

CHIASMA, INC
Form S-3
March 22, 2018
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As filed with the Securities and Exchange Commission on March 22, 2018.

Registration No. 333-

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

FORM S-3
REGISTRATION STATEMENT
UNDER
THE SECURITIES ACT OF 1933

CHIASMA, INC.
(Exact name of registrant as specified in its charter)

Delaware
(State or other jurisdiction of
incorporation or organization)

76-0722250
(I.R.S. Employer
Identification Number)

Edgar Filing: CHIASMA, INC - Form S-3

460 Totten Pond Road, Suite 530

Waltham, Massachusetts 02451

(Address of principal executive offices)

(617) 928-5300

(Registrant's telephone number, including area code)

Mark J. Fitzpatrick

Chief Executive Officer

Chiasma, Inc.

460 Totten Pond Road, Suite 530

Waltham, Massachusetts 02451

(617) 928-5300

(Name, address, including zip code, and telephone number, including area code, of agent for service)

With copies to:

Michael H. Bison, Esq.

Daniel A. Lang, Esq.

Goodwin Procter LLP

100 Northern Avenue

Boston, MA 02210

(617) 570-1000

Approximate date of commencement of proposed sale to the public: From time to time after this Registration Statement becomes effective.

If the only securities being registered on this Form are being offered pursuant to dividend or interest reinvestment plans, please check the following box.

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, as amended, other than securities offered only in connection with dividend or interest reinvestment plans, check the following box:

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

If this Form is a registration statement pursuant to General Instruction I.D. or a post-effective amendment thereto that shall become effective upon filing with the Commission pursuant to Rule 462(e) under the Securities Act, check the following box.

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If this Form is a post-effective amendment to a registration statement filed pursuant to General Instruction I.D. filed to register additional securities or additional classes of securities pursuant to Rule 413(b) under the Securities Act, check the following box.

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

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

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 7(a)(2)(B) of the Securities Act .

CALCULATION OF REGISTRATION FEE

Title of Each Class of Securities to be Registered	Amount to be Registered(1)	Proposed Maximum Offering Price Per Unit(2)	Proposed Maximum Aggregate Offering Price(3)	Amount of Registration Fee(4)
Common Stock(5)				
Preferred Stock(6)				
Debt Securities(7)				
Warrants(8)				
Units(9)				
Total	\$100,000,000	N.A.	\$100,000,000	\$12,450.00

- (1) The amount to be registered consists of up to \$100,000,000 of an indeterminate amount of common stock, preferred stock, debt securities, warrants and/or units. There is also being registered hereunder such currently indeterminate number of (i) shares of common stock or other securities of the registrant as may be issued upon conversion of, or in exchange for, convertible or exchangeable debt securities and/or preferred stock registered hereby, or (ii) shares of preferred stock, common stock, debt securities or units as may be issued upon exercise of warrants registered hereby, as the case may be. Any securities registered hereunder may be sold separately or as units with the other securities registered hereunder.

(2)

The proposed maximum aggregate offering price per unit will be determined from time to time by the registrant in connection with the issuance by the registrant of the securities registered hereunder and is not specified as to each class of security pursuant to General Instruction II.D. of Form S-3 under the Securities Act.

- (3) Estimated solely for purposes of computing the registration fee. No separate consideration will be received for (i) common stock or other securities of the registrant that may be issued upon conversion of, or in exchange for, convertible or exchangeable debt securities and/or preferred stock registered hereby, or (ii) preferred stock, common stock, debt securities or units that may be issued upon exercise of warrants registered hereby, as the case may be.
- (4) The registration fee has been calculated in accordance with Rule 457(o) under the Securities Act.
- (5) Including such indeterminate amount of common stock as may be issued from time to time at indeterminate prices or upon conversion of debt securities and/or preferred stock registered hereby, or upon exercise of warrants registered hereby, as the case may be.
- (6) Including such indeterminate amount of preferred stock as may be issued from time to time at indeterminate prices or upon conversion of debt securities and/or preferred stock registered hereby, or upon exercise of warrants registered hereby, as the case may be.
- (7) Including such indeterminate principal amount of debt securities as may be issued from time to time at indeterminate prices or upon exercise of warrants registered hereby, as the case may be.
- (8) Including such indeterminate number of warrants or other rights, including without limitation share purchase or subscription rights, as may be issued from time to time at indeterminate prices.
- (9) Each unit will be issued under a unit agreement and will represent an interest in two or more securities, which may or may not be separable from one another.

