

Mast Therapeutics, Inc.
Form 424B5
November 05, 2014
Table of Contents

Subject to completion, dated November 5, 2014

The information in this preliminary prospectus supplement is not complete and may be changed. This preliminary prospectus supplement and the accompanying prospectus are part of an effective registration statement filed with the Securities and Exchange Commission. This preliminary prospectus supplement and the accompanying prospectus are not an offer to sell these securities and are not soliciting an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

**Filed Pursuant to Rule 424(b)(5)
Registration No. 333-179989**

PROSPECTUS SUPPLEMENT

(To Prospectus dated May 1, 2012)

Series A Units consisting of Common Stock and Warrants

Series B Units consisting of Pre-Funded Warrants and Warrants

(**Shares of Common Stock Underlying the Pre-Funded Warrants**)

(**Shares of Common Stock Underlying the Warrants**)

Pursuant to this prospectus supplement and the accompanying prospectus, we are offering for sale Series A units, with each Series A unit consisting of one share of our common stock and of a warrant. Each whole warrant will be exercisable for one share of our common stock. The purchase price for each Series A unit is \$. The Series A units will not be issued or certificated. The shares of common stock and the warrants included in the Series A units will be issued separately but can only be purchased together in the Series A units in this offering.

We are also offering to those purchasers whose purchase of Series A units in this offering would result in the purchaser, together with its affiliates and certain related parties, beneficially owning more than 4.99% of our outstanding common stock following the consummation of this offering, the opportunity to purchase, in lieu of Series A units that would otherwise result in ownership in excess of 4.99% of our outstanding common stock, Series B units. Each Series B unit will consist of one pre-funded warrant and _____ of a warrant. Each pre-funded warrant will be exercisable for one share of our common stock. Each whole warrant will be exercisable for one share of our common stock. The purchase price for each Series B unit is \$ _____. The Series B units will not be issued or certificated. The pre-funded warrants and the warrants included in the Series B units will be issued separately but can only be purchased together in the Series B units in this offering.

We refer to the shares of our common stock, the warrants, and the pre-funded warrants issued in this offering, collectively, as the securities. We refer to the warrants included in the Series A units and the Series B units (but not the pre-funded warrants), collectively, as the warrants. We refer to the pre-funded warrants included in the Series B units, collectively, as the pre-funded warrants. The shares of our common stock issuable from time to time upon exercise of the pre-funded warrants and the warrants are also being offered pursuant to this prospectus supplement and the accompanying prospectus.

Each pre-funded warrant will have an initial exercise price of \$0.01 per share, will be exercisable upon issuance, and will expire five years from the date of issuance. Each warrant will have an initial exercise price of \$ _____ per share, will be exercisable upon issuance, and will expire five years from the date of issuance.

Our common stock is listed on NYSE MKT under the symbol MSTX. The last reported sale price of our common stock on November 4, 2014 was \$0.49 per share.

We do not intend to list the pre-funded warrants or the warrants on the NYSE MKT, any other national securities exchange or any other nationally recognized trading system.

Investing in our securities involves a high degree of risk. See Risk Factors, beginning on page S-6 of this prospectus supplement, as well as the documents incorporated by reference in this prospectus supplement, for a discussion of the factors you should carefully consider before deciding to purchase our securities.

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

	Per Series A Unit	Per Series B Unit	Total
Public offering price	\$ _____	\$ _____	\$ _____
Underwriting discounts and commissions ⁽¹⁾	\$ _____	\$ _____	\$ _____
Proceeds, before expenses, to us	\$ _____	\$ _____	\$ _____

(1) We have also agreed to reimburse the underwriters for fees and expenses incurred by them in connection with this offering, up to a maximum of \$100,000. See Underwriting beginning on page S-41 of this prospectus supplement for more information regarding underwriting discounts and commissions and expense reimbursement.

The underwriters expect to deliver the securities offered hereby against payment on or about November , 2014.

Sole Book-Running Manager

Cowen and Company

The date of this prospectus supplement is November , 2014

Table of Contents

TABLE OF CONTENTS

Prospectus Supplement

<u>ABOUT THIS PROSPECTUS SUPPLEMENT</u>	S-1
<u>PROSPECTUS SUPPLEMENT SUMMARY</u>	S-2
<u>THE OFFERING</u>	S-4
<u>RISK FACTORS</u>	S-6
<u>SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS</u>	S-34
<u>USE OF PROCEEDS</u>	S-35
<u>DILUTION</u>	S-36
<u>DESCRIPTION OF THE SECURITIES WE ARE OFFERING</u>	S-38
<u>UNDERWRITING</u>	S-41
<u>LEGAL MATTERS</u>	S-45
<u>EXPERTS</u>	S-45
<u>WHERE YOU CAN FIND ADDITIONAL INFORMATION</u>	S-45
<u>INCORPORATION OF CERTAIN INFORMATION BY REFERENCE</u>	S-46
TABLE OF CONTENTS	

<u>ABOUT THIS PROSPECTUS</u>	ii
<u>SUMMARY</u>	1
<u>RISK FACTORS</u>	5
<u>SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS</u>	5
<u>RATIO OF EARNINGS TO FIXED CHARGES</u>	7
<u>USE OF PROCEEDS</u>	7
<u>SECURITIES WE MAY OFFER</u>	8
<u>DESCRIPTION OF COMMON STOCK AND PREFERRED STOCK</u>	8
<u>DESCRIPTION OF DEBT SECURITIES</u>	12
<u>DESCRIPTION OF WARRANTS</u>	19
<u>DESCRIPTION OF UNITS</u>	20
<u>LEGAL OWNERSHIP OF SECURITIES</u>	22
<u>PLAN OF DISTRIBUTION</u>	25

<u>LEGAL MATTERS</u>	27
<u>EXPERTS</u>	27
<u>WHERE YOU CAN FIND MORE INFORMATION</u>	27
<u>INCORPORATION OF CERTAIN INFORMATION BY REFERENCE</u>	27

Table of Contents

ABOUT THIS PROSPECTUS SUPPLEMENT

This document is in two parts. The first part is the prospectus supplement, including the documents incorporated by reference, which describes the specific terms of this offering. The second part, the accompanying prospectus, including the documents incorporated by reference, provides more general information. Before you invest, you should carefully read this prospectus supplement, the accompanying prospectus, all information incorporated by reference herein and therein, as well as the additional information described under **Where You Can Find Additional Information** on page S-45 of this prospectus supplement. These documents contain information you should consider when making your investment decision. This prospectus supplement may add, update or change information contained in the accompanying prospectus. To the extent there is a conflict between the information contained in this prospectus supplement, on the one hand, and the information contained in the accompanying prospectus or any document incorporated by reference therein filed prior to the date of this prospectus supplement, on the other hand, you should rely on the information in this prospectus supplement. If any statement in one of these documents is inconsistent with a statement in another document having a later date—for example, a document filed after the date of this prospectus supplement and incorporated by reference in this prospectus supplement and the accompanying prospectus—the statement in the document having the later date modifies or supersedes the earlier statement.

You should rely only on the information contained or incorporated by reference in this prospectus supplement, the accompanying prospectus and in any free writing prospectuses we may provide to you in connection with this offering. We have not, and Cowen has not, authorized any other person to provide you with any information that is different. If anyone provides you with different or inconsistent information, you should not rely on it. We are offering to sell, and seeking offers to buy, shares of our common stock only in jurisdictions where offers and sales are permitted. The distribution of this prospectus supplement and the offering of the common stock in certain jurisdictions may be restricted by law. Persons outside the United States who come into possession of this prospectus supplement must inform themselves about, and observe any restrictions relating to, the offering of the common stock and the distribution of this prospectus supplement outside the United States. This prospectus supplement does not constitute, and may not be used in connection with, an offer to sell, or a solicitation of an offer to buy, any securities offered by this prospectus supplement by any person in any jurisdiction in which it is unlawful for such person to make such an offer or solicitation.

We further note that the representations, warranties and covenants made by us in any agreement that is filed as an exhibit to any document that is incorporated by reference in the accompanying prospectus were made solely for the benefit of the parties to such agreement, including, in some cases, for the purpose of allocating risk among the parties to such agreements, and should not be deemed to be a representation, warranty or covenant to you. Moreover, such representations, warranties or covenants were accurate only as of the date when made. Accordingly, such representations, warranties and covenants should not be relied on as accurately representing the current state of our affairs.

Table of Contents

PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights selected information about us, this offering and information appearing elsewhere in this prospectus supplement, in the accompanying prospectus and in the documents we incorporate by reference. This summary is not complete and does not contain all the information you should consider before investing in our securities pursuant to this prospectus supplement and the accompanying prospectus. Before making an investment decision, to fully understand this offering and its consequences to you, you should carefully read this entire prospectus supplement and the accompanying prospectus, including Risk Factors beginning on page S-6 of this prospectus supplement and the financial statements and related notes and the other information that we incorporated by reference herein, including our Annual Reports on Form 10-K and Quarterly Reports on Form 10-Q that we file from time to time.

Unless the context otherwise requires, all references in this prospectus to Mast, we, us, our, the Company or similar words refer to Mast Therapeutics, Inc., together with our consolidated subsidiaries.

Overview

We are a clinical-stage, biopharmaceutical company developing novel therapies for serious or life-threatening diseases with significant unmet needs. We are leveraging our Molecular Adhesion & Sealant Technology, or MAST, platform, derived from over two decades of clinical, nonclinical, and manufacturing experience with purified and non-purified poloxamers, to develop MST-188, our lead product candidate, for serious or life-threatening diseases and conditions typically characterized by impaired microvascular blood flow and damaged cell membranes.

We have devoted substantially all of our resources to research and development, or R&D, and to acquisition of our product candidates. We have not yet marketed or sold any products or generated any significant revenue and we have incurred significant annual operating losses since inception. We incurred a loss from operations of \$21.9 million for the nine months ended September 30, 2014. Our cash, cash equivalents, and investment securities were \$43.1 million as of September 30, 2014.

We continue to focus our resources primarily on the development of MST-188. We believe that its pharmacologic effects support its development in a wide range of serious or life-threatening diseases and conditions, and we intend to develop MST-188 in multiple clinical indications, both independently and through collaborations. Enrolling patients in EPIC, our ongoing pivotal phase 3 study of MST-188 in sickle cell disease, is one of our top priorities. We expect to enroll 388 subjects in the study from approximately 70 medical centers within and outside the United States. We have opened 50 U.S. study sites and more than ten study sites outside of the U.S. More than half of the EPIC study sites have enrolled at least one patient. Although predicting the rate of enrollment for EPIC is subject to a number of significant assumptions and the actual rate may differ materially, we expect to complete enrollment by the end of 2015. If EPIC is successful, we plan to submit a new drug application, or NDA, to the U.S. Food and Drug Administration, or FDA, based in large part on data from that study.

We also are enrolling patients with acute limb ischemia in a phase 2 clinical study of MST-188 in combination with recombinant tissue plasminogen activator (rt-PA) to evaluate whether MST-188 improves effectiveness of thrombolytic therapy. In addition, we are planning to initiate a phase 2 study of MST-188 in patients with acute decompensated heart failure in the first half of 2015. Our MST-188 pipeline also includes preclinical development programs in stroke and resuscitation following major trauma (*i.e.*, restoration of circulating blood volume and pressure).

Edgar Filing: Mast Therapeutics, Inc. - Form 424B5

In addition to our lead product candidate, we are developing AIR001, sodium nitrite inhalation solution for intermittent inhalation via nebulizer, in pulmonary hypertension (PH) associated with left heart disease. We

S-2

Table of Contents

acquired AIR001 in February 2014 through our acquisition of Aires Pharmaceuticals, Inc. In September 2014, we reported positive preliminary data from a phase 2 study of AIR001. Consistent with findings from earlier studies of AIR001, the data support AIR001's potential as an agent that can have a positive effect on hemodynamic parameters in patients with PH. We believe AIR001 may be uniquely suited to address the serious unmet need of patients with PH associated with left heart disease, or World Health Organization, or WHO, Group 2 PH, and we are supporting three institution-sponsored phase 2a studies of AIR001 in that patient population.

Corporate Information

In March 2013, we changed our name from ADVENTRX Pharmaceuticals, Inc. to Mast Therapeutics, Inc.

Our principal executive offices are located at 12390 El Camino Real, Suite 150, San Diego, CA 92130 and our telephone number is (858) 552-0866.

Table of Contents

THE OFFERING

Series A units we are offering	Series A units, with each unit consisting of one share of our common stock and of a warrant. Each whole warrant is exercisable for one share of our common stock.
Series B units we are offering	Series B units, with each Series B unit consisting of one pre-funded warrant to purchase one share of our common stock and of a warrant. Each whole warrant is exercisable for one share of our common stock. We will offer the opportunity to purchase Series B units to those purchasers whose purchase of Series A units in this offering would result in the purchaser, together with its affiliates and certain related parties, beneficially owning more than 4.99% of our outstanding common stock following the consummation of this offering, in lieu of Series A units that otherwise would result in ownership in excess of 4.99% of our outstanding common stock.
Public offering price	\$ per Series A unit and \$ per Series B unit
Pre-funded warrants we are offering	Each pre-funded warrant included in a Series B unit will have an initial exercise price of \$0.01 per share of common stock, will be exercisable upon issuance and will expire five years from the date of issuance. This prospectus supplement also relates to the offering of shares of our common stock issuable upon exercise of the pre-funded warrants.
Warrants we are offering	Each whole warrant included in Series A units and Series B units (other than the pre-funded warrant) will be exercisable for one share of our common stock, will have an initial exercise price of \$ per share of common stock, will be exercisable upon issuance and will expire five years from the date of issuance. This prospectus supplement also relates to the offering of shares of our common stock issuable upon exercise of the warrants.
Common stock to be outstanding immediately after this offering	shares (assuming none of the pre-funded warrants or warrants issued in the offering is exercised).
Use of proceeds	We currently intend to use the net proceeds from this offering primarily to fund our clinical development programs, including EPIC, our ongoing phase 3 clinical study of MST-188 in sickle cell disease, and for working capital and general corporate purposes. Please see Use of Proceeds on page S-35.
Risk factors	See Risk Factors beginning on page S-6 of this prospectus supplement, as well as the other information included in or incorporated by reference in this prospectus supplement and the accompanying prospectus, for a discussion of risks you should carefully consider before investing in our securities.
NYSE MKT symbol	MSTX
Transfer agent, warrant agent and registrar	American Stock Transfer & Trust Company, LLC

Table of Contents

The number of shares of our common stock to be outstanding immediately after this offering as shown above assumes that all of the Series A units being offered are sold, and is based on 127,508,434 shares of our common stock outstanding as of September 30, 2014 and excludes:

44,416,875 shares of our common stock issuable upon exercise of warrants outstanding as of September 30, 2014, with a weighted-average exercise price of \$1.05 per share;

13,062,271 shares of our common stock issuable upon exercise of options outstanding as of September 30, 2014, with a weighted-average exercise price of \$1.02 per share;

10,942,557 shares and 276,945 shares of our common stock available for future grants under our 2013 Omnibus Incentive Plan and 2005 Employee Stock Purchase Plan as of September 30, 2014, respectively;

12,478,050 shares of common stock that may be issued to the former stockholders of SynthRx, Inc., subject to the achievement of performance milestones, pursuant to the terms of the merger agreement with SynthRx;

1,008,840 shares of our common stock sold after September 30, 2014 pursuant to our at the market equity offering program;

shares of our common stock issuable upon exercise of the pre-funded warrants offered by this prospectus supplement and the accompanying prospectus; and

shares of our common stock issuable upon exercise of the warrants included in the Series A units and Series B units offered by this prospectus supplement and the accompanying prospectus.

