of directors of the corporation and authorized at an annual or special meeting of the stockholders by the affirmative vote of at least two-thirds of the outstanding voting stock which is not owned by the interested stockholder.

Exclusive Jurisdiction of Certain Actions.

Our certificate of incorporation provides 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 (i) any derivative

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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 arising pursuant to any provision of the Delaware General Corporation Law, our certificate of incorporation or our bylaws, or (iv) any action asserting a claim against us governed by the internal affairs doctrine. 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 have the effect of discouraging lawsuits against our directors and officers. 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.

DESCRIPTION OF DEBT SECURITIES

The paragraphs below describe the general terms and provisions of the debt securities we may issue. When we offer to sell a particular series of debt securities, we will describe the specific terms of the securities in a supplement to this prospectus, including any additional covenants or changes to existing covenants relating to such series. The prospectus supplement also will indicate whether the general terms and provisions described in this prospectus apply to a particular series of debt securities. You should read the actual indenture if you do not fully understand a term or the way we use it in this prospectus.

We may offer senior or subordinated debt securities. Each series of debt securities may have different terms. The senior debt securities will be issued under one or more senior indentures, dated as of a date prior to such issuance, between us and the trustee identified in the applicable prospectus supplement, as amended or supplemented from time to time. We will refer to any such indenture throughout this prospectus as the “senior indenture.” Any subordinated debt securities will be issued under one or more separate indentures, dated as of a date prior to such issuance, between us and the trustee identified in the applicable prospectus supplement, as amended or supplemented from time to time. We will refer to any such indenture throughout this prospectus as the “subordinated indenture” and to the trustee under the senior or subordinated indenture as the “trustee.” The senior indenture and the subordinated indenture are sometimes collectively referred to in this prospectus as the “indentures.” The indentures will be subject to and governed by the Trust Indenture Act of 1939, as amended. We included copies of the forms of the indentures as exhibits to our registration statement and they are incorporated into this prospectus by reference.

If we issue debt securities at a discount from their principal amount, then, for purposes of calculating the aggregate initial offering price of the offered securities issued under this prospectus, we will include only the initial offering price of the debt securities and not the principal amount of the debt securities.

We have summarized below the material provisions of the indentures and the debt securities, or indicated which material provisions will be described in the related prospectus supplement. The prospectus supplement relating to any particular securities offered will describe the specific terms of the securities, which may be in addition to or different from the general terms summarized in this prospectus. Because the summary in this prospectus and in any prospectus supplement does not contain all of the information that you may find useful, you should read the documents relating to the securities that are described in this prospectus or in any applicable prospectus supplement. Please read “Where You Can Find More Information” to find out how you can obtain a copy of those documents. Except as otherwise indicated, the terms of the indentures are identical. As used under this caption, the term “debt securities” includes the debt securities being offered by this prospectus and all other debt securities issued by us under the indentures.

General

The indentures:

- do not limit the amount of debt securities that we may issue;
- allow us to issue debt securities in one or more series;
- do not require us to issue all of the debt securities of a series at the same time;
- allow us to reopen a series to issue additional debt securities without the consent of the holders of the debt securities of such series; and
- provide that the debt securities will be unsecured, except as may be set forth in the applicable prospectus supplement.

Unless we give you different information in the applicable prospectus supplement, the senior debt securities will be unsubordinated obligations and will rank equally with all of our other senior unsecured and

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unsubordinated indebtedness. Payments on the subordinated debt securities will be subordinated to the prior payment in full of all of our senior indebtedness, as described under “Description of Debt Securities — Subordination” and in the applicable prospectus supplement.

Each indenture provides that we may, but need not, designate more than one trustee under an indenture. Any trustee under an indenture may resign or be removed and a successor trustee may be appointed to act with respect to the series of debt securities administered by the resigning or removed trustee. If two or more persons are acting as trustee with respect to different series of debt securities, each trustee shall be a trustee of a trust under the applicable indenture separate and apart from the trust administered by any other trustee. Except as otherwise indicated in this prospectus, any action described in this prospectus to be taken by each trustee may be taken by each trustee with respect to, and only with respect to, the one or more series of debt securities for which it is trustee under the applicable indenture.

The prospectus supplement for each offering will provide the following terms, where applicable:

- the title of the debt securities and whether they are senior or subordinated;
- the aggregate principal amount of the debt securities being offered, the aggregate principal amount of the debt securities outstanding as of the most recent practicable date and any limit on their aggregate principal amount, including the aggregate principal amount of debt securities authorized;
- the price at which the debt securities will be issued, expressed as a percentage of the principal and, if other than the principal amount thereof, the portion of the principal amount thereof payable upon declaration of acceleration of the maturity thereof or, if applicable, the portion of the principal amount of such debt securities that is convertible into common stock or other securities of ours or the method by which any such portion shall be determined;
- if convertible, the terms on which such debt securities are convertible, including the initial conversion price or rate and the conversion period and any applicable limitations on the ownership or transferability of common stock or other securities of ours received on conversion;
- the date or dates, or the method for determining the date or dates, on which the principal of the debt securities will be payable;
- the fixed or variable interest rate or rates of the debt securities, or the method by which the interest rate or rates is determined;
- the date or dates, or the method for determining the date or dates, from which interest will accrue;
- the dates on which interest will be payable;
- the record dates for interest payment dates, or the method by which such dates will be determined;
- the persons to whom interest will be payable;
- the basis upon which interest will be calculated if other than that of a 360-day year of twelve 30-day months;
- any make-whole amount, which is the amount in addition to principal and interest that is required to be paid to the holder of a debt security as a result of any optional redemption or accelerated payment of such debt security, or the method for determining the make-whole amount;
- the place or places where the principal of, and any premium or make-whole amount, and interest on, the debt securities will be payable;
- where the debt securities may be surrendered for registration of transfer or conversion or exchange;
- where notices or demands to or upon us in respect of the debt securities and the applicable indenture may be served;

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- the times, prices and other terms and conditions upon which we may redeem the debt securities;
- any obligation we have to redeem, repay or purchase the debt securities pursuant to any sinking fund or analogous provision or at the option of holders of the debt securities, and the times and prices at which we must redeem, repay or purchase the debt securities as a result of such obligation;
- the currency or currencies in which the debt securities are denominated and payable if other than United States dollars, which may be a foreign currency or units of two or more foreign currencies or a composite currency or currencies and the terms and conditions relating thereto, and the manner of determining the equivalent of such foreign currency in United States dollars;
- whether the principal of, and any premium or make-whole amount, or interest on, the debt securities of the series are to be payable, at our election or at the election of a holder, in a currency or currencies other than that in which the debt securities are denominated or stated to be payable, and other related terms and conditions;
- whether the amount of payments of principal of, and any premium or make-whole amount, or interest on, the debt securities may be determined according to an index, formula or other method and how such amounts will be determined;
- whether the debt securities will be in registered form, bearer form, or both, and (i) if in registered form, the person to whom any interest shall be payable, if other than the person in whose name the security is registered at the close of business on the regular record date for such interest, or (ii) if in bearer form, the manner in which, or the person to whom, any interest on the security shall be payable if otherwise than upon presentation and surrender upon maturity;
- any restrictions applicable to the offer, sale or delivery of securities in bearer form and the terms upon which securities in bearer form of the series may be exchanged for securities in registered form of the series and vice versa, if permitted by applicable laws and regulations;
- whether any debt securities of the series are to be issuable initially in temporary global form and whether any debt securities of the series are to be issuable in permanent global form with or without coupons and, if so, whether beneficial owners of interests in any such permanent global security may, or shall be required to, exchange their interests for other debt securities of the series, and the manner in which interest shall be paid;
- the identity of the depositary for securities in registered form, if such series are to be issuable as a global security;
- the date as of which any debt securities in bearer form or in temporary global form shall be dated if other than the original issuance date of the first security of the series to be issued;
- the applicability, if any, of the defeasance and covenant defeasance provisions described in this prospectus or in the applicable indenture;
- whether and under what circumstances we will pay any additional amounts on the debt securities in respect of any tax, assessment or governmental charge and, if so, whether we will have the option to redeem the debt securities in lieu of making such a payment;
- whether and under what circumstances the debt securities being offered are convertible into common stock or other securities of ours, as the case may be, including the conversion price or rate and the manner or calculation thereof;
- the circumstances, if any, specified in the applicable prospectus supplement, under which beneficial owners of interests in the global security may obtain definitive debt securities and the manner in which payments on a permanent global debt security will be made if any debt securities are issuable in temporary or permanent global form;
- any provisions granting special rights to holders of securities upon the occurrence of such events as specified in the applicable prospectus supplement;