THE REGISTRANT HEREBY AMENDS THIS REGISTRATION STATEMENT ON SUCH DATE OR DATES AS MAY BE NECESSARY TO DELAY ITS EFFECTIVE DATE UNTIL THE REGISTRANT SHALL FILE A FURTHER AMENDMENT WHICH SPECIFICALLY STATES THAT THIS REGISTRATION STATEMENT SHALL THEREAFTER BECOME EFFECTIVE IN ACCORDANCE WITH SECTION 8(a) OF THE SECURITIES ACT OF 1933, AS AMENDED, OR UNTIL THE REGISTRATION STATEMENT SHALL BECOME EFFECTIVE ON SUCH DATE AS THE COMMISSION ACTING PURSUANT TO SAID SECTION 8(a), MAY DETERMINE.

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The information in this preliminary prospectus is not complete and may be changed. These securities may not be sold until the registration statement filed with the Securities and Exchange Commission is effective. This preliminary prospectus is not an offer to sell nor does it seek an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

SUBJECT TO COMPLETION,

DATED MARCH 22, 2018.

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 March , 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.

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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.

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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, 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.

Table of Contents**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 $\geq 1.3 \times$ 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.

Table of Contents**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	N/A	N/A	N/A	N/A	35.22

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.

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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.

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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.

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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.

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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 successors past, present or future shareholders, employees, officers or directors.

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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.

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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.

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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.

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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.

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\$100,000,000

CHIASMA, INC.

Common Stock

Preferred Stock

Debt Securities

Warrants

Units

PROSPECTUS

, 2018

We have not authorized any dealer, salesperson or other person to give any information or represent anything not contained in this prospectus. You must not rely on any unauthorized information. If anyone provides you with different or inconsistent information, you should not rely on it. This prospectus does not offer to sell any securities in any jurisdiction where it is unlawful. Neither the delivery of this prospectus, nor any sale made hereunder, shall create any implication that the information in this prospectus is correct after the date hereof.

Table of Contents**Part II INFORMATION NOT REQUIRED IN PROSPECTUS****Item 14. Other Expenses of Issuance and Distribution**

The expenses payable by Chiasma, Inc. (the Registrant or the Company) in connection with the issuance and distribution of the securities being registered (other than underwriting discounts and commissions, if any) are set forth below. Each item listed is estimated, except for the Securities and Exchange Commission (the SEC) registration fee.

Securities and Exchange Commission registration fee	\$ 12,450
FINRA filing fee	*
Legal fees and expenses	*
Accounting fees and expenses	*
Printing fees and expenses	*
Transfer agent and trustee fees	*
Miscellaneous	*
Total	\$ *

* Estimated expenses not presently known

Item 15. Indemnification of Directors and Officers

Section 145 of the Delaware General Corporation Law permits a corporation to include in its charter documents, and in agreements between the corporation and its directors and officers, provisions expanding the scope of indemnification beyond that specifically provided by the current law.

Our certificate of incorporation provides for the indemnification of directors to the fullest extent permissible under Delaware law.

Our bylaws provide for the indemnification of officers, directors and third parties acting on our behalf if such persons act in good faith and in a manner reasonably believed to be in and not opposed to our best interest, and, with respect to any criminal action or proceeding, such indemnified party had no reason to believe his or her conduct was unlawful.

We have entered into indemnification agreements with each of our directors and certain of our executive officers. These agreements provide that we will indemnify each of our directors and certain of our executive officers to the fullest extent permitted by law. We intend to enter into indemnification agreements with any new directors and executive officers in the future.

We also maintain a general liability insurance policy which covers certain liabilities of directors and officers of our Company arising out of claims based on acts or omissions in their capacities as directors or officers.

Item 16. Exhibits

A list of exhibits filed with this registration statement on Form S-3 is set forth on the Exhibit Index and is incorporated herein by reference.

Item 17. Undertakings

The undersigned registrant hereby undertakes:

- (1) To file, during any period in which offers or sales are being made, a post-effective amendment to this registration statement:
- (i) To include any prospectus required by Section 10(a)(3) of the Securities Act of 1933;

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(ii) To reflect in the prospectus any facts or events arising after the effective date of the registration statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in the registration statement. Notwithstanding the foregoing, any increase or decrease in volume of securities offered (if the total dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of prospectus filed with the Securities and Exchange Commission pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than a 20 percent change in the maximum aggregate offering price set forth in the Calculation of Registration Fee table in the effective registration statement; and

(iii) To include any material information with respect to the plan of distribution not previously disclosed in the registration statement or any material change to such information in the registration statement;

provided, however, that paragraphs (I)(i), (I)(ii) and (I)(iii) of this section do not apply if the information required to be included in a post-effective amendment by those paragraphs is contained in reports filed with or furnished to the Securities and Exchange Commission by the registrant pursuant to Section 13 or Section 15(d) of the Securities Exchange Act of 1934 that are incorporated by reference in the registration statement, or is contained in a form of prospectus filed pursuant to Rule 424(b) that is part of the registration statement;