Table of Contents

RISK FACTORS

*Investing in our securities involves a high degree of risk and uncertainty. You should carefully consider these risk factors, together with all of the other information included or incorporated by reference in this prospectus supplement and the accompanying prospectus, as modified and superseded, before you decide to invest in our securities. The occurrence of any of the following risks could harm our business. In that case, the trading price of our common stock could decline, and you may lose all or part of your investment. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also impair our operations. You should also refer to the other information contained in this prospectus supplement, the accompanying prospectus and the documents incorporated by reference into this prospectus supplement and the accompanying prospectus, including our financial statements and the notes to those statements and the information set forth in the section entitled *Special Note Regarding Forward-Looking Statements*.*

RISKS RELATED TO OUR BUSINESS

Risks Related to Our Capital Requirements, Finances and Operations

We have incurred losses since our inception, we expect our operating expenses to continue to exceed our revenue for the foreseeable future, and we may never generate revenue sufficient to achieve profitability.

We are a clinical-stage company and have not generated sustainable revenue from operations or been profitable since inception, and we may never achieve profitability. We have devoted our resources to acquiring and developing proprietary product candidates, but such product candidates cannot be marketed until the regulatory process is completed and governmental approvals have been obtained. For the nine months ended September 30, 2014, we incurred a loss from operations of \$21.9 million. We expect to continue to incur substantial operating losses for the next several years as we advance our product candidates through clinical studies and other development activities and seek approval from the FDA to commercialize them. Accordingly, there is no current source of revenue from operations, much less profits, to sustain our present activities. Further, no revenue from operations will likely be available until, and unless, we enter into an arrangement that provides for licensing revenue or other partnering-related funding or one of our product candidates is approved by the FDA or another regulatory agency and successfully marketed, outcomes which we may not achieve.

The success of our business currently is dependent largely on the success of MST-188 and this product candidate may not receive regulatory approval or be successfully commercialized.

None of our product candidates has been approved for sale by any regulatory agency. We are focusing our resources primarily on the development of MST-188. Accordingly, the success of our business currently depends on our ability, or that of a future partner, to successfully develop, obtain regulatory approval for and then successfully commercialize this product candidate and our efforts, or those of a future partner, in this regard may prove unsuccessful. MST-188 requires considerable additional clinical development and significant manufacturing and related activities prior to commencing any commercial manufacturing, all of which require us to expend significant resources and with which we have limited experience. MST-188 may not be successful in the EPIC study or in other clinical studies we initiate, and, even if successful in clinical studies, may not receive regulatory approval in a timely manner, or at all. If MST-188 is approved by the FDA or any foreign regulatory agency, our ability to generate revenue from it will depend in substantial part on the extent to which it is accepted by the medical community and reimbursed by third-party payors, as well as our ability to market and sell the product and ensure that our third-party manufacturers produce it in quantities sufficient to meet commercial demand, if any.

Table of Contents

The process of developing and seeking regulatory approval of investigational new drug products requires expenditure of substantial resources, and we cannot estimate with reasonable certainty the duration of or costs to complete our development programs.

Our capital requirements for the foreseeable future will depend in large part on, and could increase significantly as a result of, our expenditures on our development programs. Future expenditures on our development programs are subject to many uncertainties, and will depend on, and could increase significantly as a result of, many factors, including:

the number and scope of development programs we pursue;

the number of clinical and nonclinical studies necessary to demonstrate the safety and efficacy of a product candidate in a particular indication;

the number of patients who participate in each clinical study;

the number and location of sites and the rate of site initiation in each study;

the rate of patient enrollment and ratio of randomized to evaluable patients in each clinical study;

the duration of patient treatment and follow-up;

the potential for additional safety monitoring or other studies requested by regulatory agencies;

the time and cost to manufacture clinical trial material and commercial product, including process development and scale-up activities, and to conduct stability studies, which can last several years;

the costs, requirements, timing of, and the ability to, secure regulatory approvals;

the timing and terms of any collaborative or other strategic arrangement that we may establish;

the extent to which we increase our workforce and the costs involved in recruiting, training and incentivizing new employees;

the costs related to developing, acquiring and/or contracting for sales, marketing and distribution capabilities, supply chain management capabilities, and regulatory compliance capabilities, if we obtain regulatory approval for a product candidate and commercialize it without a partner; and

the costs involved in establishing, enforcing or defending patent claims and other proprietary rights. We may not be able to raise capital when needed or reduce other expenditures to offset expenditures on our development programs, which could have a material adverse effect on our financial condition and ability to pursue our business strategy.

We will need to obtain additional funding to pursue our current business strategy and we may not be able to obtain such funding on a timely basis, or on commercially reasonable terms, or at all. Any capital-raising transaction we are able to complete may result in dilution to our existing stockholders, require us to relinquish significant rights or restrict our operations.

We anticipate that our cash, cash equivalents and investment securities, which were approximately \$43.1 million as of September 30, 2014, together with the net proceeds from this offering, will be sufficient to fund our currently planned level of operations for at least the next 12 months. However, we may determine to grow our organization and/or pursue development activities for MST-188, AIR001 or other product candidates at levels or on timelines, or we may incur unexpected expenses, that shorten the period through which our current operating funds will sustain us. Through our acquisition of Aires Pharmaceuticals in February 2014, we expanded our product pipeline to include AIR001. In the future, we may seek to further expand our product pipeline through acquisition of additional product candidates and/or technologies and the cost to acquire and develop such new product candidates and/or technologies may shorten the period through which our current operating funds will sustain us. We do not expect to generate any substantial revenue from operations in the next several years, and we will need to obtain additional capital to support our planned operating activities.

Table of Contents

For the foreseeable future, we likely will seek to fund our operations through public or private equity and debt financings and/or through collaborations, such as licensing arrangements or partnering transactions, and may execute any such transaction at any time, subject to applicable laws and regulations. Although we were able to raise significant funds in the past through equity financings, the conditions of and our access to capital markets are highly variable and adequate additional financing may not be available to us in the future on acceptable terms, or on a timely basis, or at all. Further, each of these financing alternatives carries risks. Raising capital through the issuance of our common stock, or securities convertible into or exercisable for our common stock, may depress the market price of our stock and may substantially dilute our existing stockholders. If instead we seek to raise capital through strategic transactions, such as licensing arrangements or sales of one or more of our technologies or product candidates, we may be required to relinquish valuable rights and dilute the current and future value of our assets. For example, any licensing arrangement likely would require us to share with our licensee a significant portion of any revenues generated by our licensed technologies. Additionally, our control over the development and/or marketing of any products or product candidates licensed or sold to third parties may be reduced and thus we may not realize the full value of any such products or product candidates. Debt financings would likely involve covenants that would restrict our operations. These restrictive covenants may include limitations on additional borrowing and specific restrictions on the use of our assets, as well as prohibitions on our ability to create liens or make investments and may, among other things, preclude us from making distributions to stockholders (either by paying dividends or redeeming stock) and taking other actions beneficial to our stockholders. In addition, investors could impose more one-sided investment terms and conditions on companies that have or are perceived to have limited remaining funds or limited ability to raise additional funds. The lower our cash balance, the more difficult it is likely to be for us to raise additional capital on commercially reasonable terms, or at all.

For particular development programs, such as development of MST-188 for resuscitation following major trauma, we plan to seek funding from the U.S. government. The process of obtaining government contracts is lengthy and uncertain and highly competitive. In addition, changes in government budgets and agendas may result in decreased availability of funding for drug research and development. If we do secure government funding, the contracts for such funding may contain termination and audit provisions that are unfavorable to us and cause us to incur significant additional administrative expense. In addition, the U.S. government may require march-in rights that allow it to grant licenses to inventions that arise from development programs it funds if, for example, we do not commercialize the technology within a certain timeframe or the government deems such action necessary to alleviate health or safety needs that are not being reasonably satisfied by us. If the government exercises its march-in rights, we could be obligated to license intellectual property developed by us on terms unfavorable to us and we may not receive compensation from the government for its exercise of such rights.

Notwithstanding any effort on our part to raise additional capital, adequate additional funding may not be available on acceptable terms, or on a timely basis, or at all. Even if we incur costs in pursuing, evaluating and negotiating particular capital-raising and/or strategic or partnering transactions, our efforts may not prove successful. We believe global economic conditions, such as volatility in the U.S. and international equity markets, may adversely impact our ability to raise additional capital. Our failure to raise capital as needed would have a material adverse effect on our financial condition and ability to pursue our business strategy.

Our ability to raise capital may be limited by applicable laws and regulations.

Historically, we have raised capital through the sale of our equity securities. Between June 2009 and November 2011, we completed seven equity financings and, in February 2014, we commenced an at the market equity offering program under shelf registration statements on Form S-3. Using a shelf registration statement on Form S-3 to raise additional capital generally takes less time and is less expensive than other means, such as conducting an offering under a Form S-1 registration statement. However, our ability to raise capital using a shelf registration statement may

be limited by, among other things, SEC rules and regulations. Under current SEC rules and regulations, we must meet certain requirements to use a Form S-3 registration statement to

S-8

Table of Contents

raise capital without restriction as to the amount of the market value of securities sold thereunder. One such requirement is that the market value of our outstanding common stock held by non-affiliates, or public float, be at least \$75.0 million as of a date within 60 days prior to the date of filing the Form S-3. If we do not meet that requirement, then the aggregate market value of securities sold by us or on our behalf under the Form S-3 in any 12-month period is limited to an aggregate of one-third of our public float. Moreover, even if we meet the public float requirement at the time we file a Form S-3, SEC rules and regulations require that we periodically re-evaluate the value of our public float, and if, at a re-evaluation date, our public float is less than \$75.0 million, we would become subject to the one-third of public float limitation described above. If our ability to utilize a Form S-3 registration statement for a primary offering of our securities is limited to one-third of our public float, we may conduct such an offering pursuant to an exemption from registration under the Securities Act or under a Form S-1 registration statement, which we have done in the past, including in June 2013, and we would expect either of those alternatives to increase the cost of raising additional capital relative to utilizing a Form S-3 registration statement.

In addition, under current SEC rules and regulations, our common stock must be listed and registered on a national securities exchange in order to utilize a Form S-3 registration statement (i) for a primary offering, if our public float is not at least \$75.0 million as of a date within 60 days prior to the date of filing the Form S-3, or a re-evaluation date, whichever is later, and (ii) to register the resale of our securities by persons other than us (i.e., a resale offering). While currently our common stock is listed on the NYSE MKT equities market, there can be no assurance that we will be able to maintain such listing. The NYSE MKT reviews the appropriateness of continued listing of any issuer that falls below the exchange's continued listing standards. Previously, including during part of 2010, we were not in compliance with certain NYSE MKT continued listing standards and were at risk of having our common stock delisted from the NYSE MKT equities market. For additional information regarding this risk, see the risk factor below titled "If we are unable to maintain compliance with NYSE MKT continued listing standards, our common stock may be delisted from the NYSE MKT equities market, which would likely cause the liquidity and market price of our common stock to decline."

Our ability to timely raise sufficient additional capital also may be limited by the NYSE MKT's stockholder approval requirements for transactions involving the issuance of our common stock or securities convertible into our common stock. For instance, the NYSE MKT requires that we obtain stockholder approval of any transaction involving the sale, issuance or potential issuance by us of our common stock (or securities convertible into our common stock) at a price less than the greater of book or market value, which (together with sales by our officers, directors and principal stockholders) equals 20% or more of our then outstanding common stock, unless the transaction is considered a "public offering" by the NYSE MKT staff. Based on 128,517,274 shares of our common stock outstanding as of October 31, 2014 and the closing price per share of our common stock on such date, which was \$0.51, we could not raise more than approximately \$13.1 million without obtaining stockholder approval, unless the transaction is deemed a public offering or does not involve the sale, issuance or potential issuance by us of our common stock (or securities convertible into our common stock) at a price less than the greater of book or market value. In addition, certain prior sales by us may be aggregated with any offering we may propose in the future, further limiting the amount we could raise in any future offering that is not considered a public offering by the NYSE MKT staff and involves the sale, issuance or potential issuance by us of our common stock (or securities convertible into our common stock) at a price less than the greater of book or market value. The NYSE MKT also requires that we obtain stockholder approval if the issuance or potential issuance of additional shares will be considered by the NYSE MKT staff to result in a change of control of our company.

Obtaining stockholder approval is a costly and time-consuming process. If we are required to obtain stockholder approval for a potential transaction, we would expect to spend substantial additional money and resources. In addition, seeking stockholder approval would delay our receipt of otherwise available capital, which may materially and adversely affect our ability to execute our current business strategy, and there is no guarantee our stockholders

ultimately would approve a proposed transaction. A public offering under the NYSE MKT rules typically involves broadly announcing the proposed transaction, which often times has the effect of depressing

S-9

Table of Contents

the issuer's stock price. Accordingly, the price at which we could sell our securities in a public offering may be less, and the dilution existing stockholders experience may in turn be greater, than if we were able to raise capital through other means.