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- if the debt securities of such series are to be issuable in definitive form only upon receipt of certain certificates or other documents or satisfaction of other conditions, then the form and/or terms of such certificates, documents or conditions;
- the name of the applicable trustee and the nature of any material relationship with us or any of our affiliates, and the percentage of debt securities of the class necessary to require the trustee to take action;
- any deletions from, modifications of or additions to our events of default or covenants with regard to such debt securities and any change in the right of any trustee or any of the holders to declare the principal amount of any of such debt securities due and payable;
- applicable CUSIP numbers; and
- any other terms of such debt securities not inconsistent with the provisions of the applicable indenture.

We may issue debt securities that provide for less than the entire principal amount thereof to be payable upon declaration of acceleration of the maturity of the debt securities. We refer to any such debt securities throughout this prospectus as “original issue discount securities.” The applicable prospectus supplement will describe the United States federal income tax consequences and other relevant considerations applicable to original issue discount securities.

We also may issue indexed debt securities. Payments of principal of, and premium and interest on, indexed debt securities are determined with reference to the rate of exchange between the currency or currency unit in which the debt security is denominated and any other currency or currency unit specified by us, to the relationship between two or more currencies or currency units or by other similar methods or formulas specified in the prospectus supplement.

Except as described under “— Merger, Consolidation or Sale of Assets” or as may be set forth in any prospectus supplement, the debt securities will not contain any provisions that (i) would limit our ability to incur indebtedness or (ii) would afford holders of debt securities protection in the event of (a) a highly leveraged or similar transaction involving us, or (b) a change of control or reorganization, restructuring, merger or similar transaction involving us that may adversely affect the holders of the debt securities. In the future, we may enter into transactions, such as the sale of all or substantially all of our assets or a merger or consolidation, that may have an adverse effect on our ability to service our indebtedness, including the debt securities, by, among other things, substantially reducing or eliminating our assets.

Our governing instruments do not define the term “substantially all” as it relates to the sale of assets. Additionally, Delaware cases interpreting the term “substantially all” rely upon the facts and circumstances of each particular case. Consequently, to determine whether a sale of “substantially all” of our assets has occurred, a holder of debt securities must review the financial and other information that we have disclosed to the public.

We will provide you with more information in the applicable prospectus supplement regarding any deletions, modifications, or additions to the events of default or covenants that are described below, including any addition of a covenant or other provision providing event risk or similar protection.

Payment

Unless we give you different information in the applicable prospectus supplement, the principal of, and any premium or make-whole amount, and interest on, any series of the debt securities will be payable at the corporate trust office of the trustee. We will provide you with the address of the trustee in the applicable prospectus supplement. We may also pay interest by mailing a check to the address of the person entitled to it as it appears in the applicable register for the debt securities or by wire transfer of funds to that person at an account maintained within the United States.

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All monies that we pay to a paying agent or a trustee for the payment of the principal of, and any premium or make-whole amount, or interest on, any debt security will be repaid to us if unclaimed at the end of two years after the obligation underlying payment becomes due and payable. After funds have been returned to us, the holder of the debt security may look only to us for payment, without payment of interest for the period which we hold the funds.

Denomination, Interest, Registration and Transfer

Unless otherwise described in the applicable prospectus supplement, the debt securities of any series will be issuable in denominations of \$1,000 and integral multiples of \$1,000.

Subject to the limitations imposed upon debt securities that are evidenced by a computerized entry in the records of a depository company rather than by physical delivery of a note, a holder of debt securities of any series may:

- exchange them for any authorized denomination of other debt securities of the same series and of a like aggregate principal amount and kind upon surrender of such debt securities at the corporate trust office of the applicable trustee or at the office of any transfer agent that we designate for such purpose; and
- surrender them for registration of transfer or exchange at the corporate trust office of the applicable trustee or at the office of any transfer agent that we designate for such purpose.

Every debt security surrendered for registration of transfer or exchange must be duly endorsed or accompanied by a written instrument of transfer satisfactory to the applicable trustee or transfer agent. Payment of a service charge will not be required for any registration of transfer or exchange of any debt securities, but we or the trustee may require payment of a sum sufficient to cover any tax or other governmental charge payable in connection therewith. If in addition to the applicable trustee, the applicable prospectus supplement refers to any transfer agent initially designated by us for any series of debt securities, we may at any time rescind the designation of any such transfer agent or approve a change in the location through which any such transfer agent acts, except that we will be required to maintain a transfer agent in each place of payment for such series. We may at any time designate additional transfer agents for any series of debt securities.

Neither we, nor any trustee, will be required to:

- issue, register the transfer of or exchange debt securities of any series during a period beginning at the opening of business 15 days before the day that the notice of redemption of any debt securities selected for redemption is mailed and ending at the close of business on the day of such mailing;
- register the transfer of or exchange any debt security, or portion thereof, so selected for redemption, in whole or in part, except the unredeemed portion of any debt security being redeemed in part; and
- issue, register the transfer of or exchange any debt security that has been surrendered for repayment at the option of the holder, except the portion, if any, of such debt security not to be so repaid.

Merger, Consolidation or Sale of Assets

The indentures provide that we may, without the consent of the holders of any outstanding debt securities, (i) consolidate with, (ii) sell, lease or convey all or substantially all of our assets to, or (iii) merge with or into, any other entity provided that:

- either we are the continuing entity, or the successor entity, if other than us, assumes the obligations (a) to pay the principal of, and any premium or make-whole amount, and interest on, all of the debt securities and (b) to duly perform and observe all of the covenants and conditions contained in each indenture;

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- after giving effect to the transaction, there is no event of default under the indentures and no event which, after notice or the lapse of time, or both, would become such an event of default, occurs and continues; and
- an officers' certificate and legal opinion covering such conditions are delivered to each applicable trustee.

Covenants

Existence. Except as described under “— Merger, Consolidation or Sale of Assets,” the indentures require us to do or cause to be done all things necessary to preserve and keep in full force and effect our existence, rights and franchises. However, the indentures do not require us to preserve any right or franchise if we determine that any right or franchise is no longer desirable in the conduct of our business.

Payment of taxes and other claims. The indentures require us to pay, discharge or cause to be paid or discharged, before they become delinquent (i) all taxes, assessments and governmental charges levied or imposed on us, and (ii) all lawful claims for labor, materials and supplies which, if unpaid, might by law become a lien upon our property. However, we will not be required to pay, discharge or cause to be paid or discharged any such tax, assessment, charge or claim whose amount, applicability or validity is being contested in good faith by appropriate proceedings.

Provision of financial information. The indentures require us to (i) within 15 days of each of the respective dates by which we are required to file our annual reports, quarterly reports and other documents with the SEC, file with the trustee copies of the annual report, quarterly report and other documents that we file with the SEC under Section 13 or 15(d) of the Exchange Act, (ii) file with the trustee and the SEC any additional information, documents and reports regarding compliance by us with the conditions and covenants of the indentures, as required, (iii) within 30 days after the filing with the trustee, mail to all holders of debt securities, as their names and addresses appear in the applicable register for such debt securities, without cost to such holders, summaries of any documents and reports required to be filed by us pursuant to (i) and (ii) above, and (iv) supply, promptly upon written request and payment of the reasonable cost of duplication and delivery, copies of such documents to any prospective holder.