(2) That, for the purpose of determining any liability under the Securities Act of 1933, each such post-effective amendment shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof;

(3) To remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of the offering;

(4) That, for the purpose of determining liability under the Securities Act of 1933 to any purchaser:

(i) Each prospectus filed by the registrant pursuant to Rule 424(b)(3) shall be deemed to be part of the registration statement as of the date the filed prospectus was deemed part of and included in the registration statement; and

(ii) Each prospectus required to be filed pursuant to Rule 424(b)(2), (b)(5), or (b)(7) as part of a registration statement in reliance on Rule 430B relating to an offering made pursuant to Rule 415(a)(1)(i), (vii), or (x) for the purpose of providing the information required by Section 10(a) of the Securities Act of 1933 shall be deemed to be part of and included in the registration statement as of the earlier of the date such form of prospectus is first used after effectiveness or the date of the first contract of sale of securities in the offering described in the prospectus. As provided in Rule 430B, for liability purposes of the issuer and any person that is at that date an underwriter, such date shall be deemed to be a new effective date of the registration statement relating to the securities in the registration statement to which that prospectus relates, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof; *provided, however*, that no statement made in a registration statement or prospectus that is part of the registration statement or made in a document incorporated or deemed incorporated by reference into the registration statement or prospectus that is part of the registration statement will, as to a purchaser with a time of contract of sale prior to such effective date, supersede or modify any statement that was made in the registration statement or prospectus that was part of the registration statement or made in any such document immediately prior to such effective date;

(5) That, for the purpose of determining liability of the registrant under the Securities Act of 1933 to any purchaser in the initial distribution of the securities, the undersigned registrant undertakes that in a primary offering of securities of the undersigned registrant pursuant to this registration statement, regardless of the underwriting method used to sell

the securities to the purchaser, if the securities are offered or sold to such

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purchaser by means of any of the following communications, the undersigned registrant will be a seller to the purchaser and will be considered to offer or sell such securities to such purchaser:

(i) Any preliminary prospectus or prospectus of the undersigned registrant relating to the offering required to be filed pursuant to Rule 424;

(ii) Any free writing prospectus relating to the offering prepared by or on behalf of the undersigned registrant or used or referred to by the undersigned registrant;

(iii) The portion of any other free writing prospectus relating to the offering containing material information about the undersigned registrant or its securities provided by or on behalf of the undersigned registrant; and

(iv) Any other communication that is an offer in the offering made by the undersigned registrant to the purchaser;

(6) That, for purposes of determining any liability under the Securities Act of 1933, each filing of the registrant's annual report pursuant to Section 13(a) or Section 15(d) of the Securities Exchange Act of 1934 (and, where applicable, each filing of an employee benefit plan's annual report pursuant to Section 15(d) of the Securities Exchange Act of 1934) that is incorporated by reference in the registration statement shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof;

(7) Insofar as indemnification for liabilities arising under the Securities Act of 1933 may be permitted to directors, officers and controlling persons of the registrant pursuant to the foregoing provisions, or otherwise, the registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Securities Act of 1933 and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the registrant of expenses incurred or paid by a director, officer or controlling person of the registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act of 1933 and will be governed by the final adjudication of such issue;

(8) That, for purposes of determining any liability under the Securities Act of 1933, the information omitted from the form of prospectus filed as part of this registration statement in reliance upon Rule 430A and contained in a form of prospectus filed by the registrant pursuant to Rule 424(b)(1) or (4) or 497(h) under the Securities Act of 1933 shall be deemed to be part of this registration statement as of the time it was declared effective;

(9) That, for the purpose of determining any liability under the Securities Act of 1933, each post-effective amendment that contains a form of prospectus shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof; and

(10) To file an application for the purpose of determining the eligibility of the trustee to act under subsection (a) of Section 310 of the Trust Indenture Act of 1939 in accordance with the rules and regulations prescribed by the Securities and Exchange Commission under Section 305(b)(2) of the Trust Indenture Act of 1939.