If we are unable to raise sufficient additional capital as needed, we may be forced to delay, scale back or discontinue our development of our product candidates, partner them at inopportune times or pursue less expensive but higher-risk and/or lower-return development paths.

If we are not able to raise sufficient additional capital as needed, we may be required to delay, scale back or discontinue one or more of our development programs, or to seek collaborators at an earlier stage than otherwise would be desirable or on terms less favorable than might otherwise be available. For example, if we do not have sufficient capital, we may determine not to investigate certain additional indications for MST-188 or to conduct other studies or activities intended to enhance our intellectual property position, improve the probability of regulatory approval, or expand the scope of MST-188's clinical benefit and market potential. Delays in and/or reduction of development activities could impair our ability to realize the full clinical and market potential of a product candidate and have a material adverse effect on our business and financial condition. In addition, discontinuation of a development program may be viewed negatively, which could adversely affect our stock price.

To the extent we discontinue independent development of a product candidate, we may not realize any value from our investment in the discontinued program. Even if we pursue a strategic option, such as partnering, selling or exclusively licensing the program to a third party, such an option may be not be available on acceptable terms or at all. For example, in prior years, we were focused on developing Exelbine and ANX-514 and expended significant resources on their development; however, in 2011 and 2012, respectively, we elected to discontinue independent development of those programs. Although we are evaluating other opportunities for further development of those agents, such as partnering and licensing arrangements, none may be available and we may not realize any return on our investment in those programs.

Our business may suffer if we are unable to retain and attract highly qualified personnel and manage internal growth.

Currently, we have a small number of employees and we rely on third parties to perform many essential services for us. Our ability to execute on our business strategy and compete in the highly competitive biopharmaceutical, specialty pharmaceutical, pharmaceutical and biotechnology industries depends, in part, on our ability to attract and retain highly qualified personnel. We are highly dependent on certain personnel, including our chief executive officer, our president and chief operating officer, our chief medical officer, and our senior vice president, development. Our industries in general and our company in particular historically have experienced a high rate of turnover of management personnel. If we lose any of our key employees, our ability to successfully implement our current business strategy could be seriously harmed. Replacing key employees may be a difficult, costly and protracted process, particularly due to the fact that we currently do not have other executive officers or personnel to assume all of the responsibilities of these key employees. In addition, we may seek to increase the size of our organization as development of our product candidates progresses. Competition for qualified personnel, particularly for key positions, is intense among companies in our field, universities and other research organizations, particularly in the San Diego, California area, and many of the organizations against which we compete for qualified personnel have greater financial and other resources and different risk profiles than our company, which may make them more attractive employers. Our ability to compete for qualified personnel may be adversely affected by our highly volatile stock price. The value of stock options we offer to candidates to induce their employment and to our employees to retain and incentivize them is significantly affected by movements in our stock price that we cannot control and may at any time be insufficient to counteract more lucrative offers from other companies. All of our employees, including our

executive officers, may terminate their employment with us at any time without notice. If we cannot attract and retain skilled personnel, as needed, we may not achieve our development and other goals.

S-10

Table of Contents

Future internal growth could impose significant added responsibilities on our management, including the need to identify, recruit, maintain, motivate and integrate additional employees. We may need to devote a significant amount of time to managing these activities and may not be able to do so effectively. If we are unable to effectively manage future internal growth, our expenses may increase more than expected, we may not be able to achieve our development goals, and our ability to generate and/or grow revenue could be diminished. In the meantime, the success of our business also depends, in part, on our ability to develop and maintain relationships with respected service providers and industry-leading consultants and advisers. If we cannot develop and maintain such relationships, as needed, the rate and success at which we can develop and commercialize product candidates may be limited. In addition, our outsourcing strategy, which has included engaging consultants that spend considerable time in our office to manage key functional areas, may subject us to scrutiny under labor laws and regulations, which may divert management time and attention and have an adverse effect on our business and financial condition.

If we determine to grow our business through the acquisition of new technologies and/or product candidates, our existing stockholders may experience substantial dilution, we may fail to realize the benefits of any future strategic acquisition or investment and we may incur unexpected costs and disruptions to our business.

From time to time, we may evaluate pipeline expansion opportunities and execute the acquisition of new technologies and/or product candidates that we believe will increase the long-term value of our company. The process of identifying, evaluating, negotiating and implementing the purchase or license of new assets is lengthy and complex and may disrupt other development programs and distract our personnel. We have limited resources with respect to identifying, evaluating, negotiating and implementing the acquisition of new assets or rights thereto and integrating them into our current infrastructure. Supplementing our current resources to complete one or more of these transactions may be costly.

We may use cash, shares of our common stock, securities convertible into our common stock or a combination of cash and our securities to pay the purchase price or license fee for any future strategic transaction. The use of cash could negatively impact our financial position and ability to advance our current development programs. The use of shares of our common stock or securities convertible into shares of our common stock would dilute the holdings of our existing stockholders and such dilution could be substantial. For example, to acquire SynthRx we agreed to issue up to such number of shares that represented a 41% ownership stake in our company at the time we completed the acquisition in April 2011, if development of MST-188 fully achieved the milestones under the merger agreement. The issuance of shares in connection with future strategic transactions, if any, may result in the stockholders who own the majority of our voting securities prior to one or more of such transactions owning less than a majority after such transactions.

Further, strategic transactions may entail numerous operational and financial risks, including:

exposure to unknown liabilities;

disruption of our business and diversion of our management's time and attention to develop and/or commercialize acquired technologies and/or products candidates;

incurrence of substantial debt to pay for acquisitions;

greater than anticipated difficulty and cost in combining the operations and personnel of any acquired businesses with our operations and personnel;

impairment of relationships with key suppliers of any acquired business due to changes in management and ownership; and

inability to retain key employees of any acquired business.

Our stockholders will be required to rely on the judgment of our management and board of directors as to which new product candidates and/or technologies we pursue and may have limited or no opportunity to evaluate

S-11

Table of Contents

potential new assets prior to completion of a transaction, including the terms of acquisition, the costs of their future development and their commercial potential. We may devote resources to potential acquisition or in-licensing opportunities that are never completed, or we may fail to realize the anticipated benefits of such efforts. Any technology and/or product candidate that we acquire or to which we acquire rights likely will require additional development efforts prior to commercial sale, including extensive clinical testing and approval by the FDA and applicable foreign regulatory authorities. All product candidates are subject to risks of failure typical of pharmaceutical product development, including the possibility that a product candidate will not be shown to be sufficiently safe and effective for approval by regulatory authorities and other risks described under the section titled Risks Related to Drug Development and Commercialization.

We expend substantial resources to comply with laws and regulations relating to public companies, and any failure to maintain compliance could subject us to regulatory scrutiny and cause investors to lose confidence in our company, which could harm our business and have a material adverse effect on our stock price.

Laws and regulations affecting public companies, including provisions of the Dodd-Frank Wall Street Reform and Consumer Protection Act of 2010 and the Sarbanes-Oxley Act of 2002, or SOX, and the related rules and regulations adopted by the SEC and by the NYSE MKT have resulted in, and will continue to result in, significant costs to us as we evaluate the implications of these rules and respond to their requirements. For example, compliance with Section 404 of SOX, including performing the system and process documentation and evaluation necessary to issue our annual report on the effectiveness of our internal control over financial reporting and, if applicable, obtain the required attestation report from our independent registered public accounting firm, requires us to incur substantial expense and expend significant management time. Further, we have in the past discovered, and may in the future discover, areas of internal controls that need improvement. If we identify deficiencies in our internal controls that are deemed to be material weaknesses, we could become subject to scrutiny by regulatory authorities and lose investor confidence in the accuracy and completeness of our financial reports, which could have a material adverse effect on our stock price. Internal control over financial reporting cannot provide absolute assurance of achieving financial reporting objectives because of its inherent limitations, including the possibility of human error and circumvention by collusion or overriding of controls. Accordingly, even an effective internal control system may not prevent or detect material misstatements on a timely basis, or at all. Also, previously effective controls may become inadequate over time as a result of changes in our business or operating structure, and we may fail to take measures to evaluate the adequacy of and update these controls, as necessary, which could lead to a material misstatement.

In addition, new laws and regulations could make it more difficult or more costly for us to obtain certain types of insurance, including director and officer liability insurance, and we may be forced to accept reduced policy limits and coverage or incur substantially higher costs to obtain the coverage that is the same or similar to our current coverage. The impact of these events could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors or board committees, and as our executive officers. We cannot predict or estimate with any reasonable accuracy the total amount or timing of the costs we may incur to comply with these laws and regulations.

Our ability to use net operating loss carry forwards and research and development tax credits to offset future taxable income or future tax will be limited and may be limited further in the future due to changes in ownership (within the meaning of IRC Section 382) that have occurred and may occur in the future.

In general, under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, or IRC, a corporation that undergoes an ownership change is subject to limitations on its ability to utilize its pre-change net operating losses, or NOLs, and certain other tax assets to offset future taxable income, and an ownership change is generally defined as a cumulative change of 50% or more in the ownership positions of certain stockholders during a rolling three year period. In 2012, we identified several ownership changes within the meaning of IRC Section 382 that had occurred

during 2010 and 2011, with the most recent as a result of our November 2011 common stock and warrant financing. As a result of those ownership changes, we do not expect

S-12

Table of Contents

to be eligible to utilize the NOL carry forwards and research and development tax credits we had accumulated as of November 11, 2011. In addition, although we have not yet conducted a formal study to identify ownership changes within the meaning of IRC Section 382 for periods after December 31, 2011, we believe that the common stock and warrant financing we completed in June 2013 may be an ownership change for purposes of Sections 382 and 383 of the IRC, which would further limit the availability of our NOL carry forwards. Other ownership changes within the meaning of IRC Section 382 may occur in the future, including as a result of this offering, and such future ownership changes could eliminate or restrict our ability to use NOL carry forwards and research and development tax credits generated after June 19, 2013. Limitations on our ability to use NOL carry forwards and research and development tax credits to offset future taxable income could require us to pay U.S. federal income taxes earlier than would be required if such limitations were not in effect. Similar rules and limitations may apply for state income tax purposes.

Our operations might be interrupted by the occurrence of a natural disaster or other catastrophic event.

Our corporate headquarters are located in a single commercial facility in San Diego, California. Important documents and records, including copies of our regulatory documents and other records for our product candidates, are located at our facilities and we depend on our facilities for the continued operation of our business. Natural disasters and other catastrophic events, such as wildfires and other fires, earthquakes and extended power interruptions, which have impacted San Diego businesses in the past, and terrorist attacks or severe weather conditions, could significantly disrupt our operations and result in additional, unplanned expense. As a small company, we have limited capability to establish and maintain a comprehensive disaster recovery program and, accordingly, we do not have a formal business continuity or disaster recovery plan, and any natural disaster or catastrophic event could disrupt our business operations and result in setbacks to our development programs. Even though we believe we carry commercially reasonable insurance, we might suffer losses that are not covered by or exceed the coverage available under these insurance policies.

Risks Related to Drug Development and Commercialization

Further testing and validation of our product candidates and related manufacturing processes are required and regulatory approval may be delayed or denied, which would delay or prevent us from marketing our product candidates and substantially harm our business.

Human pharmaceutical products generally are subject to rigorous nonclinical testing and clinical studies and other approval procedures mandated by the FDA and foreign regulatory authorities. Various federal and foreign statutes and regulations also govern or influence the manufacturing, safety, labeling, storage, record keeping and marketing of pharmaceutical products. The process of obtaining these approvals and the subsequent compliance with appropriate U.S. and foreign statutes and regulations is time-consuming and requires the expenditure of substantial resources. In addition, these requirements and processes vary widely from country to country. Government regulation and the need for FDA and other regulatory agency approval will delay commercialization of our product candidates, impose costly procedures upon our activities, and may put us at a disadvantage relative to other companies with which we compete. There can be no assurance that FDA or any other regulatory agency will grant marketing approval for any of our product candidates on a timely basis, or at all, including due to factors not within our control. For example, federal government shut-down or budget sequestration, such as occurred during 2013, may result in significant reductions to the FDA's budget and operations, which may lead to slower response times and longer review periods, potentially affecting our ability to progress development of or obtain approval for our product candidates.

Clinical studies typically involve a lengthy and expensive process with an uncertain outcome.

Clinical testing typically is expensive and can take years to complete, and its outcome is inherently uncertain. Clinical studies may not commence on time or be completed on schedule, if at all. The commencement and completion of clinical studies can be delayed for a variety of reasons, including difficulties and delays related to:

obtaining regulatory approval to commence a clinical study;

S-13

Table of Contents

obtaining institutional review board, or IRB, approval to conduct a clinical study at a prospective site;

identifying appropriate study sites and reaching agreement on acceptable terms with prospective study sites and investigators, the terms of which can be subject to extensive negotiation and may vary significantly among study sites;

reaching agreement on acceptable terms with prospective contract research organizations, or CROs, for the conduct of clinical studies and contract manufacturing organizations, or CMOs, for the production of clinical trial material, the terms of which agreements can be subject to extensive negotiation and may vary significantly among different CROs and CMOs;

failures on the part of our CROs and CMOs in developing procedures and protocols or otherwise conducting activities on timelines requested by us;

identifying and hiring or engaging, as applicable, additional employees or consultants to assist us in managing CRO and/or CMO activities, managing a clinical study and analyzing the data resulting from a study;

recruiting and enrolling patients to participate in a clinical study;

manufacturing sufficient quantities of clinical trial material due, among other things, to lack of availability of capacity at a CMO or of the component materials, including the active pharmaceutical ingredient, or API;

having patients complete a study and/or return for and complete post-treatment follow-up; and

unforeseen results from other clinical studies or nonclinical testing that require us to amend a study design or halt or terminate a clinical study.

Patient enrollment, a critical component to successful completion of a clinical study, is affected by many factors, including the size and nature of the study subject population, the proximity of patients to clinical sites, the eligibility criteria for the study, the design of the clinical study, competing clinical studies and clinicians and patients' perceptions as to the potential advantages of the drug being studied in relation to available alternatives, including therapies being investigated by other companies. Further, completion of a clinical study and/or its results may be adversely affected by failure to retain subjects who enroll in a study but withdraw due to adverse side effects, lack of efficacy, improvement in condition before treatment has been completed or for personal issues or who fail to return for or complete post-treatment follow-up.