Additional covenants. The applicable prospectus supplement will set forth any of our additional covenants relating to any series of debt securities.

Events of Default, Notice and Waiver

Unless the applicable prospectus supplement states otherwise, when we refer to “events of default” as defined in the indentures with respect to any series of debt securities, we mean:

- default in the payment of any installment of interest on any debt security of such series continuing for 30 days;
- default in the payment of principal of, or any premium or make-whole amount on, any debt security of such series for five business days at its stated maturity;
- default in making any sinking fund payment as required for any debt security of such series for five business days;
- default in the performance or breach of any covenant or warranty in the debt securities or in the indenture by us continuing for 60 days after written notice as provided in the applicable indenture, but not of a covenant added to the indenture solely for the benefit of a series of debt securities issued thereunder other than such series;
- a default under any bond, debenture, note, mortgage, indenture or instrument:
 - (i) having an aggregate principal amount of at least \$30,000,000; or

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- (ii) under which there may be issued, secured or evidenced any existing or later created indebtedness for money borrowed by us, if we are directly responsible or liable as obligor or guarantor,
- if the default results in the indebtedness becoming or being declared due and payable prior to the date it otherwise would have, without such indebtedness having been discharged, or such acceleration having been rescinded or annulled, within 30 days after notice to the issuing company specifying such default. Such notice shall be given to us by the trustee, or to us and the trustee by the holders of at least 10% in principal amount of the outstanding debt securities of that series. The written notice shall specify such default and require us to cause such indebtedness to be discharged or cause such acceleration to be rescinded or annulled and shall state that such notice is a "Notice of Default" under such indenture;
- bankruptcy, insolvency or reorganization, or court appointment of a receiver, liquidator or trustee of us; and
 - any other event of default provided with respect to a particular series of debt securities.

If an event of default occurs and is continuing with respect to debt securities of any series outstanding, then the applicable trustee or the holders of 25% or more in principal amount of the debt securities of that series will have the right to declare the principal amount of all the debt securities of that series to be due and payable. If the debt securities of that series are original issue discount securities or indexed securities, then the applicable trustee or the holders of 25% or more in principal amount of the debt securities of that series will have the right to declare the portion of the principal amount as may be specified in the terms thereof to be due and payable. However, at any time after such a declaration of acceleration has been made, but before a judgment or decree for payment of the money due has been obtained by the applicable trustee, the holders of at least a majority in principal amount of outstanding debt securities of such series or of all debt securities then outstanding under the applicable indenture may rescind and annul such declaration and its consequences if:

- we have deposited with the applicable trustee all required payments of the principal, any premium or make-whole amount, interest and, to the extent permitted by law, interest on overdue installment of interest, plus applicable fees, expenses, disbursements and advances of the applicable trustee; and
- all events of default, other than the non-payment of accelerated principal, or a specified portion thereof, and any premium or make-whole amount, have been cured or waived.

The indentures also provide that the holders of at least a majority in principal amount of the outstanding debt securities of any series or of all debt securities then outstanding under the applicable indenture may, on behalf of all holders, waive any past default with respect to such series and its consequences, except a default:

- in the payment of the principal, any premium or make-whole amount, or interest;
- in respect of a covenant or provision contained in the applicable indenture that cannot be modified or amended without the consent of the holders of the outstanding debt security that is affected by the default; or
- in respect of a covenant or provision for the benefit or protection of the trustee, without its express written consent.

The indentures require each trustee to give notice to the holders of debt securities within 90 days of a default unless such default has been cured or waived. However, the trustee may withhold notice if specified persons of such trustee consider such withholding to be in the interest of the holders of debt securities. The trustee may not withhold notice of a default in the payment of principal, any premium or interest on any debt security of such series or in the payment of any sinking fund installment in respect of any debt security of such series.

The indentures provide that holders of debt securities of any series may not institute any proceedings, judicial or otherwise, with respect to such indenture or for any remedy under the indenture, unless the trustee fails to act for a period of 60 days after the trustee has received a written request to institute proceedings in

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respect of an event of default from the holders of 25% or more in principal amount of the outstanding debt securities of such series, as well as an offer of indemnity reasonably satisfactory to the trustee. However, this provision will not prevent any holder of debt securities from instituting suit for the enforcement of payment of the principal of, and any premium or make-whole amount, and interest on, such debt securities at the respective due dates thereof.

The indentures provide that, subject to provisions in each indenture relating to its duties in the case of a default, a trustee has no obligation to exercise any of its rights or powers at the request or direction of any holders of any series of debt securities then outstanding under the indenture, unless the holders have offered to the trustee reasonable security or indemnity. The holders of at least a majority in principal amount of the outstanding debt securities of any series or of all debt securities then outstanding under an indenture shall have the right to direct the time, method and place of conducting any proceeding for any remedy available to the applicable trustee, or of exercising any trust or power conferred upon such trustee. However, a trustee may refuse to follow any direction which:

- is in conflict with any law or the applicable indenture;
- may involve the trustee in personal liability; or
- may be unduly prejudicial to the holders of debt securities of the series not joining the proceeding.

Within 120 days after the close of each fiscal year, we will be required to deliver to each trustee a certificate, signed by one of our several specified officers, stating whether or not that officer has knowledge of any default under the applicable indenture. If the officer has knowledge of any default, the notice must specify the nature and status of the default.

Modification of the Indentures

The indentures provide that modifications and amendments may be made only with the consent of the affected holders of a majority in principal amount of all outstanding debt securities issued under that indenture. However, no such modification or amendment may, without the consent of the holders of the debt securities affected by the modification or amendment:

- change the stated maturity of the principal of, or any premium or make-whole amount on, or any installment of principal of or interest on, any such debt security;
- reduce the principal amount of, the rate or amount of interest on, or any premium or make-whole amount payable on redemption of, any such debt security;
- reduce the amount of principal of an original issue discount security that would be due and payable upon declaration of acceleration of the maturity thereof or would be provable in bankruptcy, or adversely affect any right of repayment of the holder of any such debt security;
- change the place of payment or the coin or currency for payment of principal of, or any premium or make-whole amount, or interest on, any such debt security;
- impair the right to institute suit for the enforcement of any payment on or with respect to any such debt security;
- reduce the percentage in principal amount of any outstanding debt securities necessary to modify or amend the applicable indenture with respect to such debt securities, to waive compliance with particular provisions thereof or defaults and consequences thereunder or to reduce the quorum or voting requirements set forth in the applicable indenture; and
- modify any of the foregoing provisions or any of the provisions relating to the waiver of particular past defaults or covenants, except to increase the required percentage to effect such action or to provide that some of the other provisions may not be modified or waived without the consent of the holder of such debt security.

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The holders of a majority in aggregate principal amount of the outstanding debt securities of each series may, on behalf of all holders of debt securities of that series, waive, insofar as that series is concerned, our compliance with material restrictive covenants of the applicable indenture.

We and our respective trustee may make modifications and amendments of an indenture without the consent of any holder of debt securities for any of the following purposes:

- to evidence the succession of another person to us as obligor under such indenture;
- to add to our covenants for the benefit of the holders of all or any series of debt securities or to surrender any right or power conferred upon us in such indenture;
- to add events of default for the benefit of the holders of all or any series of debt securities;
- to add or change any provisions of an indenture (i) to change or eliminate restrictions on the payment of principal of, or premium or make-whole amount, or interest on, debt securities in bearer form, or (ii) to permit or facilitate the issuance of debt securities in uncertificated form, provided that such action shall not adversely affect the interests of the holders of the debt securities of any series in any material respect;
- to change or eliminate any provisions of an indenture, provided that any such change or elimination shall become effective only when there are no debt securities outstanding of any series created prior thereto which are entitled to the benefit of such provision;
- to secure the debt securities;
- to establish the form or terms of debt securities of any series;
- to provide for the acceptance of appointment by a successor trustee or facilitate the administration of the trusts under an indenture by more than one trustee;
- to cure any ambiguity, defect or inconsistency in an indenture, provided that such action shall not adversely affect the interests of holders of debt securities of any series issued under such indenture; and
- to supplement any of the provisions of an indenture to the extent necessary to permit or facilitate defeasance and discharge of any series of such debt securities, provided that such action shall not adversely affect the interests of the holders of the outstanding debt securities of any series.