Table of Contents**EXHIBIT INDEX**

Exhibit No.	Description
1.1*	Form of Underwriting Agreement
3.1	<u>Amended and Restated Certificate of Incorporation of the Registrant (incorporated by reference to Exhibit 3.1 of the Registrant's Form 8-K filed on July 21, 2015)</u>
3.2	<u>Amended and Restated Bylaws of the Registrant (incorporated by reference to Exhibit 3.2 of the Registrant's Form 8-K filed on July 21, 2015)</u>
4.1	<u>Form of indenture for senior debt securities and the related form of senior debt security</u>
4.2	<u>Form of indenture for subordinated debt securities and the related form of subordinated debt security</u>
4.3	<u>Form of Common Stock certificate of the Registrant (incorporated by reference to Exhibit 4.1 to the Registrant's Amendment No. 1 to Registration Statement on Form S-1/A (File No. 333-204949) filed on July 6, 2015)</u>
4.4	<u>Amended and Restated Investors' Rights Agreement, by and between the Registrant and the Investors named therein, dated as of December 16, 2014 (incorporated by reference to Exhibit 4.2 to the Registrant's Registration Statement on Form S-1 (File No. 333-204949) filed on June 15, 2015)</u>
4.5	<u>Form of Warrant to Purchase Shares of Common Stock (issued in connection with the Registrant's Series D preferred stock financing) (incorporated by reference to Exhibit 4.3 to the Registrant's Registration Statement on Form S-1 (File No. 333-204949) filed on June 15, 2015)</u>
4.6	<u>Form of Warrant to Purchase Shares of Common Stock (issued in connection with the Registrant's Series E preferred stock financing) (incorporated by reference to Exhibit 4.4 to the Registrant's Registration Statement on Form S-1 (File No. 333-204949) filed on June 15, 2015)</u>
4.7*	Form of Certificate of Designations
4.8*	Form of Warrant Agreements
4.9*	Form of Unit Certificate
4.10*	Form of Preferred Stock Certificate
5.1	<u>Opinion of Goodwin Procter LLP</u>
12.1	<u>Computation of Ratio of Earnings to Fixed Charges</u>
23.1	<u>Consent of Deloitte & Touche LLP</u>
23.2	<u>Consent of Kost Forer Gabbay & Kasierer</u>
23.3	<u>Consent of Goodwin Procter LLP (included in Exhibit 5.1 hereto)</u>
24.1	<u>Power of Attorney (included on the signature pages to this registration statement)</u>
25.1**	Form T-1 Statement of Eligibility of Trustee for Senior Indenture under the Trust Indenture Act of 1939
25.2**	Form T-1 Statement of Eligibility of Trustee for Subordinated Indenture under the Trust Indenture Act

of 1939

- * To be filed if necessary by amendment or as an exhibit to a document to be incorporated or deemed to be incorporated by reference in this registration statement, including a Current Report on Form 8-K.
- ** To be filed by amendment pursuant to Section 305(b)(2) of the Trust Indenture Act of 1939.

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Table of Contents**SIGNATURES**

Pursuant to the requirements of the Securities Act of 1933, the registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-3 and has duly caused this registration statement to be signed on its behalf by the undersigned, thereunto duly authorized, in Waltham, Massachusetts, on this 22nd day of March 2018.

CHIASMA, INC.

By: */s/ Mark J. Fitzpatrick*
Mark J. Fitzpatrick
Chief Executive Officer

KNOW ALL BY THESE PRESENTS, that each person whose signature appears below hereby severally constitutes and appoints each of Mark J. Fitzpatrick and Drew Enamait, and each of them singly, as such person's true and lawful attorneys-in-fact and agents, with full power of substitution and resubstitution, for such person and in such person's name, place and stead, in any and all capacities, to sign any or all amendments (including, without limitation, post-effective amendments) to this registration statement (or any registration statement for the same offering that is to be effective upon filing pursuant to Rule 462(b) under the Securities Act of 1933), and to file the same, with all exhibits thereto, and all documents in connection therewith, with the Securities and Exchange Commission, granting unto each said attorney-in-fact and agent full power and authority to do and perform each and every act and thing requisite and necessary to be done in and about the premises, as fully to all intents and purposes as such person might or could do in person, hereby ratifying and confirming all that any said attorney-in-fact and agent, or any substitute or substitutes of any of them, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Act of 1933, this registration statement has been signed by the following persons in the capacities and on the dates indicated.

Signature	Title	Date
<i>/s/ Mark J. Fitzpatrick</i>	Chief Executive Officer and Director	March 22, 2018
Mark J. Fitzpatrick	(Principal Executive Officer and Principal Financial Officer)	
<i>/s/ Drew Enamait</i>	Vice President, Finance and Administration	March 22, 2018
Drew Enamait	(Principal Accounting Officer)	
<i>/s/ David Stack</i>	Director	March 22, 2018
David Stack		
<i>/s/ John F. Thero</i>	Director	March 22, 2018

John F. Thero

/s/ Todd Foley

Director

March 22, 2018

Todd Foley

/s/ Bard Geesaman, M.D., Ph.D.

Director

March 22, 2018

Bard Geesaman, M.D., Ph.D.

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Signature	Title	Date
<i>/s/ Scott Minick</i>	Director	March 22, 2018
Scott Minick		
<i>/s/ John Scarlett, M.D.</i>	Director	March 22, 2018
John Scarlett, M.D.		
<i>/s/ Roni Mamluk, Ph.D.</i>	Director	March 22, 2018
Roni Mamluk, Ph.D.		

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