In addition, a clinical study may be suspended or terminated by us, an IRB, a data safety monitoring board, the FDA or other regulatory authorities due to a number of factors, including:

failure to conduct the study in accordance with regulatory requirements or the study's protocol;

inspection of clinical study operations or sites by the FDA or other regulatory authorities resulting in the imposition of a clinical hold;

unforeseen safety issues, including adverse side effects;

changes in governmental regulations or administrative actions; or

lack of adequate funding to continue the study.

Changes in governmental regulations and guidance relating to clinical studies may occur and we may need to amend study protocols to reflect these changes, or we may amend study protocols for other reasons. Amendments may require us to resubmit protocols to IRBs for reexamination or renegotiate terms with CROs, study sites and investigators, all of which may adversely impact the costs or timing of or our ability to successfully complete a trial.

S-14

Table of Contents

Clinical studies may not begin on time or be completed in the timeframes we anticipate and may be more costly than we anticipate for a variety of reasons, including one or more of those described above. For example, although we expect to move MST-188 directly into phase 2 studies for most new indications we plan to pursue, an IRB or the FDA or another regulatory agency may require additional clinical or nonclinical studies prior to initiation of any planned phase 2 study, which likely would increase the total time and cost of development in that indication. The length of time necessary to complete clinical studies varies significantly and is difficult to predict accurately. We may make statements regarding anticipated timing for completion of enrollment in and/or availability of results from our clinical studies, but such predictions are subject to a number of significant assumptions and actual timing may differ materially for a variety of reasons, including patient enrollment rates and other factors described above. If we experience delays in the completion of a clinical study or if a clinical study is terminated, the commercial prospects for our product candidate may be harmed and our ability to generate product revenue will be delayed. In addition, any delays in completing our clinical studies likely will increase our development costs. Further, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical studies may ultimately lead to the denial of regulatory approval of a product candidate. Even if we are able to ultimately commercialize our product candidates, other therapies for the same indications may be introduced to the market in the interim and establish a competitive advantage or diminish the need for our products.

Positive results in nonclinical testing and prior clinical studies do not ensure that ongoing or future clinical studies will be successful or that our product candidates will receive the regulatory approvals necessary for their commercialization.

Before obtaining regulatory approval for the commercial sale of any of our product candidates, we must demonstrate through nonclinical testing and clinical studies that each product is safe and effective for use in each target indication. Based on extensive nonclinical testing, we believe we understand our product candidates' respective mechanisms of action; however, previously observed pharmacologic effects and clinical benefits may not be observed in ongoing or future nonclinical or clinical studies. Success in nonclinical testing and prior clinical studies does not ensure that subsequent or larger-scale studies will be successful. For example, non-purified poloxamer 188 was tested in more than 2,000 human subjects in various indications before the program was discontinued, principally due to concerns regarding acute renal dysfunction observed in patients who received the study drug. In contrast, MST-188 was generally well-tolerated in seven completed clinical studies and no clinically significant changes in renal function were observed. However, patient safety concerns may be observed in ongoing or future clinical studies, including EPIC. With respect to efficacy, although there is compelling data from nonclinical and clinical studies of poloxamer 188 in multiple indications, ongoing and future studies may fail to demonstrate clinical benefits to human subjects.

Further, clinical study results frequently are susceptible to varying interpretations. Medical professionals, investors and/or regulatory authorities may analyze or weigh study data differently than we do. In addition, determining the value of clinical data typically requires application of assumptions and extrapolations to raw data. Alternative methodologies may lead to differing conclusions, including with respect to the safety or efficacy of our product candidates. For example, alternative methods for applying missing or imputed data may have impacted the treatment effect observed in the prior-sponsor phase 3 study of MST-188 in sickle cell disease. If regulatory authorities disagree with us as to the appropriate methods for analyzing study data, regulatory approval for our product candidates may be delayed, limited or withheld. For instance, despite positive nonclinical testing that indicated bioequivalence between ANX-514 and the reference product, Taxotere, our bioequivalence study of ANX-514 did not demonstrate bioequivalence between ANX-514 and Taxotere based on the FDA's benchmark regulatory standards and the FDA determined ANX-514 could not be approved based on the findings from that study.

In addition, if we license to third parties rights to develop our product candidates in other geographic areas or in other indications, we may have limited control over nonclinical testing or clinical studies that may be

S-15

Table of Contents

conducted by such third-party licensees in those territories or indications. If data from third-party testing identifies a safety or efficacy concern, such data could adversely affect our or another licensee's development of our product candidates.

There is significant risk that our product candidates, including MST-188, could fail to show anticipated results in ongoing and future nonclinical testing and/or clinical studies and, as a result, we may elect to discontinue one or more of our development programs. A failure to obtain requisite regulatory approvals or to obtain approvals of the scope requested will delay or preclude us from marketing our products or limit the commercial use of the products, and would have a material adverse effect on our business, financial condition and results of operations.

We do not have, and do not have plans to establish, any manufacturing facilities and are dependent on third parties for the manufacture and supply of MST-188, and the loss of any of these manufacturers, or their failure to provide to us with an adequate supply of drug product in a timely manner and on commercially acceptable terms, or at all, could harm our business.

We do not have, and do not have plans to establish, our own manufacturing facilities. For clinical trial material, we have entered into supply agreements with third parties for both API and finished drug product, but our current agreements may not cover all of our clinical trial material needs and we may need to negotiate new or amended agreements with these CMOs or rely on individual proposals or statements of work, which inherently involves uncertainty as to ongoing supply and may result in delays in the completion of ongoing clinical studies or initiation of new studies. In addition, as development of our product candidates progress, we will need to negotiate agreements for commercial supply.

If we fail to maintain relationships with our current CMOs, we may not be able to complete development of our product candidates, including MST-188, or market them, if approved, on a timely basis, or at all, which would have a material and adverse effect on our business. Third-party manufacturers and suppliers may not perform as agreed or may terminate their agreements with us. For example, because these third parties provide manufacturing services to a number of other pharmaceutical companies, they may experience capacity constraints or choose to prioritize one or more of their other customers over us. Any significant problem that our manufacturers or suppliers experience could delay or interrupt our supply of clinical trial material or commercial product until the manufacturer or supplier cures the problem or until we locate, negotiate for and validate an alternative source of supply, if one is available.

In addition to our reliance on third parties to manufacture clinical trial material, we rely on them to conduct or assist us in conducting key manufacturing development activities, including qualification of equipment, developing and validating methods, defining critical process parameters, releasing component materials and conducting stability testing, among other things. If these third parties are unable to perform successfully in a timely manner, whether for technical, financial or other reasons, we may be unable to secure clinical trial material, which likely would delay the initiation, conduct or completion of our clinical studies, which, in turn, likely would have a material and adverse effect on our business.

All manufacturers of our clinical trial material and, as applicable, commercial product, including API manufacturers, must comply with cGMP requirements enforced by the FDA through its facilities inspection program and applicable requirements of foreign regulatory authorities. These requirements include quality control, quality assurance and the maintenance of records and documentation. Manufacturers of our clinical trial material may be unable to comply with these cGMP requirements and with other FDA, state and foreign regulatory requirements. While we or our representatives generally monitor and audit our manufacturers' systems, we have little control over their ongoing compliance with these regulations. Failure to comply with these requirements may result in fines and civil penalties, suspension of production, suspension or delay in product approval, product seizure or recall, or withdrawal of product

approval.

S-16

Table of Contents

Currently, we do not have alternative sources to backup our primary sources of clinical trial material. Therefore, if our primary sources become unable or unwilling to perform, we could experience protracted delays or interruptions in the supply of clinical trial material and, ultimately, product for commercial sale, which could materially and adversely affect our development programs, commercial activities, operating results and financial condition. For example, if we are unable to maintain our relationship with our current supplier of MST-188 API, we may be unable to identify or establish a relationship with an alternate CMO that has the technical capabilities and desire to perform the development and supply services that we require for MST-188 API on commercially reasonable terms, or at all. Production of the API in MST-188 requires application of our proprietary fluid extraction process. This extraction process is complex and requires highly specialized equipment and there are a limited number of CMOs capable of performing and willing to perform the process as we require, which makes identifying and establishing relationships with CMOs more difficult and may provide them with leverage over us in any negotiations. In addition, we use commercially-available poloxamer 188 as API starting material. There are a limited number of sources of poloxamer 188, and we are not aware of any that currently manufacture it to cGMP requirements applicable to API. The current supplier of our MST-188 API starting material manufactures it under excipient-grade cGMP conditions. Prior to approval of MST-188, the FDA or other regulatory agencies may require our API starting material to be manufactured consistent with cGMP requirements applicable to API, in which case regulatory approval and commercialization of MST-188 could be delayed significantly and require substantial additional financial resources as we seek to contract with a third party to manufacture poloxamer 188 consistent with cGMP requirements applicable to API or undertake to manufacture it ourselves, and conduct any additional clinical or nonclinical activities with such material as the FDA may require. Even if the FDA accepts our current approach with respect to API starting material, we do not have any control over its production and the third-party supplier may change its manufacturing process and/or limit the availability of its poloxamer 188 product in the future. If the supplier makes changes to its poloxamer 188 product, the FDA may determine that it is not acceptable API starting material and we may have difficulty obtaining an alternate supply of API starting material that the FDA finds acceptable without our conducting additional clinical or nonclinical activities or taking other remedial measures, which could require substantial time and financial resources. As a result, we could experience significant disruption in our ability to manufacture MST-188, which likely would add significant cost to the overall development and commercialization of MST-188 and adversely affect our ability to develop MST-188 on a timely basis.

Any new manufacturer or supplier of finished drug product or its component materials, including API, would be required to qualify under applicable regulatory requirements and would need to have sufficient rights under applicable intellectual property laws to the method of manufacturing such product or ingredients. The FDA may require us to conduct additional clinical studies, collect stability data and provide additional information concerning any new supplier, or change in a validated manufacturing process, including scaling-up production, before we could distribute products from that manufacturer or supplier or revised process. For example, if we were to engage a third party other than our current CMO to supply API for future MST-188 clinical trial material or commercial product, the FDA may require us to conduct additional clinical and nonclinical studies to ensure comparability of the drug product containing API manufactured by our current CMO to API manufactured by the new supplier. In addition to the potential for such requirements to result in significant interruption to development and commercialization of MST-188, we likely would incur substantial additional costs to comply with the additional requirements.

The manufacture of pharmaceutical products requires significant expertise and capital investment, including the development of advanced manufacturing techniques and process controls. Manufacturers of pharmaceutical products often encounter difficulties in production, particularly in scaling-up initial production. These problems include difficulties with production costs and yields, quality control, including stability of the product candidate and quality assurance testing, and shortages of qualified personnel. None of our product candidates, including MST-188, has been manufactured at the scale we believe will be necessary to maximize its commercial value and, accordingly, we may encounter difficulties in attempting to scale-up production and may not succeed in that effort. In addition, the FDA or

other regulatory authorities may impose additional requirements as we scale-up initial production capabilities, which may delay our scale-up activities or add expense.

S-17

Table of Contents

If our manufacturers encounter any of these difficulties or otherwise fail to comply with their contractual obligations, we may have insufficient quantities of clinical trial material for our clinical studies, including EPIC or any other then-ongoing studies. In addition, any delay or interruption in the supply of materials necessary or useful to manufacture our product candidates could delay the completion of our clinical studies, increase the costs associated with our development programs and, depending upon the period of delay, require us to commence new clinical studies at significant additional expense or terminate the studies completely. We cannot ensure that manufacturing or quality control problems will not arise in connection with the manufacture of our clinical trial material, or that third-party manufacturers will be able to maintain the necessary governmental licenses and approvals to continue manufacturing such clinical trial material. In addition, our current CMOs are located outside the U.S. and, as a result, we may experience interruptions in supply due to shipping or customs difficulties or regional instability. Any of the above factors could cause us to delay or suspend anticipated or ongoing trials, regulatory submissions or commercialization of our product candidates, entail higher costs or result in our being unable to effectively commercialize our products. Our dependence upon third parties for the manufacture of our clinical trial material may adversely affect our future costs and our ability to develop and commercialize our product candidates on a timely and competitive basis.

We rely significantly on third parties to conduct our nonclinical testing and clinical studies and other aspects of our development programs and if those third parties do not satisfactorily perform their contractual obligations or meet anticipated deadlines, the development of our product candidates could be adversely affected.

We do not employ personnel or possess the facilities necessary to conduct many of the activities associated with our programs. We engage consultants, advisors, CROs, CMOs and others to assist in the design and conduct of nonclinical and clinical studies of our product candidates and with interpretation of the results of those studies, and we expect to continue to outsource a significant amount of such activities. As a result, many important aspects of our development programs are and will continue to be outside our direct control. Consultants and contractors may not be as committed to the success of our programs as employees and, therefore, may not be willing to devote the same time, thoughtfulness or creativity as would an employee. There can be no assurance that such third parties will perform all of their obligations under arrangements with us or will perform those obligations satisfactorily.

The CROs that we engage to execute our clinical studies play a significant role in the conduct of the studies and subsequent collection and analysis of data, and we likely will depend on CROs and clinical investigators to conduct future clinical studies and to assist in analyzing completed studies and developing regulatory strategies for our product candidates. Individuals working at the CROs with which we contract, as well as investigators at the sites at which our studies are conducted, are not our employees, and we have limited control over the amount or timing of resources that they devote to our programs. If these CROs and/or investigators fail to devote sufficient time and resources to our studies, if they do not comply with all regulatory and contractual requirements or if their performance is substandard, it may delay commencement and/or completion of our studies, submission of our new drug applications to the FDA and other regulatory agencies and approval of our applications by those agencies, and commercialization of our products. Moreover, these CROs may have relationships with other commercial entities, some of which may compete with us. If they assist our competitors at our expense, it could harm our competitive position. Failure of these CROs to meet their obligations could adversely affect development of our product candidates. For example, in 2006, we engaged a CRO to assist with the primary conduct of our bioequivalence study of Exelbine, including monitoring participating clinical sites to ensure compliance with regulatory requirements. FDA guidance recommends that clinical sites randomly select and retain reserve samples of study drugs used in bioequivalence studies. However, the clinical sites that participated in our bioequivalence study of Exelbine failed to do so. In August 2011, we received a complete response letter from the FDA stating that the authenticity of the study drugs used in that bioequivalence study could not be verified and, consequently, the study would need to be repeated to address that deficiency.