Voting

The indentures provide that in determining whether the holders of the requisite principal amount of outstanding debt securities of a series have given any request, demand, authorization, direction, notice, consent or waiver under the indentures or whether a quorum is present at a meeting of holders of debt securities:

- the principal amount of an original issue discount security that shall be deemed to be outstanding shall be the amount of the principal thereof that would be due and payable as of the date of such determination upon declaration of acceleration of the maturity thereof;
- the principal amount of any debt security denominated in a foreign currency that shall be deemed outstanding shall be the United States dollar equivalent, determined on the issue date for such debt security, of the principal amount or, in the case of an original issue discount security, the United States dollar equivalent on the issue date of such debt security of the amount determined as provided in the preceding bullet point;
- the principal amount of an indexed security that shall be deemed outstanding shall be the principal face amount of such indexed security at original issuance, unless otherwise provided for such indexed security under such indenture; and
- debt securities owned by us or any other obligor upon the debt securities or by any affiliate of ours or of such other obligor shall be disregarded.

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The indentures contain provisions for convening meetings of the holders of debt securities of a series. A meeting will be permitted to be called at any time by the applicable trustee, and also, upon request, by us or the holders of at least 25% in principal amount of the outstanding debt securities of such series, in any such case upon notice given as provided in such indenture. Except for any consent that must be given by the holder of each debt security affected by the modifications and amendments of an indenture described above, any resolution presented at a meeting or adjourned meeting duly reconvened at which a quorum is present may be adopted by the affirmative vote of the holders of a majority of the aggregate principal amount of the outstanding debt securities of that series represented at such meeting.

Notwithstanding the preceding paragraph, except as referred to above, any resolution relating to a request, demand, authorization, direction, notice, consent, waiver or other action that may be made, given or taken by the holders of a specified percentage, which is less than a majority of the aggregate principal amount of the outstanding debt securities of a series, may be adopted at a meeting or adjourned meeting duly reconvened at which a quorum is present by the affirmative vote of such specified percentage.

Any resolution passed or decision taken at any properly held meeting of holders of debt securities of any series will be binding on all holders of such series. The quorum at any meeting called to adopt a resolution, and at any reconvened meeting, will be persons holding or representing a majority in principal amount of the outstanding debt securities of a series. However, if any action is to be taken relating to a consent or waiver which may be given by the holders of at least a specified percentage in principal amount of the outstanding debt securities of a series, the persons holding such percentage will constitute a quorum.

Notwithstanding the foregoing provisions, the indentures provide that if any action is to be taken at a meeting with respect to any request, demand, authorization, direction, notice, consent, waiver or other action that such indenture expressly provides may be made, given or taken by the holders of a specified percentage in principal amount of all outstanding debt securities affected by such action, or of the holders of such series and one or more additional series:

- there shall be no minimum quorum requirement for such meeting; and
- the principal amount of the outstanding debt securities of such series that vote in favor of such request, demand, authorization, direction, notice, consent, waiver or other action shall be taken account in determining whether such request, demand, authorization, direction, notice, consent, waiver or other action has been made, given or taken under such indenture.

Subordination

Unless otherwise provided in the applicable prospectus supplement, subordinated debt securities will be subject to the following subordination provisions.

Upon any distribution to our creditors in a liquidation, dissolution or reorganization, the payment of the principal of and interest on any subordinated debt securities will be subordinated to the extent provided in the applicable indenture in right of payment to the prior payment in full of all senior debt. However, our obligation to make payments of the principal of and interest on such subordinated debt securities otherwise will not be affected. No payment of principal or interest will be permitted to be made on subordinated debt securities at any time if a default on senior debt exists that permits the holders of such senior debt to accelerate its maturity and the default is the subject of judicial proceedings or we receive notice of the default. After all senior debt is paid in full and until the subordinated debt securities are paid in full, holders of subordinated debt securities will be subrogated to the rights of holders of senior debt to the extent that distributions otherwise payable to holders of subordinated debt securities have been applied to the payment of senior debt. The subordinated indenture will not restrict the amount of senior debt or other indebtedness of ours. As a result of these subordination provisions, in the event of a distribution of assets upon insolvency, holders of subordinated debt securities may recover less, ratably, than our general creditors.

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The term “senior debt” will be defined in the applicable indenture as the principal of and interest on, or substantially similar payments to be made by us in respect of, other outstanding indebtedness, whether outstanding at the date of execution of the applicable indenture or subsequently incurred, created or assumed. The prospectus supplement may include a description of additional terms implementing the subordination feature.

No restrictions will be included in any indenture relating to subordinated debt securities upon the creation of additional senior debt.

If this prospectus is being delivered in connection with the offering of a series of subordinated debt securities, the accompanying prospectus supplement or the information incorporated in this prospectus by reference will set forth the approximate amount of senior debt outstanding as of the end of our most recent fiscal quarter.

Discharge, Defeasance and Covenant Defeasance

Unless otherwise indicated in the applicable prospectus supplement, the indentures allow us to discharge our obligations to holders of any series of debt securities issued under any indenture when:

- either (i) all securities of such series have already been delivered to the applicable trustee for cancellation; or (ii) all securities of such series have not already been delivered to the applicable trustee for cancellation but (a) have become due and payable, (b) will become due and payable within one year, or (c) if redeemable at our option, are to be redeemed within one year, and we have irrevocably deposited with the applicable trustee, in trust, funds in such currency or currencies, currency unit or units or composite currency or currencies in which such debt securities are payable, an amount sufficient to pay the entire indebtedness on such debt securities in respect of principal and any premium or make-whole amount, and interest to the date of such deposit if such debt securities have become due and payable or, if they have not, to the stated maturity or redemption date;
- we have paid or caused to be paid all other sums payable; and
- an officers’ certificate and an opinion of counsel stating the conditions to discharging the debt securities have been satisfied has been delivered to the trustee.

Unless otherwise indicated in the applicable prospectus supplement, the indentures provide that, upon our irrevocable deposit with the applicable trustee, in trust, of an amount, in such currency or currencies, currency unit or units or composite currency or currencies in which such debt securities are payable at stated maturity, or government obligations, or both, applicable to such debt securities, which through the scheduled payment of principal and interest in accordance with their terms will provide money in an amount sufficient to pay the principal of, and any premium or make-whole amount, and interest on, such debt securities, and any mandatory sinking fund or analogous payments thereon, on the scheduled due dates therefor, the issuing company may elect either:

- to defease and be discharged from any and all obligations with respect to such debt securities; or
- to be released from its obligations with respect to such debt securities under the applicable indenture or, if provided in the applicable prospectus supplement, its obligations with respect to any other covenant, and any omission to comply with such obligations shall not constitute an event of default with respect to such debt securities.

Notwithstanding the above, we may not elect to defease and be discharged from the obligation to pay any additional amounts upon the occurrence of particular events of tax, assessment or governmental charge with respect to payments on such debt securities and the obligations to register the transfer or exchange of such debt securities, to replace temporary or mutilated, destroyed, lost or stolen debt securities, to maintain an office or agency in respect of such debt securities, or to hold monies for payment in trust.

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The indentures only permit us to establish the trust described in the paragraph above if, among other things, we have delivered to the applicable trustee an opinion of counsel to the effect that the holders of such debt securities will not recognize income, gain or loss for United States federal income tax purposes as a result of such defeasance or covenant defeasance and will be subject to United States federal income tax on the same amounts, in the same manner and at the same times as would have been the case if such defeasance or covenant defeasance had not occurred. Such opinion of counsel, in the case of defeasance, will be required to refer to and be based upon a ruling received from or published by the Internal Revenue Service or a change in applicable United States federal income tax law occurring after the date of the indenture. In the event of such defeasance, the holders of such debt securities would be able to look only to such trust fund for payment of principal, any premium or make-whole amount, and interest.

When we use the term “government obligations,” we mean securities that are:

- direct obligations of the United States or the government that issued the foreign currency in which the debt securities of a particular series are payable, for the payment of which its full faith and credit is pledged; or
- obligations of a person controlled or supervised by and acting as an agency or instrumentality of the United States or other government that issued the foreign currency in which the debt securities of such series are payable, the payment of which is unconditionally guaranteed as a full faith and credit obligation by the United States or such other government, which are not callable or redeemable at the option of the issuer thereof and shall also include a depository receipt issued by a bank or trust company as custodian with respect to any such government obligation or a specific payment of interest on or principal of any such government obligation held by such custodian for the account of the holder of a depository receipt. However, except as required by law, such custodian is not authorized to make any deduction from the amount payable to the holder of such depository receipt from any amount received by the custodian in respect of the government obligation or the specific payment of interest on or principal of the government obligation evidenced by such depository receipt.

Unless otherwise provided in the applicable prospectus supplement, if after we have deposited funds and/or government obligations to effect defeasance or covenant defeasance with respect to debt securities of any series, (i) the holder of a debt security of such series is entitled to, and does, elect under the terms of the applicable indenture or the terms of such debt security to receive payment in a currency, currency unit or composite currency other than that in which such deposit has been made in respect of such debt security, or (ii) a conversion event occurs in respect of the currency, currency unit or composite currency in which such deposit has been made, the indebtedness represented by such debt security will be deemed to have been, and will be, fully discharged and satisfied through the payment of the principal of, and premium or make-whole amount, and interest on, such debt security as they become due out of the proceeds yielded by converting the amount so deposited in respect of such debt security into the currency, currency unit or composite currency in which such debt security becomes payable as a result of such election or such cessation of usage based on the applicable market exchange rate.

When we use the term “conversion event,” we mean the cessation of use of:

- a currency, currency unit or composite currency both by the government of the country that issued such currency and for the settlement of transactions by a central bank or other public institutions of or within the international banking community;
- the European Currency Unit both within the European Monetary System and for the settlement of transactions by public institutions of or within the European Communities; or
- any currency unit or composite currency other than the European Currency Unit for the purposes for which it was established.

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Unless otherwise provided in the applicable prospectus supplement, all payments of principal of, and any premium or make-whole amount, and interest on, any debt security that is payable in a foreign currency that ceases to be used by its government of issuance shall be made in United States dollars.

In the event that (i) we effect covenant defeasance with respect to any debt securities and (ii) those debt securities are declared due and payable because of the occurrence of any event of default, the amount in the currency, currency unit or composite currency in which such debt securities are payable, and government obligations on deposit with the applicable trustee, will be sufficient to pay amounts due on such debt securities at the time of their stated maturity but may not be sufficient to pay amounts due on such debt securities at the time of the acceleration resulting from such event of default. However, the issuing company would remain liable to make payments of any amounts due at the time of acceleration.

The applicable prospectus supplement may further describe the provisions, if any, permitting such defeasance or covenant defeasance, including any modifications to the provisions described above, with respect to the debt securities of or within a particular series.

Conversion Rights

The terms and conditions, if any, upon which the debt securities are convertible into common stock or other securities of ours will be set forth in the applicable prospectus supplement. The terms will include whether the debt securities are convertible into shares of common stock or other securities of ours, the conversion price, or manner of calculation thereof, the conversion period, provisions as to whether conversion will be at the issuing company's option or the option of the holders, the events requiring an adjustment of the conversion price and provisions affecting conversion in the event of the redemption of the debt securities and any restrictions on conversion.

Global Securities

The debt securities of a series may be issued in whole or in part in the form of one or more global securities that will be deposited with, or on behalf of, a depository identified in the applicable prospectus supplement relating to such series. Global securities, if any, issued in the United States are expected to be deposited with The Depository Trust Company, or DTC, as depository. We may issue global securities in either registered or bearer form and in either temporary or permanent form. We will describe the specific terms of the depository arrangement with respect to a series of debt securities in the applicable prospectus supplement relating to such series. We expect that unless the applicable prospectus supplement provides otherwise, the following provisions will apply to depository arrangements.

Once a global security is issued, the depository for such global security or its nominee will credit on its book-entry registration and transfer system the respective principal amounts of the individual debt securities represented by such global security to the accounts of participants that have accounts with such depository. Such accounts shall be designated by the underwriters, dealers or agents with respect to such debt securities or by us if we offer such debt securities directly. Ownership of beneficial interests in such global security will be limited to participants with the depository or persons that may hold interests through those participants.

We expect that, under procedures established by DTC, ownership of beneficial interests in any global security for which DTC is the depository will be shown on, and the transfer of that ownership will be effected only through, records maintained by DTC or its nominee, with respect to beneficial interests of participants with the depository, and records of participants, with respect to beneficial interests of persons who hold through participants with the depository. Neither we nor the trustee will have any responsibility or liability for any aspect of the records of DTC or for maintaining, supervising or reviewing any records of DTC or any of its participants relating to beneficial ownership interests in the debt securities. The laws of some states require that certain purchasers of securities take physical delivery of such securities in definitive form. Such limits and laws may impair the ability to own, pledge or transfer beneficial interest in a global security.

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So long as the depository for a global security or its nominee is the registered owner of such global security, such depository or such nominee, as the case may be, will be considered the sole owner or holder of the debt securities represented by the global security for all purposes under the applicable indenture. Except as described below or in the applicable prospectus supplement, owners of beneficial interest in a global security will not be entitled to have any of the individual debt securities represented by such global security registered in their names, will not receive or be entitled to receive physical delivery of any such debt securities in definitive form and will not be considered the owners or holders thereof under the applicable indenture. Beneficial owners of debt securities evidenced by a global security will not be considered the owners or holders thereof under the applicable indenture for any purpose, including with respect to the giving of any direction, instructions or approvals to the trustee under the indenture. Accordingly, each person owning a beneficial interest in a global security with respect to which DTC is the depository must rely on the procedures of DTC and, if such person is not a participant with the depository, on the procedures of the participant through which such person owns its interests, to exercise any rights of a holder under the applicable indenture. We understand that, under existing industry practice, if DTC requests any action of holders or if an owner of a beneficial interest in a global security desires to give or take any action which a holder is entitled to give or take under the applicable indenture, DTC would authorize the participants holding the relevant beneficial interest to give or take such action, and such participants would authorize beneficial owners through such participants to give or take such actions or would otherwise act upon the instructions of beneficial owners holding through them.

Payments of principal of, and any premium or make-whole amount, and interest on, individual debt securities represented by a global security registered in the name of a depository or its nominee will be made to or at the direction of the depository or its nominee, as the case may be, as the registered owner of the global security under the applicable indenture. Under the terms of the applicable indenture, we and the trustee may treat the persons in whose name debt securities, including a global security, are registered as the owners thereof for the purpose of receiving such payments. Consequently, neither we nor the trustee have or will have any responsibility or liability for the payment of such amounts to beneficial owners of debt securities including principal, any premium or make-whole amount, or interest. We believe, however, that it is currently the policy of DTC to immediately credit the accounts of relevant participants with such payments, in amounts proportionate to their respective holdings of beneficial interests in the relevant global security as shown on the records of DTC or its nominee. We also expect that payments by participants to owners of beneficial interests in such global security held through such participants will be governed by standing instructions and customary practices, as is the case with securities held for the account of customers in bearer form or registered in street name, and will be the responsibility of such participants. Redemption notices with respect to any debt securities represented by a global security will be sent to the depository or its nominee. If less than all of the debt securities of any series are to be redeemed, we expect the depository to determine the amount of the interest of each participant in such debt securities to be redeemed to be determined by lot. Neither we, the trustee, any paying agent nor the security registrar for such debt securities will have any responsibility or liability for any aspect of the records relating to or payments made on account of beneficial ownership interests in the global security for such debt securities or for maintaining any records with respect thereto.