Table of Contents

If any of our current CRO relationships were to terminate, particularly those with the CROs we have engaged to conduct the EPIC study, we may not be able to enter into arrangements with alternative CROs on acceptable terms or in a timely manner, or at all. Switching CROs would involve additional cost and divert management time and attention. In addition, there likely would be a transition period when a new CRO commences work. These challenges could result in delays in the commencement or completion of our clinical studies, which could materially impact our ability to meet our desired development timelines and have a material adverse impact on our business and financial condition.

Our product candidates may cause undesirable side effects or have other properties that could delay or prevent their clinical development, regulatory approval or commercialization.

Undesirable side effects caused by our product candidates could interrupt, delay or halt clinical studies and could result in the denial of regulatory approval by the FDA or other regulatory authorities for any or all indications, and in turn prevent us from commercializing our product candidates. For example, while we believe our proprietary purification process has addressed the cause of the acute renal dysfunction observed in clinical studies of non-purified poloxamer 188, we cannot provide assurance that the purification process has fully addressed the issue or that renal toxicity will not be observed in ongoing or future studies of MST-188, particularly if we conduct studies in patients with impaired renal function. In addition, transient, generally mild to moderate elevations in liver enzymes were associated with treatment with MST-188 in prior clinical studies. If in our clinical studies of MST-188 we observe more pronounced increases in liver enzymes, or we observe other previously unidentified adverse events, whether or not statistically significant, we may be required to conduct additional clinical studies of MST-188 or to investigate the clinical significance of the adverse event and MST-188 may not receive regulatory approval.

If any of our product candidates receive marketing approval and we or others later identify undesirable side effects caused by the product or, if applicable, the reference product:

regulatory authorities may require the addition of labeling statements, such as a black box warning or a contraindication;

regulatory authorities may withdraw their approval of the product;

we may be required to change the way the product is administered, conduct additional clinical studies or change the labeling of the product; and

our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of the affected product or could substantially increase the costs and expenses of commercializing the product, which in turn could delay or prevent us from generating significant revenue from its sale.

We may not achieve our projected development goals in the time frames we announce.

We set goals for and make public statements regarding our estimates of the timing for accomplishing certain objectives material to successful development of our product candidates. The actual timing of these events can vary,

sometimes dramatically, due to many factors, including delays or failures in our nonclinical testing, clinical studies and manufacturing and regulatory activities and the uncertainties inherent in the regulatory approval process. For example, we had expected to initiate the EPIC study in 2012, but unforeseen delays related to the manufacture of clinical trial material delayed initiation of the study to 2013. In addition, we have estimated that patient enrollment in EPIC will complete by the end of 2015. However, predicting the rate of enrollment for any clinical study, including EPIC, requires us to make a number of significant assumptions that may prove to be incorrect. If, as a clinical study progresses, we gain reliable information that materially impacts our assumptions, we will adjust our estimates. Even so, our estimated enrollment rates and the actual rates may differ materially and the time required to complete enrollment of any clinical study may be considerably longer than we estimate. For additional discussion of these risks, see the risk factors above in this section, Risks Related to Drug Development and Commercialization.

S-19

Table of Contents

Even if we complete a clinical study with successful results, we may not achieve our projected development goals in the time frames we initially anticipate or announce. The FDA may require nonclinical testing and/or clinical studies prior to its review or approval of a new drug application for MST-188 in sickle cell disease in addition to the EPIC study and the other testing that we are conducting or plan to conduct in parallel with EPIC. If the development plan for MST-188 or any other product candidate becomes more extensive and costly than anticipated, we may determine that the associated time and cost are not financially justifiable and, as a result, discontinue development in a particular indication or of the product candidate as a whole. Any such action may be viewed negatively, which could adversely affect our stock price.

In addition, changes may occur in regulatory requirements or policy during the period of product development and/or regulatory review of an NDA that relate to the data required to be included in NDAs. For example, despite including in our initial Exelbine NDA submission in December 2009 data that we believe met the filing requirements for a new drug promulgated by the International Conference on Harmonization, or ICH, as well as site-specific stability data from lots manufactured at the intended commercial manufacturing site, we received a refusal-to-file letter from the FDA indicating that the data included in that submission was insufficient to support a commercially-viable expiration dating period. Consequently, we had to generate 12 months of stability data from material manufactured at our intended commercial manufacturing site before resubmitting the Exelbine NDA, which we did in November 2010. A change in regulatory policy, which may not have been formalized or publicly disseminated, may have been a factor underlying the FDA's refusal to file our December 2009 submission.

Further, throughout development, we must provide adequate assurance to the FDA and other regulatory authorities that we can consistently produce our product candidates in conformance with current good manufacturing practices, or cGMP, and other regulatory standards. We rely on CMOs for the manufacture of clinical, and future commercial, quantities of our product candidates. If future FDA or other regulatory authority inspections identify cGMP compliance issues at these third-party facilities, production of our clinical trial material or, in the future, commercial product, could be disrupted, causing potentially substantial delay in development or commercialization of our product candidates.

Even if we receive regulatory approval for a product candidate, we may face development and regulatory difficulties that could materially and adversely affect our business, financial condition and results of operations and cause our stock price to decline.

Even if initial regulatory approval is obtained, or as a condition to the initial approval, the FDA or a foreign regulatory agency may impose significant restrictions on a product's indicated uses or marketing or impose ongoing requirements for potentially costly post-approval studies or marketing surveillance programs, any of which would limit the commercial potential of the product. Our product candidates also will be subject to ongoing FDA requirements related to the manufacturing processes, labeling, packaging, storage, distribution, advertising, promotion, record-keeping and submission of safety and other post-market information regarding the product. For instance, the FDA may require changes to approved drug labels, require post-approval clinical studies and impose distribution and use restrictions on certain drug products. In addition, approved products, manufacturers and manufacturers' facilities are subject to continuing regulatory review and periodic inspections. If previously unknown problems with a product are discovered, such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured, the FDA may impose restrictions on that product or us, including requiring withdrawal of the product from the market. If we or a CMO of ours fail to comply with applicable regulatory requirements, a regulatory agency may:

issue warning letters or untitled letters;

impose civil or criminal penalties;

suspend or withdraw regulatory approval;

suspend or terminate any ongoing clinical studies;

S-20

Table of Contents

refuse to approve pending applications or supplements to approved applications;

exclude our product from reimbursement under government healthcare programs, including Medicaid or Medicare;

impose restrictions or affirmative obligations on our or our CMO's operations, including costly new manufacturing requirements;

close the facilities of a CMO; or

seize or detain products or require a product recall.

We currently have limited marketing capabilities and no sales capability and our failure to acquire or develop these and related capabilities internally or contract with third parties to perform these activities successfully could delay and/or limit our ability to generate revenue in the event MST-188 or any other product candidate obtains regulatory approval.

We currently have limited marketing capabilities and no sales capability and our company has never marketed or sold products. To commercialize MST-188 or any other product candidate, we will have to acquire or develop marketing, distribution, sales and associated regulatory compliance capabilities, or rely on marketing partners or other third parties for the marketing, distribution and sale of our products. There is no guarantee that we will be able to establish adequate marketing, distribution or sales capabilities or make arrangements with third parties to perform those activities on terms satisfactory to us, or at all, or that any internal capabilities or third-party arrangements will be cost-effective. The acquisition or development of commercialization and associated regulatory compliance capabilities likely will require substantial financial and other resources and divert the attention of our management and key personnel, and, if not completed on time, could delay the launch of an approved product, and otherwise negatively impact our product development and commercialization efforts.

To the extent we establish marketing, distribution or sales arrangements with third parties, those third parties may hold significant control over important aspects of the commercialization of our products, including market identification, marketing methods, pricing, composition of sales force and promotional activities. Even if we are successful in establishing and maintaining these arrangements, there can be no assurance that we will be able to control the amount and timing of resources that any third party may devote to our products or prevent any third party from pursuing alternative technologies or products that could result in the development of products that compete with, or the withdrawal of support for, our products. If we retain third-party service providers to perform functions related to the marketing, distribution and sale of our products, key aspects of those functions that may be out of our direct control could include warehousing and inventory management, distribution, contract administration and chargeback processing, accounts receivable management and call center management. In this event, we would place substantial reliance on third-party providers to perform services for us, including entrusting our inventories of products to their care and handling. If these third-party service providers fail to comply with applicable laws and regulations, fail to meet expected deadlines, encounter natural or other disasters at their facilities or otherwise fail to perform in a satisfactory manner, or at all, our ability to deliver product to meet commercial demand could be significantly impaired. In addition, we may use third parties to perform various other services for us relating to sample accountability and regulatory monitoring, including adverse event reporting, safety database management and other product maintenance services. If the quality or accuracy of the data maintained by these service providers is

insufficient, our ability to continue to market our products could be jeopardized or we could be subject to regulatory sanctions.

If any of our product candidates for which we receive regulatory approval fails to achieve significant market acceptance among the medical community, patients or third-party payors, the revenue we generate from its sales will be limited and our business may not be profitable.

S-21

Table of Contents

Our success will depend in substantial part on the extent to which our products candidates, if approved, are accepted by the medical community and patients and reimbursed by third-party payors, including government payors. The degree of market acceptance with respect to each of our approved products, if any, will depend upon a number of factors, including:

the safety and efficacy of our product demonstrated in clinical studies;

acceptance in the medical and patient communities of our product as a safe and effective treatment;

the perceived advantages of our product over alternative treatments, including with respect to the incidence and severity of any adverse side effects and the cost of treatment;

the indications for which our product is approved;

claims or other information (including limitations or warnings) in our product's approved labeling;

reimbursement and coverage policies of government and other third-party payors;

pricing and cost-effectiveness of our product relative to alternative treatments;

availability of alternative treatments;

the prevalence of off-label substitution of chemically equivalent products or alternative treatments; and

the resources we devote to marketing our product and restrictions on promotional claims we can make with respect to the product.

We cannot predict with reasonable accuracy whether physicians, patients, healthcare insurers or maintenance organizations, or the medical community in general, will accept or utilize any of our products. If our product candidates are approved but do not achieve an adequate level of acceptance by these parties, we may not generate sufficient revenue to become or remain profitable. In addition, our efforts to educate the medical community and third-party payors regarding benefits of our products may require significant resources and may never be successful.

If we determine that a product candidate may not achieve adequate market acceptance or that the potential market size does not justify additional expenditure on the program, we may reduce our expenditures on the development and/or the process of seeking regulatory approval of the product candidate while we evaluate whether and on what timeline to move the program forward.

Even if we receive regulatory approval to market one or more of our product candidates in the U.S., we may never receive approval or commercialize our products outside of the U.S., which would limit our ability to realize the full commercial potential of our product candidates.

In order to market any products outside of the U.S., we must establish and comply with numerous and varying regulatory requirements of other countries regarding safety and efficacy. Approval procedures vary among countries and can involve additional product testing and validation and additional administrative review periods. The time required to obtain approval in other countries might differ from that required to obtain FDA approval. The regulatory approval process in other countries may include all of the risks detailed above regarding FDA approval in the U.S., as well as other risks. Regulatory approval in one country does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country may have a negative effect on the regulatory process in others. Failure to obtain regulatory approval in other countries or any delay or setback in obtaining such approval could have the same adverse effects detailed above regarding FDA approval in the U.S. As described above, such effects include the risks that our product candidates may not be approved for all indications requested, which could limit the uses of our product candidates and have an adverse effect on product sales, and that such approval may be subject to limitations on the indicated uses for which the product may be marketed or require costly, post-marketing follow-up studies.

Table of Contents

Risks Related to Our Intellectual Property

Our success will depend on patents and other intellectual property protection we obtain that cover our product candidates and proprietary technology.

Our success will depend in part on our ability to:

obtain and maintain patent and other exclusivity with respect to our products;

prevent third parties from infringing upon our proprietary rights;

maintain proprietary know-how and trade secrets;

operate without infringing upon the patents and proprietary rights of others; and

obtain appropriate licenses to patents or proprietary rights held by third parties if infringement would otherwise occur, both in the U.S. and in foreign countries.

The patent and intellectual property positions of biopharmaceutical companies, including ours, are uncertain and involve complex legal and factual questions. There is no guarantee that we have or will develop or obtain the rights to products or processes that are patentable, that patents will issue from any pending applications or that claims allowed will be sufficient to protect the technology we develop or have developed or that is used by us, our CMOs or our other service providers. In addition, any patents that are issued to us may be challenged, invalidated, infringed or circumvented, including by our competitors, and rights we have under issued patents may not provide competitive advantages to us.

Patent applications in the U.S. are confidential for a period of time until they are published, and publication of discoveries in scientific or patent literature typically lags actual discoveries by several months. As a result, we cannot be certain that the inventors listed in any patent or patent application owned by us were the first to conceive of the inventions covered by such patents and patent applications (for U.S. patent applications filed before March 16, 2013), or that such inventors were the first to file patent applications for such inventions outside the United States and, after March 15, 2013, in the United States.

We also rely on unpatented know-how and trade secrets and continuing technological innovation to develop and maintain our competitive position, which we seek to protect, in part, through confidentiality agreements with employees, consultants, collaborators and others. We also have invention or patent assignment agreements with our employees and certain consultants. There can be no assurance, however, that binding agreements will not be breached, that we will have adequate remedies for any breach, or that trade secrets or other proprietary information will not otherwise become known or be independently discovered by competitors. In addition, it is possible that inventions relevant to our business could be developed by a person not bound by an invention assignment agreement with us.

For exclusivity for our product candidates in rare or orphan diseases, such as MST-188 in sickle cell disease and acute limb ischemia, we expect to rely primarily on orphan drug designation in the U.S. and European Union. However,

orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review or approval process. Our product candidates may not receive the marketing exclusivity periods available with orphan drug status if they are not the first drug products to obtain marketing approval for the treatment of the disease or condition for which they received the orphan designation. In addition, orphan drug exclusive marketing rights may be lost if the FDA later determines that the request for designation was materially defective or if we are unable to assure sufficient quantity of the drug. Furthermore, if the FDA later determines another drug or biologic to be clinically superior to or different from our product for treatment of disease or condition for which it received orphan status, the FDA may approve such other product for marketing during our product's exclusivity period.

S-23

Table of Contents

Our success depends in large part on our ability to prevent competitors from duplicating or developing equivalent versions of our product candidates, but patent protection for our product candidates, including MST-188, may be difficult to obtain and any issued claims may be limited.