Neither we nor the trustee will be liable for any delay by the holders of a global security or the depository in identifying the beneficial owners of debt securities, and we and the trustee may conclusively rely on, and will be protected in relying on, instructions from the holder of a global security or the depository for all purposes. The rules applicable to DTC and its participants are on file with the SEC.

If a depository for any debt securities is at any time unwilling, unable or ineligible to continue as depository and we do not appoint a successor depository within 90 days, we will issue individual debt securities in exchange for the global security representing such debt securities. In addition, we may at any time and at our sole discretion, subject to any limitations described in the applicable prospectus supplement relating to such debt securities, determine not to have any of such debt securities represented by one or more global securities and in such event will issue individual debt securities in exchange for the global security or securities representing such

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debt securities. Individual debt securities so issued will be issued in denominations of \$1,000 and integral multiples of \$1,000.

The debt securities of a series may also be issued in whole or in part in the form of one or more bearer global securities that will be deposited with a depository, or with a nominee for such depository, identified in the applicable prospectus supplement. Any such bearer global securities may be issued in temporary or permanent form. The specific terms and procedures, including the specific terms of the depository arrangement, with respect to any portion of a series of debt securities to be represented by one or more bearer global securities will be described in the applicable prospectus supplement.

No Recourse

There is no recourse under any obligation, covenant or agreement in the applicable indenture or with respect to any security against any of our or our successor's past, present or future shareholders, employees, officers or directors.

DESCRIPTION OF WARRANTS

The following description, together with the additional information we may include in any applicable prospectus supplements, summarizes the material terms and provisions of the warrants that we may offer under this prospectus and the related warrant agreements and warrant certificates. While the terms summarized below will apply generally to any warrants that we may offer, we will describe the particular terms of any series of warrants in more detail in the applicable prospectus supplement. If we indicate in the prospectus supplement, the terms of any warrants offered under that prospectus supplement may differ from the terms described below. Specific warrant agreements will contain additional important terms and provisions and will be incorporated by reference as an exhibit to the registration statement, which includes this prospectus.

General

We may issue warrants for the purchase of common stock, preferred stock and/or debt securities in one or more series. We may issue warrants independently or together with common stock, preferred stock and/or debt securities, and the warrants may be attached to or separate from these securities.

We will evidence each series of warrants by warrant certificates that we will issue under a separate warrant agreement. We will enter into the warrant agreement with a warrant agent. We will indicate the name and address of the warrant agent in the applicable prospectus supplement relating to a particular series of warrants.

We will describe in the applicable prospectus supplement the terms of the series of warrants, including:

- the offering price and aggregate number of warrants offered;
- the currency for which the warrants may be purchased;
- if applicable, the designation and terms of the securities with which the warrants are issued and the number of warrants issued with each such security or each principal amount of such security;
- if applicable, the date on and after which the warrants and the related securities will be separately transferable;
- in the case of warrants to purchase debt securities, the principal amount of debt securities purchasable upon exercise of one warrant and the price at, and currency in which, this principal amount of debt securities may be purchased upon such exercise;
- in the case of warrants to purchase common stock or preferred stock, the number of shares of common stock or preferred stock, as the case may be, purchasable upon the exercise of one warrant and the price at which these shares may be purchased upon such exercise;
- the effect of any merger, consolidation, sale or other disposition of our business on the warrant agreement and the warrants;
- the terms of any rights to redeem or call the warrants;
- any provisions for changes to or adjustments in the exercise price or number of securities issuable upon exercise of the warrants;
- the periods during which, and places at which, the warrants are exercisable;
- the manner of exercise;
- the dates on which the right to exercise the warrants will commence and expire;
- the manner in which the warrant agreement and warrants may be modified;
- federal income tax consequences of holding or exercising the warrants;
- the terms of the securities issuable upon exercise of the warrants; and
- any other specific terms, preferences, rights or limitations of or restrictions on the warrants.

DESCRIPTION OF UNITS

We may issue units comprised of shares of common stock, shares of preferred stock, debt securities and warrants in any combination. We may issue units in such amounts and in as many distinct series as we wish. This section outlines certain provisions of the units that we may issue. If we issue units, they will be issued under one or more unit agreements to be entered into between us and a bank or other financial institution, as unit agent. The information described in this section may not be complete in all respects and is qualified entirely by reference to the unit agreement with respect to the units of any particular series. The specific terms of any series of units offered will be described in the applicable prospectus supplement. If so described in a particular supplement, the specific terms of any series of units may differ from the general description of terms presented below. We urge you to read any prospectus supplement related to any series of units we may offer, as well as the complete unit agreement and unit certificate that contain the terms of the units. If we issue units, forms of unit agreements and unit certificates relating to such units will be incorporated by reference as exhibits to the registration statement, which includes this prospectus.

Each unit that we may issue will be issued so that the holder of the unit is also the holder of each security included in the unit. Thus, the holder of a unit will have the rights and obligations of a holder of each included security. The unit agreement under which a unit is issued may provide that the securities included in the unit may not be held or transferred separately, at any time or at any time before a specified date. The applicable prospectus supplement may describe:

- the designation and terms of the units and of the securities comprising the units, including whether and under what circumstances those securities may be held or transferred separately;
- any provisions of the governing unit agreement;
- the price or prices at which such units will be issued;
- the applicable United States federal income tax considerations relating to the units;
- any provisions for the issuance, payment, settlement, transfer or exchange of the units or of the securities comprising the units; and
- any other terms of the units and of the securities comprising the units.

The provisions described in this section, as well as those described under “Description of Capital Stock,” “Description of Debt Securities” and “Description of Warrants” will apply to the securities included in each unit, to the extent relevant and as may be updated in any prospectus supplements.

Issuance in Series

We may issue units in such amounts and in as many distinct series as we wish. This section summarizes terms of the units that apply generally to all series. Most of the financial and other specific terms of your series will be described in the applicable prospectus supplement.

Unit Agreements

We will issue the units under one or more unit agreements to be entered into between us and a bank or other financial institution, as unit agent. We may add, replace or terminate unit agents from time to time. We will identify the unit agreement under which each series of units will be issued and the unit agent under that agreement in the applicable prospectus supplement.

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The following provisions will generally apply to all unit agreements unless otherwise stated in the applicable prospectus supplement:

Modification without Consent

We and the applicable unit agent may amend any unit or unit agreement without the consent of any holder:

- to cure any ambiguity, including modifying any provisions of the governing unit agreement that differ from those described below;
- to correct or supplement any defective or inconsistent provision; or
- to make any other change that we believe is necessary or desirable and will not adversely affect the interests of the affected holders in any material respect.

We do not need any approval to make changes that affect only units to be issued after the changes take effect. We may also make changes that do not adversely affect a particular unit in any material respect, even if they adversely affect other units in a material respect. In those cases, we do not need to obtain the approval of the holder of the unaffected unit; we need only obtain any required approvals from the holders of the affected units.

Modification with Consent

We may not amend any particular unit or a unit agreement with respect to any particular unit unless we obtain the consent of the holder of that unit, if the amendment would:

- impair any right of the holder to exercise or enforce any right under a security included in the unit if the terms of that security require the consent of the holder to any changes that would impair the exercise or enforcement of that right; or
- reduce the percentage of outstanding units or any series or class the consent of whose holders is required to amend that series or class, or the applicable unit agreement with respect to that series or class, as described below.

Any other change to a particular unit agreement and the units issued under that agreement would require the following approval:

- If the change affects only the units of a particular series issued under that agreement, the change must be approved by the holders of a majority of the outstanding units of that series; or
- If the change affects the units of more than one series issued under that agreement, it must be approved by the holders of a majority of all outstanding units of all series affected by the change, with the units of all the affected series voting together as one class for this purpose.

These provisions regarding changes with majority approval also apply to changes affecting any securities issued under a unit agreement, as the governing document.

In each case, the required approval must be given by written consent.

Unit Agreements Will Not Be Qualified under Trust Indenture Act

No unit agreement will be qualified as an indenture, and no unit agent will be required to qualify as a trustee, under the Trust Indenture Act. Therefore, holders of units issued under unit agreements will not have the protections of the Trust Indenture Act with respect to their units.

Mergers and Similar Transactions Permitted; No Restrictive Covenants or Events of Default

The unit agreements will not restrict our ability to merge or consolidate with, or sell our assets to, another corporation or other entity or to engage in any other transactions. If at any time we merge or consolidate with, or

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sell our assets substantially as an entirety to, another corporation or other entity, the successor entity will succeed to and assume our obligations under the unit agreements. We will then be relieved of any further obligation under these agreements.

The unit agreements will not include any restrictions on our ability to put liens on our assets, nor will they restrict our ability to sell our assets. The unit agreements also will not provide for any events of default or remedies upon the occurrence of any events of default.

Governing Law

The unit agreements and the units will be governed by Delaware law.

Form, Exchange and Transfer

Unless the accompanying prospectus supplement states otherwise, we will issue each unit in global — i.e., book-entry — form only. Units in book-entry form will be represented by a global security registered in the name of a depositary, which will be the holder of all the units represented by the global security. Those who own beneficial interests in a unit will do so through participants in the depositary's system, and the rights of these indirect owners will be governed solely by the applicable procedures of the depositary and its participants. We will describe book-entry securities, and other terms regarding the issuance and registration of the units in the applicable prospectus supplement.

Unless the accompanying prospectus supplement states otherwise, each unit and all securities comprising the unit will be issued in the same form.

If we issue any units in registered, non-global form, the following will apply to them.

The units will be issued in the denominations stated in the applicable prospectus supplement. Holders may exchange their units for units of smaller denominations or combined into fewer units of larger denominations, as long as the total amount is not changed.

- Holders may exchange or transfer their units at the office of the unit agent. Holders may also replace lost, stolen, destroyed or mutilated units at that office. We may appoint another entity to perform these functions or perform them ourselves.
- Holders will not be required to pay a service charge to transfer or exchange their units, but they may be required to pay for any tax or other governmental charge associated with the transfer or exchange. The transfer or exchange, and any replacement, will be made only if our transfer agent is satisfied with the holder's proof of legal ownership. The transfer agent may also require an indemnity before replacing any units.
- If we have the right to redeem, accelerate or settle any units before their maturity, and we exercise our right as to less than all those units or other securities, we may block the exchange or transfer of those units during the period beginning 15 days before the day we mail the notice of exercise and ending on the day of that mailing, in order to freeze the list of holders to prepare the mailing. We may also refuse to register transfers of or exchange any unit selected for early settlement, except that we will continue to permit transfers and exchanges of the unsettled portion of any unit being partially settled. We may also block the transfer or exchange of any unit in this manner if the unit includes securities that are or may be selected for early settlement.

Only the depositary will be entitled to transfer or exchange a unit in global form, since it will be the sole holder of the unit.

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Payments and Notices

In making payments and giving notices with respect to our units, we will follow the procedures as described in the applicable prospectus supplement.

PLAN OF DISTRIBUTION

We may sell securities:

- through underwriters;
- through dealers;
- through agents;
- directly to purchasers; or
- through a combination of any of these methods or any other method permitted by law.

In addition, we may issue the securities as a dividend or distribution or in a subscription rights offering to our existing security holders.

We may directly solicit offers to purchase securities, or agents may be designated to solicit such offers. In the prospectus supplement relating to such offering, we will name any agent that could be viewed as an underwriter under the Securities Act and describe any commissions that we must pay to any such agent. Any such agent will be acting on a best efforts basis for the period of its appointment or, if indicated in the applicable prospectus supplement, on a firm commitment basis. This prospectus may be used in connection with any offering of our securities through any of these methods or other methods described in the applicable prospectus supplement.

The distribution of the securities may be effected from time to time in one or more transactions:

- at a fixed price, or prices, which may be changed from time to time;
- at market prices prevailing at the time of sale;
- at prices related to such prevailing market prices; or
- at negotiated prices.

Each prospectus supplement will describe the method of distribution of the securities and any applicable restrictions.

The prospectus supplement with respect to the securities of a particular series will describe the terms of the offering of the securities, including the following:

- the name of the agent or any underwriters;
- the public offering or purchase price;
- any discounts and commissions to be allowed or paid to the agent or underwriters;
- all other items constituting underwriting compensation;
- any discounts and commissions to be allowed or paid to dealers; and
- any exchanges on which the securities will be listed.

If any underwriters or agents are used in the sale of the securities in respect of which this prospectus is delivered, we will enter into an underwriting agreement, sales agreement or other agreement with them at the time of sale to them, and we will set forth in the prospectus supplement relating to such offering the names of the underwriters or agents and the terms of the related agreement with them.

In connection with the offering of securities, we may grant to the underwriters an option to purchase additional securities with an additional underwriting commission, as may be set forth in the accompanying prospectus supplement. If we grant any such option, the terms of such option will be set forth in the prospectus supplement for such securities.

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If a dealer is used in the sale of the securities in respect of which the prospectus is delivered, we will sell such securities to the dealer, as principal. The dealer, who may be deemed to be an “underwriter” as that term is defined in the Securities Act, may then resell such securities to the public at varying prices to be determined by such dealer at the time of resale.

If we offer securities in a subscription rights offering to our existing security holders, we may enter into a standby underwriting agreement with dealers, acting as standby underwriters. We may pay the standby underwriters a commitment fee for the securities they commit to purchase on a standby basis. If we do not enter into a standby underwriting arrangement, we may retain a dealer-manager to manage a subscription rights offering for us.

Agents, underwriters, dealers and other persons may be entitled under agreements which they may enter into with us to indemnification by us against certain civil liabilities, including liabilities under the Securities Act, and may be customers of, engage in transactions with or perform services for us in the ordinary course of business.

If so indicated in the applicable prospectus supplement, we will authorize underwriters or other persons acting as our agents to solicit offers by certain institutions to purchase securities from us pursuant to delayed delivery contracts providing for payment and delivery on the date stated in the prospectus supplement. Each contract will be for an amount not less than, and the aggregate amount of securities sold pursuant to such contracts shall not be less nor more than, the respective amounts stated in the prospectus supplement. Institutions with whom the contracts, when authorized, may be made include commercial and savings banks, insurance companies, pension funds, investment companies, educational and charitable institutions and other institutions, but shall in all cases be subject to our approval. Delayed delivery contracts will not be subject to any conditions except that:

- the purchase by an institution of the securities covered under that contract shall not at the time of delivery be prohibited under the laws of the jurisdiction to which that institution is subject; and
- if the securities are also being sold to underwriters acting as principals for their own account, the underwriters shall have purchased such securities not sold for delayed delivery. The underwriters and other persons acting as our agents will not have any responsibility in respect of the validity or performance of delayed delivery contracts.