The potential therapeutic benefits of poloxamer 188 have been known for decades and there is substantial prior art describing the use of poloxamer 188 in a wide range of diseases and conditions. As a result, our ability to find novel and non-obvious uses of poloxamer 188 is limited. Further, a patent examiner may combine numerous, disparate references in order to reject a claimed use for obviousness. If the prior art suggests, even implicitly, the desirability of combining previously known elements, such as the use of poloxamer 188 in a particular indication, the subsequent use of MST-188 in that indication may be unpatentable.

While we have filed for patent protection covering various methods of using poloxamers, as well as a novel composition of poloxamer material, we cannot provide assurance that our pending patent applications will issue as patents, that any issued patents will provide us with significant competitive advantages, or that the validity or enforceability of any of our patents will not be challenged or, if instituted, that these challenges will not be successful. For instance, our patent application covering a purportedly novel composition of poloxamer material may be limited to the specific method by which we manufacture the material. Even if claims issue, a competitor may develop a method to manufacture our poloxamer material using a different process, in which case the competitor may not infringe our product-by-process claims. The cost of litigation to uphold the validity and prevent infringement of our patents could be substantial. Furthermore, one or more parties may independently develop similar technologies or duplicate our technologies or design around the patented aspects of our technologies. We can provide no assurance that our technologies will not infringe patents or rights owned by others, licenses to which might not be available to us in a timely manner or on acceptable terms, or at all.

If we are sued for infringing the proprietary rights of third parties, it will be costly and time consuming, and an unfavorable outcome would have an adverse effect on our business.

Our commercial success depends on our ability and the ability of our CMOs and component suppliers to develop, manufacture, market and sell our products and product candidates and use our proprietary technologies without infringing the proprietary rights of third parties. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we are or may be developing products. As the industries in which we operate (biopharmaceutical, specialty pharmaceutical, biotechnology and pharmaceutical) expand and more patents are issued, the risk increases that we will be subject to claims that our products or product candidates, or their use or manufacture, infringe the rights of others. Because patent applications can take many years to publish and issue, there currently may be pending applications, unknown to us, that may later result in issued patents that our products, product candidates or technologies infringe, or that the process of manufacturing our products or any of their respective component materials, or the component materials themselves, infringe, or that the use of our products, product candidates or technologies infringe.

We or our CMOs or component material suppliers may be exposed to, or threatened with, litigation by third parties alleging that our products, product candidates and/or technologies infringe their patents and/or other intellectual property rights, or that one or more of the processes for manufacturing our products or any of their respective component materials, or the component materials themselves, or the use of our products, product candidates or technologies, infringe their patents and/or other intellectual property rights. If a third-party patent or other intellectual property right is found to cover our products, product candidates, technologies or their uses, or any of the underlying manufacturing processes or components, we could be required to pay damages and could be unable to commercialize our products or use our technologies or methods unless we are able to obtain a license to the patent or intellectual property right. A license may not be available to us in a timely manner or on acceptable terms, or at all. In addition,

during litigation, the third-party alleging infringement could obtain a preliminary injunction or other equitable remedy that could prohibit us from making, using or selling our products, technologies or methods.

S-24

Table of Contents

There generally is a substantial amount of litigation involving patent and other intellectual property rights in the industries in which we operate. If a third party claims that we or our CMOs or component material suppliers infringe its intellectual property rights, we may face a number of issues, including, but not limited to:

infringement and other intellectual property claims which, with or without merit, may be expensive and time consuming to litigate and may divert our management's time and attention from our core business;

substantial damages for infringement, including the potential for treble damages and attorneys' fees, which we may have to pay if it is determined that the product at issue infringes or violates the third party's rights;

a court prohibiting us from selling or licensing the product unless the third-party licenses its intellectual property rights to us, which it may not be required to do;

if a license is available from the third party, we may have to pay substantial royalties, fees and/or grant cross-licenses to the third party; and

redesigning our products or processes so they do not infringe, which may not be possible or may require substantial expense and time.

No assurance can be given that patents do not exist, have not been filed, or could not be filed or issued, which contain claims covering our products, product candidates or technology or those of our CMOs or component material suppliers or the use of our products, product candidates or technologies. Because of the large number of patents issued and patent applications filed in the industries in which we operate, there is a risk that third parties may allege they have patent rights encompassing our products, product candidates or technologies, or those of our CMOs or component material suppliers, or uses of our products, product candidates or technologies.

In addition, it may be necessary for us to enforce our proprietary rights, or to determine the scope, validity and unenforceability of other parties' proprietary rights, through litigation or other dispute proceedings, which may be costly, and to the extent we are unsuccessful, adversely affect our rights. In these proceedings, a court or administrative body could determine that our claims, including those related to enforcing patent rights, are not valid or that an alleged infringer has not infringed our rights. The uncertainty resulting from the mere institution and continuation of any patent- or other proprietary rights-related litigation or interference proceeding could have a material and adverse effect on us.

RISKS RELATED TO OUR INDUSTRY

We expect intense competition in the marketplace for our product candidates, should any of them receive regulatory approval.

The industries in which we operate (biopharmaceutical, specialty pharmaceutical, biotechnology and pharmaceutical) are highly competitive and subject to rapid and significant change. We are aware of many other organizations developing drug products and other therapies intended to treat or cure the diseases or conditions in which we are developing or plan to develop our product candidates. Developments by others may render potential application of any

of our product candidates in a particular indication obsolete or noncompetitive, even prior to completion of its development and approval for that indication. If successfully developed and approved, we expect our product candidates will face intense competition. We may not be able to compete successfully against organizations with competitive products, particularly large pharmaceutical companies. Many of our potential competitors have significantly greater financial, technical and human resources than we do, and may be better equipped to develop, manufacture, market and distribute products. Many of these companies operate large, well-funded research, development and commercialization programs, have extensive experience in nonclinical and clinical studies, obtaining FDA and other regulatory approvals and manufacturing and marketing products, and have multiple products that have been approved or are in late-stage development. Smaller companies may

S-25

Table of Contents

also prove to be significant competitors, particularly through collaborative arrangements with large pharmaceutical and biotechnology companies. Furthermore, heightened awareness on the part of academic institutions, government agencies and other public and private research organizations of the potential commercial value of their inventions have led them to actively seek to commercialize the technologies they develop, which increases competition for investment in our programs. In addition, there is increasing interest in developing drugs for rare diseases, which may have the effect of increasing the development of agents to treat sickle cell disease, acute limb ischemia and other orphan indications we may pursue. Legislative action, such as the Food and Drug Administration Safety and Innovation Act, which was signed into law in 2012, may generate further interest. Competitive products may be more effective, or more effectively marketed and sold, than ours, which would have a material adverse effect on our ability to generate revenue.

With respect to competition for MST-188 in sickle cell disease, we are aware of numerous companies with product candidates in varying stages of development. Some of our potential competitors in sickle cell disease are large, well-financed and experienced pharmaceutical and biotechnology companies or have partnered with such companies, which may give them development, regulatory and/or marketing advantages over us. For example, Pfizer and Novartis have each invested in privately-held companies, GlycoMimetics, Inc. and Selexys Pharmaceuticals Corporation, respectively, which have clinical-stage agents for the treatment of vaso-occlusive crisis. Pfizer is expected to commence a phase 3 study of GlycoMimetics GMI-1070 in vaso-occlusive crisis of sickle cell disease; however, in September 2014, GlycoMimetics announced that the study would be significantly delayed due to a manufacturing development issue impacting drug supply. Eli Lilly and Company is conducting a phase 3 study of prasugrel in pediatric patients with sickle cell disease to assess whether it reduces the rate of vaso-occlusive crisis. In March 2014, Emmaus Life Sciences, Inc. announced that top-line data from its phase 3 clinical study of L-glutamine in sickle cell disease showed a statistically significant reduction in the frequency of sickle cell crisis and, in August 2014, it disclosed plans to submit complete study results for pre-NDA review to the FDA during the third quarter of 2014. In addition, numerous non-profit or non-commercial foundations and interest groups are committed to improving outcomes for patients with sickle cell disease. Advances in the understanding of the signaling pathways associated with sickle cell disease may lead to further interest and development of treatment options. If an effective treatment or cure for vaso-occlusive crisis or sickle cell disease receives regulatory approval, the potential commercial success of MST-188 could be severely jeopardized.

With respect to competition for MST-188 for complications of arterial disease, although we intend first to develop MST-188 as an adjunct to thrombolytics, it could compete with current revascularization methods, including thrombolytics. In addition, we are aware of a number of potentially competitive investigational therapies for severe forms of thrombotic arterial disease, including angiogenic growth factors, vasoactive drugs, anticoagulants, thrombolytics, anti-platelet agents, cytoprotectives, and blood substitutes, certain of which are in late-stage clinical development. Should any of these other investigational therapies receive regulatory approval prior to MST-188, they may become entrenched in the standard of care, diminish the need for MST-188, or be difficult to displace.

We are subject to uncertainty relating to healthcare reform measures and reimbursement policies that, if not favorable to our products, could hinder or prevent our products' commercial success, if any of our product candidates are approved.

Our ability to commercialize our products successfully will depend in part on the extent to which reimbursement for the costs of such products and related treatments will be available from government health administration authorities, private health insurers and other third-party payors. Significant uncertainty exists as to the reimbursement status of newly approved medical products. The continuing efforts of the government, insurance companies, managed care organizations and other payors of healthcare services to contain or reduce costs of healthcare may adversely affect:

our ability to set an appropriate price for our products;

the rate and scope of adoption of our products by healthcare providers;

S-26

Table of Contents

our ability to generate revenue or achieve or maintain profitability;

the future revenue and profitability of our potential customers, suppliers and collaborators; and

our access to additional capital.

Our ability to successfully commercialize our products will depend in part on the extent to which governmental authorities, private health insurers and other organizations establish what we believe are appropriate coverage and reimbursement for our products. These payors are increasingly attempting to contain healthcare costs by limiting both coverage and the level of reimbursement, particularly for new therapeutic products or if there is a perception that the target indication of the new product is well-served by existing drugs or other treatments. Accordingly, even if coverage and reimbursement are provided, market acceptance of our products would be adversely affected if the level of coverage and/or reimbursement for our products proved to be unprofitable for healthcare providers or less profitable than alternative treatments.

There have been federal and state proposals to subject the pricing of healthcare goods and services to government control and to make other changes to the U.S. healthcare system. While we cannot predict the outcome of current or future legislation, we anticipate that the U.S. Congress and state legislatures will continue to introduce initiatives directed at lowering the total cost of healthcare. In addition, in certain foreign markets, the pricing of drug products is subject to government control and reimbursement may in some cases be unavailable or insufficient. It is uncertain if future legislative proposals, whether domestic or abroad, will be adopted that might affect our products or product candidates or what actions federal, state, or private payors for healthcare treatment and services may take in response to any such healthcare reform proposals or legislation. Any such healthcare reforms could have a material and adverse effect on the marketability of any products for which we ultimately receive FDA or other regulatory agency approval.

We face potential product liability exposure and, if successful claims are brought against us, we may incur substantial liability for a product or product candidate and may have to limit its commercialization. In the future, we anticipate that we will need to obtain additional or increased product liability insurance coverage and it is uncertain whether such increased or additional insurance coverage can be obtained on commercially reasonable terms, if at all.

Our business (in particular, the use of our product candidates in clinical studies and the sale of any products for which we obtain marketing approval) will expose us to product liability risks. Product liability claims might be brought against us by patients, healthcare providers, pharmaceutical companies or others selling our products. If we cannot successfully defend ourselves against any such claims, we will incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

decreased demand for our products and loss of revenue;

impairment of our business reputation;

delays in enrolling patients to participate in our clinical studies;

withdrawal of clinical study participants;

a clinical hold, suspension or termination of a clinical study or amendments to a study design;

significant costs of related litigation;

substantial monetary awards to patients or other claimants; and

the inability to commercialize our products and product candidates.

We maintain limited product liability insurance for our clinical studies, but our insurance coverage may not reimburse us or may not be sufficient to reimburse us for all expenses or losses we may suffer. Moreover, insurance coverage is becoming increasingly expensive and, in the future, we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses.

S-27

Table of Contents

We expect that we would expand our insurance coverage to include the sale of commercial products if we obtain marketing approval of any of our product candidates, but we may be unable to obtain product liability insurance on commercially acceptable terms or may not be able to maintain such insurance at a reasonable cost or in sufficient amounts to protect us against potential losses. Large judgments have been awarded in class action lawsuits based on drug products that had unanticipated side effects. A successful product liability claim or series of claims brought against us could cause our stock price to fall and, if judgments exceed our insurance coverage, could decrease our cash and adversely affect our business.

RISKS RELATED TO OUR COMMON STOCK

If we are unable to maintain compliance with NYSE MKT continued listing standards, our common stock may be delisted from the NYSE MKT equities market, which would likely cause the liquidity and market price of our common stock to decline.

Our common stock currently is listed on the NYSE MKT equities market. The NYSE MKT will consider suspending dealings in, or delisting, securities of an issuer that does not meet its continued listing standards, including specified stockholders' equity levels. In addition, the NYSE MKT will consider suspending dealings in, or delisting, securities selling for a substantial period of time at a low price per share if the issuer fails to effect a reverse split of such stock within a reasonable time after being notified that the NYSE MKT deems such action to be appropriate under the circumstances.

In the past, though not since 2010, we were notified of non-compliance with certain NYSE MKT stockholders' equity continued listing standards; specifically, (1) Section 1003(a)(ii) of the NYSE MKT Company Guide, or the Company Guide, because we reported stockholders' equity of less than \$4,000,000 and losses from continuing operations and net losses in three of our four most recent fiscal years, and (2) Section 1003(a)(iii) of the Company Guide, because we reported stockholders' equity of less than \$6,000,000 and losses from continuing operations and net losses in our five most recent fiscal years. In addition, we were notified, in accordance with Section 1003(f)(v) of the Company Guide, that the NYSE MKT determined it was appropriate for us to effect a reverse stock split of our common stock to address our low selling price per share. In April 2010, we announced that we had resolved the stockholders' equity continued listing deficiencies and we implemented a 1-for-25 reverse split of our common stock, in part to address the NYSE MKT's requirement that we address our low stock price.