Offered securities may also be offered and sold, if so indicated in the prospectus supplement, in connection with a remarketing upon their purchase, in accordance with a redemption or repayment pursuant to their terms, or otherwise, by one or more remarketing firms, acting as principals for their own accounts or as agents for us. Any remarketing firm will be identified and the terms of its agreement, if any, with us and its compensation will be described in the applicable prospectus supplement. Remarketing firms may be deemed to be underwriters in connection with their remarketing of offered securities.

Certain agents, underwriters and dealers, and their associates and affiliates, may be customers of, have borrowing relationships with, engage in other transactions with, or perform services, including investment banking services, for us or one or more of our respective affiliates in the ordinary course of business.

In order to facilitate the offering of the securities, any underwriters may engage in transactions that stabilize, maintain or otherwise affect the price of the securities or any other securities the prices of which may be used to determine payments on such securities. Specifically, any underwriters may overallocate in connection with the offering, creating a short position for their own accounts. In addition, to cover overallocations or to stabilize the price of the securities or of any such other securities, the underwriters may bid for, and purchase, the securities or any such other securities in the open market. Finally, in any offering of the securities through a syndicate of underwriters, the underwriting syndicate may reclaim selling concessions allowed to an underwriter or a dealer for distributing the securities in the offering if the syndicate repurchases previously distributed securities in transactions to cover syndicate short positions, in stabilization transactions or otherwise. Any of these activities

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may stabilize or maintain the market price of the securities above independent market levels. Any such underwriters are not required to engage in these activities and may end any of these activities at any time.

We may engage in at the market offerings into an existing trading market in accordance with Rule 415(a)(4) under the Securities Act. In addition, we may enter into derivative transactions with third parties, or sell securities not covered by this prospectus to third parties in privately negotiated transactions. If the applicable prospectus supplement so indicates, in connection with those derivatives, the third parties may sell securities covered by this prospectus and the applicable prospectus supplement, including in short sale transactions. If so, the third party may use securities pledged by us or borrowed from us or others to settle those sales or to close out any related open borrowings of stock, and may use securities received from us in settlement of those derivatives to close out any related open borrowings of stock. The third party in such sale transactions will be an underwriter and, if not identified in this prospectus, will be named in the applicable prospectus supplement (or a post-effective amendment). In addition, we may otherwise loan or pledge securities to a financial institution or other third party that in turn may sell the securities short using this prospectus and an applicable prospectus supplement. Such financial institution or other third party may transfer its economic short position to investors in our securities or in connection with a concurrent offering of other securities.

Under Rule 15c6-1 of the Exchange Act, trades in the secondary market generally are required to settle in two business days, unless the parties to any such trade expressly agree otherwise. The applicable prospectus supplement may provide that the original issue date for your securities may be more than two scheduled business days after the trade date for your securities. Accordingly, in such a case, if you wish to trade securities on any date prior to the second business day before the original issue date for your securities, you will be required, by virtue of the fact that your securities initially are expected to settle in more than two scheduled business days after the trade date for your securities, to make alternative settlement arrangements to prevent a failed settlement.

The securities may be new issues of securities and may have no established trading market. The securities may or may not be listed on a national securities exchange. We can make no assurance as to the liquidity of or the existence of trading markets for any of the securities.

The specific terms of any lock-up provisions in respect of any given offering will be described in the applicable prospectus supplement.

The underwriters, dealers and agents may engage in transactions with us, or perform services for us, in the ordinary course of business for which they receive compensation.

The anticipated date of delivery of offered securities will be set forth in the applicable prospectus supplement relating to each offer.

LEGAL MATTERS

Certain legal matters in connection with this offering will be passed upon for us by Goodwin Procter LLP, Boston, Massachusetts. Any underwriters will also be advised about the validity of the securities and other legal matters by their own counsel, which will be named in the prospectus supplement.

EXPERTS

Kost Forer Gabbay & Kasierer, independent registered public accounting firm, has audited our consolidated financial statements for the year ended December 31, 2015 included in our Annual Report on Form 10-K for the year ended December 31, 2017 as set forth in their report, which is incorporated by reference in this prospectus and elsewhere in the registration statement. Our financial statements are incorporated by reference in reliance on Kost Forer Gabbay & Kasierer's report, given on their authority as experts in accounting and auditing.

The financial statements incorporated in this Prospectus by reference from the Company's Annual Report on Form 10-K have been audited by Deloitte & Touche LLP, an independent registered public accounting firm, as stated in their report, which is incorporated herein by reference. Such financial statements have been so incorporated in reliance upon the report of such firm given upon their authority as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We are subject to the information requirements of the Exchange Act and, in accordance therewith, file annual, quarterly and special reports, proxy statements and other information with the SEC. You may read and copy any document we file at the SEC's Public Reference Room at 100 F Street, N.E., Washington, D.C. 20549. You may call the SEC at 1-800-SEC-0330 for further information on the operation of the Public Reference Room. These documents also may be accessed through the SEC's electronic data gathering, analysis and retrieval system, or EDGAR, via electronic means, including the SEC's home page on the Internet (www.sec.gov).

We have the authority to designate and issue more than one class or series of stock having various preferences, conversion and other rights, voting powers, restrictions, limitations as to dividends, qualifications, and terms and conditions of redemption. See "Description of Capital Stock." We will furnish a full statement of the relative rights and preferences of each class or series of our stock which has been so designated and any restrictions on the ownership or transfer of our stock to any shareholder upon request and without charge. Written requests for such copies should be directed to Chiasma, Inc., 460 Totten Pond Road, Suite 530, Waltham, MA 02451, Attention: Secretary, or by telephone request to (617) 928-5300. Our website is located at www.chiasmapharma.com. Information contained on our website is not incorporated by reference into this prospectus and, therefore, is not part of this prospectus or any accompanying prospectus supplement.

INCORPORATION BY REFERENCE

The SEC allows us to incorporate by reference the information and reports we file with it, which means that we can disclose important information to you by referring you to these documents. The information incorporated by reference is an important part of this prospectus, and information that we file later with the SEC will automatically update and supersede the information already incorporated by reference. We are incorporating by reference the documents listed below, which we have already filed with the SEC, and any future filings we make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act, including all filings made after the date of the filing of this registration statement and prior to the effectiveness of this registration statement, except

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as to any portion of any future report or document that is not deemed filed under such provisions, until we sell all of the securities:

- Annual Report on [Form 10-K](#) for the year ended December 31, 2017;
- The information specifically incorporated by reference into our Annual Report on [Form 10-K](#) for the year ended December 31, 2016 from our [definitive proxy statement](#) on Schedule 14A (other than information furnished rather than filed), which was filed with the SEC on April 25, 2017;
- Current Reports on Form 8-K filed with the SEC on [February 28, 2018](#), and [March 20, 2018](#); and
- The description of our common stock contained in our registration statement on [Form 8-A](#), which was filed with the SEC on July 14, 2015, including any amendment or report filed for the purpose of updating such description.

Upon request, we will provide, without charge, to each person, including any beneficial owner, to whom a copy of this prospectus is delivered, a copy of the documents incorporated by reference into this prospectus but not delivered with the prospectus. You may request a copy of these filings, and any exhibits we have specifically incorporated by reference as an exhibit in this prospectus, at no cost by writing or telephoning us at the following address:

Chiasma, Inc., 460 Totten Pond Road, Suite 530, Waltham, MA 02451, Attention: Secretary, or by telephone request to (617) 928-5300.

This prospectus is part of a registration statement we filed with the SEC. We have incorporated exhibits into this registration statement. You should read the exhibits carefully for provisions that may be important to you.

You should rely only on the information incorporated by reference or provided in this prospectus or any prospectus supplement. We have not authorized anyone to provide you with different information. We are not making an offer of these securities in any state where the offer is not permitted. You should not assume that the information in this prospectus or in the documents incorporated by reference is accurate as of any date other than the date on the front of this prospectus or those documents.

Shares



Common Stock

PROSPECTUS SUPPLEMENT

Book Running Managers

Piper Jaffray

Cantor

, 2019