There is no assurance, however, that we will continue to maintain compliance with NYSE MKT continued listing standards. For example, we may determine to pursue development or other activities or grow our organization or product pipeline or at levels or on timelines that reduces our stockholders' equity below the level required to maintain compliance with NYSE MKT continued listing standards. In addition, the market price for our common stock historically has been highly volatile, as more fully described below under the risk titled "The market price of our common stock historically has been and likely will continue to be highly volatile." The NYSE MKT may again determine that the selling price per share of our common stock is low and require that we effect a reverse stock split of our common stock, which would require stockholder approval that we may be unable to obtain. Our failure to maintain compliance with NYSE MKT continued listing standards could result in the delisting of our common stock from the NYSE MKT.

The delisting of our common stock from the NYSE MKT likely would reduce the trading volume and liquidity in our common stock and may lead to decreases in the trading price of our common stock. The delisting of our common stock may also materially impair our stockholders' ability to buy and sell shares of our common stock. In addition, the delisting of our common stock could significantly impair our ability to raise capital, which is critical to the execution of our current business strategy.

Table of Contents

If our common stock were delisted and determined to be a penny stock, a broker-dealer may find it more difficult to trade our common stock and an investor may find it more difficult to acquire or dispose of our common stock in the secondary market.

If our common stock were removed from listing with the NYSE MKT, it may be subject to the so-called penny stock rules. The SEC has adopted regulations that define a penny stock to be any equity security that has a market price per share of less than \$5.00, subject to certain exceptions, such as any securities listed on a national securities exchange. For any transaction involving a penny stock, unless exempt, the rules impose additional sales practice requirements on broker-dealers, subject to certain exceptions. If our common stock were delisted and determined to be a penny stock, a broker-dealer may find it more difficult to trade our common stock and an investor may find it more difficult to acquire or dispose of our common stock on the secondary market.

The market price of our common stock historically has been and likely will continue to be highly volatile.

The market price for our common stock historically has been highly volatile, and the market for our common stock has from time to time experienced significant price and volume fluctuations, based both on our operating performance and for reasons that appear to us unrelated to our operating performance. For instance, on August 10, 2011, the market price for our common stock dropped almost 60% following our announcement of our receipt of a complete response letter to our NDA for Exelbine, which letter stated that the FDA could not approve Exelbine in its present form. Conversely, the market price for our common stock increased by more than 55% during one trading day in January 2014, in the absence of any news release by us or rumors of which we were aware. The market price of our common stock may fluctuate significantly in response to a number of factors, including:

the level of our financial resources;

announcements of entry into or consummation of a financing or strategic transaction;

changes in the regulatory status of our product candidates, including results of any clinical studies and other research and development programs;

FDA or international regulatory actions and regulatory developments in the U.S. and foreign countries;

announcements of new products or technologies, commercial relationships or other events (including clinical study results and regulatory events and actions) by us or our competitors;

market conditions in the pharmaceutical, biopharmaceutical, specialty pharmaceutical and biotechnology sectors;

developments concerning intellectual property rights generally or those of us or our competitors;

changes in securities analysts' estimates of our financial performance or deviations in our business and the trading price of our common stock from the estimates of securities analysts;

events affecting any future collaborations, commercial agreements and grants;

fluctuations in stock market prices and trading volumes of similar companies;

sales of large blocks of our common stock, including sales by significant stockholders, our executive officers or our directors or pursuant to shelf or resale registration statements that register shares of our common stock that may be sold by us or certain of our current or future stockholders;

discussion of us or our stock price by the financial and scientific press and in online investor communities;

commencement of delisting proceedings by the NYSE MKT;

Table of Contents

additions or departures of key personnel; and

changes in third-party payor reimbursement policies.

As evidenced by the August 10, 2011 decline, the realization of any of the foregoing could have a dramatic and adverse impact on the market price of our common stock. In addition, class action litigation has often been instituted against companies whose securities have experienced a substantial decline in market price. Moreover, regulatory entities often undertake investigations of investor transactions in securities that experience volatility following an announcement of a significant event or condition. Any such litigation brought against us or any such investigation involving our investors could result in substantial costs and a diversion of management's attention and resources, which could hurt our business, operating results and financial condition.

Our stock price could decline significantly based on progress with and results of clinical studies of MST-188 and regulatory agency decisions affecting development of MST-188.

We expect announcements of progress with and results of clinical studies of MST-188 and regulatory decisions (by us, the FDA, or another regulatory agency) to affect our stock price. Stock prices of companies in our industry have declined significantly when such results and decisions were unfavorable or perceived to be negative or discouraging or when a product candidate did not otherwise meet expectations. If progress in clinical studies of MST-188 or MST-188 study results are not viewed favorably by us or third parties, including investors, analysts, potential collaborators, the academic and medical communities and regulators, our stock price could decline significantly and you could lose your investment in our common stock.

We may report top-line clinical and nonclinical study data from time to time, which is based on preliminary analysis of then-available data. Such preliminary findings and conclusions are subject to change following a more comprehensive review of the study data. In addition, results of clinical and nonclinical studies often are subject to different interpretations. We may interpret or weigh the importance of study data differently than third parties, including those noted above. Others may not accept or agree with our analysis of study data, which could impact the approvability of our product candidates and/or the value of our development programs and our company in general.

Sales of substantial amounts of our common stock or the perception that such sales may occur could cause the market price of our common stock to drop significantly, even if our business is performing well.

The market price of our common stock could decline as a result of sales by, or the perceived possibility of sales by, us or our existing stockholders of shares of our common stock. Sales by our existing stockholders might also make it more difficult for us to sell equity securities at a time and price that we deem appropriate. In February 2014, we commenced a \$30 million at the market offering program, or ATM program. As of September 30, 2014, we had raised gross proceeds of \$14.8 million under the ATM program. In addition, the shelf registration statement on Form S-3 under which the ATM program is registered may be used to register the sale and issuance of up to \$120 million of additional securities, subject to the aggregate amount sold as a result of this offering as well as limitations if our public float is less than \$75 million at certain re-evaluation dates. Further, we have outstanding warrants to purchase more than 44 million additional shares of our common stock. Collectively, the ATM program, the shelf registration statement and any outstanding, in-the-money warrants, may increase the likelihood of sales of substantial amounts of our shares, or the perception that substantial sales may occur, by us or our existing securityholders from time to time, which could cause the market price of our common stock to drop significantly.

Table of Contents

We have voting control over shares held by the former principal stockholders of SynthRx and Aires Pharmaceuticals and we will have voting control over shares issuable to former principal SynthRx stockholders in the future, and we may determine to cause those shares to be voted in such a manner that does not necessarily coincide with the interests of individual stockholders or particular groups of stockholders.

We have voting control with respect to approximately 5% of our outstanding common stock (based on shares outstanding as of October 31, 2014), pursuant to agreements we entered into with the former principal stockholders of each of SynthRx and Aires Pharmaceuticals in connection with our acquisition of those companies. Pursuant to the voting and transfer restriction agreement between us and each of the former principal stockholders of SynthRx, we have an irrevocable proxy to vote the shares of our common stock beneficially owned by those stockholders with respect to every action or approval by written consent of our stockholders in such manner as directed by us, except in limited circumstances. If the development of MST-188 achieves the remaining milestones set forth in our merger agreement with SynthRx, we will issue an additional 12,478,050 shares of our common stock to the former stockholders of SynthRx and the amount of those shares held by the stockholder parties to the voting and transfer restriction agreement will also be subject to the irrevocable proxy held by us. In addition, pursuant to the stockholder agreements between us and the former principal stockholders of Aires, we have an irrevocable proxy to vote the shares of our common stock issued to such stockholders pursuant to the merger agreement governing the Aires acquisition and then held by such stockholders with respect to every action or approval by written consent of our stockholders in such manner as directed by us, except in limited circumstances. Accordingly, pursuant to our agreements with the former principal stockholders of SynthRx and Aires, assuming achievement of the remaining milestones under our merger agreement with SynthRx and issuance of all 12,478,050 milestone shares, based on 128,517,274 shares of our common stock outstanding as of October 31, 2014, we would have voting control with respect to approximately 13% of our outstanding common stock. As a result, in the future, we may have significant control over substantially all matters requiring approval by our stockholders, including the election of directors and the approval of certain mergers and other business combination transactions. Even if less than all potential milestone-related and holdback shares are issued, our ability to control a potentially significant block of stockholder votes pursuant to these voting agreements may enable us to substantially affect the outcome of proposals brought before our stockholders. Although our board of directors acts in a manner it believes is in the best interest of our stockholders as a whole, the interests of our stockholders as a whole may not always coincide with the interests of individual stockholders or particular groups of stockholders.

Anti-takeover provisions in our charter documents and under Delaware law may make an acquisition of us, which may be beneficial to our stockholders, more difficult, which could depress our stock price.

We are incorporated in Delaware. Certain anti-takeover provisions of Delaware law and our charter documents as currently in effect may make a change in control of our company more difficult, even if a change in control would be beneficial to our stockholders. Our bylaws limit who may call a special meeting of stockholders and establish advance notice requirements for nomination of individuals for election to our board of directors or for proposing matters that can be acted upon at stockholders' meetings. Delaware law also prohibits corporations from engaging in a business combination with any holders of 15% or more of their capital stock until the holder has held the stock for three years unless, among other possibilities, the board of directors approves the transaction. Our board of directors may use these provisions to prevent changes in the management and control of our company. Also, under applicable Delaware law, our board of directors may adopt additional anti-takeover measures in the future. In addition, provisions of certain compensatory contracts with our management, such as equity award agreements, may have an anti-takeover effect by resulting in accelerated vesting of outstanding equity securities held by our executive officers. In particular, in the event of a change in control, the vesting of options we granted since July 2009 to certain key executives will accelerate with respect to fifty percent of the then unvested shares on the day prior to the date of the change in control and, subject to the respective executive's continuous service, with respect to the remaining fifty percent of the then

unvested shares on the one year anniversary of the date of the change in control, and could accelerate in full at the time of the change in control if the acquirer does not assume or substitute for the options. As a result, if an acquirer desired to retain the services of those executives following an acquisition, it may be required to provide additional incentive to them, which could increase the cost of the acquisition to the acquirer and may deter or adversely affect the terms of the potential acquisition.

S-31

Table of Contents

Because we do not expect to pay dividends with respect to our common stock in the foreseeable future, you must rely on stock appreciation for any return on your investment.

We have paid no cash dividends on any of our common stock to date, and we currently intend to retain our future earnings, if any, to fund the development and growth of our business. As a result, with respect to our common stock, we do not expect to pay any cash dividends in the foreseeable future, and payment of cash dividends, if any, will also depend on our financial condition, results of operations, capital requirements and other factors and will be at the discretion of our board of directors. Furthermore, we are subject to various laws and regulations that may restrict our ability to pay dividends and we may in the future become subject to contractual restrictions on, or prohibitions against, the payment of dividends. Due to our intent to retain any future earnings rather than pay cash dividends on our common stock and applicable laws, regulations and contractual obligations that may restrict our ability to pay dividends on our common stock, the success of your investment in our common stock will likely depend entirely upon any future appreciation and our common stock may not appreciate.

If we were to issue shares of our common stock or preferred stock that are available for issuance, our stock price could decline.

We have 500,000,000 shares of authorized common stock and, as of October 31, 2014, more than 290 million of such authorized shares were not outstanding or reserved for issuance under outstanding warrants, options, equity incentive plans or other rights. Subject to applicable securities laws and stock exchange listing requirements, our board of directors is authorized under our charter documents to sell and issue our authorized, but unissued, common stock without stockholder approval and may do so to satisfy our capital requirements or expand our product pipeline. Our board of directors also is authorized to issue and sell up to 1,000,000 shares of preferred stock without stockholder approval, at a purchase price approved by the board. The preferred stock may have rights that are superior to the rights of the holders of our common stock. The sale or the proposed sale of substantial amounts of our common stock, preferred stock and/or securities convertible into shares of our common or preferred stock in the public markets may adversely affect the market price of our common stock. Our stockholders may also experience substantial dilution.

RISKS RELATED TO THIS OFFERING

Our management will have broad discretion over the use of the net proceeds from this offering, you may not agree with how we use the proceeds and the proceeds may not be invested successfully.

Our management will have broad discretion as to the use of the net proceeds from this offering and could use them for purposes other than those contemplated currently and described under **Use of Proceeds** on page S-35. Accordingly, you will be relying on the judgment of our management with regard to the use of these net proceeds, and you will not have the opportunity, as part of your investment decision, to assess whether the proceeds are being used appropriately. It is possible that, pending their use, we may invest the net proceeds in a way that does not yield a favorable, or any, return for our company.

We currently intend to use the net proceeds from this offering primarily to fund our clinical development programs, including EPIC, our ongoing phase 3 clinical study of MST-188 in sickle cell disease, and for working capital and general corporate purposes. If EPIC is successful, we plan to submit a NDA to the FDA based in large part on data from that study. We may not achieve the progress we currently expect with respect to EPIC and submission of the NDA because actual costs and timing of clinical development activities, including patient enrollment, and regulatory activities are difficult predict and subject to substantial

Table of Contents

risks and delays, as discussed elsewhere in this prospectus supplement and the accompanying prospectus, in which case our costs to complete EPIC and submit an NDA to the FDA may be materially greater than anticipated currently.

There may be future sales or other dilution of our equity, which may adversely affect the market price of our common stock.

We are generally not restricted from issuing additional common stock, including any securities that are convertible into or exchangeable for, or that represent the right to receive, common stock. The market price of our common stock could decline as a result of sales of common stock or securities that are convertible into or exchangeable for, or that represent the right to receive, common stock after this offering or the perception that such sales could occur.

You will experience immediate and substantial dilution in the net tangible book value per share of our common stock.

Because the purchase price per Series A unit and Series B unit in this offering is substantially higher than the net tangible book value per share of our common stock, investors in this offering will suffer immediate and substantial dilution in the net tangible book value per share of common stock. Based on the public offering price of \$ per Series A unit and \$ per Series B unit and assuming the exercise of all of the pre-funded warrants being offered in this offering, if you purchase securities in this offering, you will suffer immediate and substantial dilution of approximately \$ per share in net tangible book value of our common stock. See Dilution for a more detailed discussion of the dilution you may incur in connection with this offering.

There is no public market for the pre-funded warrants or the warrants to purchase shares of our common stock being offered by us in this offering.

There is no established public trading market for the pre-funded warrants or the warrants being offered in this offering, and a public market may never develop. In addition, we do not intend to apply to list the pre-funded warrants or the warrants on any national securities exchange or other nationally recognized trading system, including the NYSE MKT. Without an active market, the liquidity of the pre-funded warrants and the warrants will be limited.

Holders of our warrants will have no rights as a common stockholder until such holders exercise their warrants and acquire our common stock.

Until holders of warrants acquire shares of our common stock upon exercise of the warrants, holders of warrants will have no rights with respect to the shares of our common stock underlying such warrants. Upon exercise of the warrants, the holders thereof will be entitled to exercise the rights of a common stockholder only as to matters for which the record date occurs after the exercise date.

The warrants included in this offering may not have any value.

Each warrant has an initial exercise price of \$ per share of common stock, will be exercisable upon issuance and will expire five years from the date of issuance. In the event our common stock price does not exceed the exercise price of the warrants during the period when the warrants are exercisable, the warrants may not have any value.

Table of Contents

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement, the accompanying prospectus and the SEC filings that are incorporated by reference into this prospectus supplement and the accompanying prospectus contain or incorporate by reference forward-looking statements within the meaning of Section 27A of the Securities Act and Section 21E of the Securities Exchange Act of 1934, as amended. All statements, other than statements of historical fact, included or incorporated by reference in this prospectus supplement or the accompanying prospectus regarding our strategy, plans, objectives, expectations, prospects, future operations, capital resources, financial position, projected costs of and progress with development of our product candidates, regulatory requirements, collaborations, competition, market exclusivity, intellectual property, and compliance with NYSE MKT listing standards are forward-looking statements. The words believe, anticipate, estimate, plan, expect, intend, may, could, should, potential, likely, projects, continue, will, expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. We cannot guarantee that we actually will achieve the plans, intentions or expectations expressed in our forward-looking statements and you should not place undue reliance on our forward-looking statements. There are a number of important factors that could cause our actual results to differ materially from those indicated or implied by forward-looking statements. These important factors include those set forth above under Risk Factors. These factors and the other cautionary statements made in this prospectus supplement and the accompanying prospectus should be read as being applicable to all related forward-looking statements whenever they appear in this prospectus supplement and the accompanying prospectus. Except as required by law, we do not assume any obligation to update any forward-looking statement. We disclaim any intention or obligation to update or revise any forward-looking statement, whether as a result of new information, future events or otherwise.

Table of Contents

USE OF PROCEEDS

We expect the net proceeds from this offering to be approximately \$ million, after deducting the underwriting discounts and commissions and estimated offering expenses. Our estimated net proceeds do not include proceeds that we may receive upon exercise of the pre-funded warrants and warrants that we are offering. We will not receive any proceeds from the sale of common stock issuable upon exercise of the pre-funded warrants and warrants unless and until such warrants are exercised for cash. If all of the pre-funded warrants and warrants are exercised for cash, we will receive additional proceeds of \$ million. We will not pay the underwriters any discounts, commissions or other fees with respect to shares of our common stock issued upon exercise of the warrants.

We currently intend to use the net proceeds from this offering primarily to fund our clinical development programs, including EPIC, our ongoing phase 3 clinical study of MST-188 in sickle cell disease, and for working capital and general corporate purposes.

Pending the application of the net proceeds as described above, we expect to invest the net proceeds from this offering in short-term, interest-bearing, marketable securities.

S-35

Table of Contents**DILUTION**

Purchasers of the securities offered by this prospectus supplement and the accompanying prospectus will suffer immediate and substantial dilution in the net tangible book value per share of our common stock. Dilution in net tangible book value per share represents the difference between the amount per share paid by purchasers in this offering and the net tangible book value per share of our common stock immediately after this offering.

The net tangible book value of our common stock as of September 30, 2014, was approximately \$33.7 million, or approximately \$0.26 per share. Net tangible book value per share represents the amount of our total tangible assets, less the amount of our total tangible liabilities, divided by the total number of shares of our common stock outstanding. Dilution per share to new investors represents the difference between the amount per share paid by purchasers for each share of common stock in this offering and the net tangible book value per share of our common stock immediately following the completion of this offering.

Assuming the exercise of all of the pre-funded warrants being offered in this offering for \$0.01 per share and after giving effect to the sale of Series A units at the public offering price of \$ per unit and Series B units at the public offering price of \$ per unit (which equals the public offering price of a Series A unit, less the \$0.01 exercise price per share of each pre-funded warrant), and after deducting underwriting discounts and commissions and estimated offering expenses payable by us, and excluding the proceeds, if any, from the exercise of the warrants issued pursuant to this offering, the net tangible book value of our common stock as of September 30, 2014 would have been approximately \$ million, or approximately \$ per share. This represents an immediate increase in net tangible book value of approximately \$ per share to our existing stockholders and an immediate dilution in as-adjusted net tangible book value of approximately \$ per share to purchasers of our securities in this offering, as illustrated by the following table:

Assumed offering price per Series A unit	\$
Assumed offering price per Series B unit	\$
Exercise price per share of the pre-funded warrants	\$ 0.01
Net tangible book value per share as of September 30, 2014	\$ 0.26
Increase per share attributable to this offering	\$
As-adjusted net tangible book value per share as of September 30, 2014, after giving effect to this offering	\$
Dilution per share to new investors participating in this offering	\$

The foregoing table is based on 127,508,434 shares of our common stock outstanding as of September 30, 2014, and assumes the issuance of shares of our common stock upon the exercise of all of the pre-funded warrants being offered in this offering and excludes:

44,416,875 shares of our common stock issuable upon exercise of warrants outstanding as of September 30, 2014, with a weighted-average exercise price of \$1.05 per share;

Edgar Filing: Mast Therapeutics, Inc. - Form 424B5

13,062,271 shares of our common stock issuable upon exercise of options outstanding as of September 30, 2014, with a weighted-average exercise price of \$1.02 per share;

10,942,557 shares and 276,945 shares of our common stock available for future grants under our 2013 Omnibus Incentive Plan and 2005 Employee Stock Purchase Plan as of September 30, 2014, respectively;

12,478,050 shares of common stock that may be issued to the former stockholders of SynthRx, Inc., subject to the achievement of performance milestones, pursuant to the terms of the merger agreement with SynthRx;

S-36

Table of Contents

1,008,840 shares of our common stock sold after September 30, 2014 pursuant to our at the market equity offering program; and

shares of our common stock issuable upon exercise of the warrants included in the Series A units and Series B units offered by this prospectus supplement and the accompanying prospectus.

To the extent that any outstanding options or warrants are exercised, new options are issued under our equity incentive plan, additional shares of common shares are sold under our at the market offering program, shares of common stock are sold under our employee stock purchase plan or we otherwise issue additional shares of common stock in the future at prices per share below the price per share for any shares sold in this offering, there will be further dilution to new investors.

S-37

Table of Contents

DESCRIPTION OF THE SECURITIES WE ARE OFFERING

In this offering, we are offering for sale Series A units, with each Series A unit consisting of one share of our common stock and of a warrant. Each whole warrant will be exercisable for one share of our common stock. The purchase price for each Series A unit is \$. The Series A units will not be issued or certificated. The shares of common stock and the warrants included in the Series A units will be issued separately but can only be purchased together in the Series A units in this offering.

We are also offering to those purchasers whose purchase of Series A units in this offering would result in the purchaser, together with its affiliates and certain related parties, beneficially owning more than 4.99% of our outstanding common stock following the consummation of this offering, the opportunity to purchase, in lieu of Series A units that otherwise would result in ownership in excess of 4.99% of our outstanding common stock, Series B units. Each Series B unit will consist of one pre-funded warrant and of a warrant. Each pre-funded warrant will be exercisable for one share of our common stock. Each whole warrant will be exercisable for one share of our common stock. The purchase price for each Series B unit is \$. The Series B units will not be issued or certificated. The pre-funded warrants and the warrants included in the Series B units will be issued separately but can only be purchased together in the Series B units in this offering.

Each pre-funded warrant will have an initial exercise price of \$0.01 per share, will be exercisable upon issuance, and will expire five years from the date of issuance. Each warrant will have an initial exercise price of \$ per share, will be exercisable upon issuance, and will expire five years from the date of issuance.

Common Stock

The material terms and provisions of our common stock are described in the section titled Description of Common Stock and Preferred Stock Common Stock in the accompanying prospectus.

Securities Exchange Listing

Our common stock is listed on the NYSE MKT under the symbol MSTX.

Transfer Agent and Registrar

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

Warrants

The material terms and provisions of the pre-funded warrants and other warrants being offered pursuant to this prospectus supplement and the accompanying prospectus are summarized below. This summary is subject to and qualified in its entirety by each form of warrant, which will be filed with a Current Report on Form 8-K to be filed by us with the SEC in connection with this offering. You should review a copy of each form of warrant for a complete description of the terms and conditions applicable to the pre-funded warrants and the warrants included in the Series A units and Series B units.

Pre-Funded Warrants

The pre-funded warrants will provide for an exercise price of \$0.01 per share and will be exercisable at the option of the holder at any time on or after their date of issuance, which will be the closing date of this offering, through close

of business on the date that is five years of their original issuance date.

The pre-funded warrants will be issued pursuant to the terms of the warrant agent agreement between American Stock Transfer & Trust Company, as warrant agent, and us. We will initially issue the pre-funded

S-38

Table of Contents

warrants in the form of global securities held in book-entry form. The pre-funded warrants initially will be represented by one or more permanent global certificates in fully registered form and will be deposited with a custodian for, and registered in the name of, a nominee of The Depository Trust Company, New York, New York (DTC), as depository. Owners of beneficial interests in the pre-funded warrants represented by the global securities will hold their interests pursuant to the procedures and practices of DTC and must exercise any rights in respect of their interests in accordance with the procedures and practices of DTC. As a result, beneficial interests in any such securities will be shown on, and transfers will be effected only through, records maintained by DTC and its direct and indirect participants and any such interest may not be exchanged for certificated securities, except in limited circumstances. Beneficial owners will not be holders and will not be entitled to any rights provided to the holders of the pre-funded warrants under the global securities or the global warrant. Our company and any of our agents may treat DTC as the sole holder and registered owner of the global securities.

A pre-funded warrant holder will not have the right to exercise any portion of the pre-funded warrant if the holder, together with its affiliates, would beneficially own in excess of 4.99% of the number of shares of our common stock outstanding immediately after giving effect to the exercise, as such percentage ownership is determined in accordance with the terms of the pre-funded warrants. However, any holder may increase or decrease such percentage to any other percentage upon at least 61 days' prior notice from the holder to us.

The exercise price of the pre-funded warrants, and in some cases the number of shares issuable upon exercise of the pre-funded warrants, will be subject to adjustment in the event of stock splits, stock dividends, combinations, rights offerings and similar events affecting our common stock. In addition, in the event we consummate a merger or consolidation with or into another person or other reorganization event in which our common stock is converted or exchanged for securities, cash or other property, or we sell, lease, license or otherwise dispose of all or substantially all of our assets or we or another person acquire 50% or more of our outstanding common stock, then following such event, the holders of the pre-funded warrants will be entitled to receive upon exercise of the pre-funded warrants the same kind and amount of securities, cash or property which the holders would have received had they exercised the pre-funded warrants immediately prior to such fundamental transaction. Any successor to us or surviving entity shall assume the obligations under the pre-funded warrants.

The pre-funded warrant holders must surrender payment in cash of the aggregate exercise price of the shares being acquired upon exercise of the pre-funded warrants. If, however, we are unable to offer and sell the shares underlying the pre-funded warrants pursuant to this prospectus due to the ineffectiveness of the registration statement of which this prospectus is a part, then the pre-funded warrants may only be exercised on a net or cashless basis. In addition, any time after two years from the date of original issuance of the pre-funded warrants, a holder may, in its discretion, elect to exercise the pre-funded warrants on a net or cashless basis. No fractional shares of common stock will be issued in connection with the exercise of a pre-funded warrant. In lieu of fractional shares, we will pay the holder an amount in cash equal to the fractional amount multiplied by the exercise price.

We do not intend to list the pre-funded warrants on any securities exchange or automated quotation system.

Subject to applicable laws, the pre-funded warrants may be offered for sale, sold, transferred or assigned without our consent. Except by virtue of such holder's ownership of shares of our common stock, the holder of a pre-funded warrant does not have the rights or privileges of a holder of our common stock, including any voting rights, until the holder exercises the pre-funded warrant.

Table of Contents

Warrants

The warrants will provide for an exercise price of \$ _____ per share and will be exercisable at the option of the holder at any time on or after their date of issuance, which will be the closing date of this offering, through close of business on the date that is five years of their original issuance date.

The warrants will be issued pursuant to the terms of the warrant agent agreement between American Stock Transfer & Trust Company, as warrant agent, and us. We will initially issue the warrants in the form of global securities held in book-entry form. The warrants initially will be represented by one or more permanent global certificates in fully registered form and will be deposited with a custodian for, and registered in the name of, a nominee of DTC, as depository. Owners of beneficial interests in the warrants represented by the global securities will hold their interests pursuant to the procedures and practices of DTC and must exercise any rights in respect of their interests in accordance with the procedures and practices of DTC. As a result, beneficial interests in any such securities will be shown on, and transfers will be effected only through, records maintained by DTC and its direct and indirect participants and any such interest may not be exchanged for certificated securities, except in limited circumstances. Beneficial owners will not be holders and will not be entitled to any rights provided to the holders of the warrants under the global securities or the global warrant. Our company and any of our agents may treat DTC as the sole holder and registered owner of the global securities.

A warrant holder will not have the right to exercise any portion of the warrant if the holder, together with its affiliates, would beneficially own in excess of 4.99% of the number of shares of our common stock outstanding immediately after giving effect to the exercise, as such percentage ownership is determined in accordance with the terms of the warrants. However, any holder may increase or decrease such percentage to any other percentage upon at least 61 days prior notice from the holder to us.

The exercise price of the warrants, and in some cases the number of shares issuable upon exercise of the warrants, will be subject to adjustment in the event of stock splits, stock dividends, combinations, rights offerings and similar events affecting our common stock. In addition, in the event we consummate a merger or consolidation with or into another person or other reorganization event in which our common stock is converted or exchanged for securities, cash or other property, or we sell, lease, license or otherwise dispose of all or substantially all of our assets or we or another person acquire 50% or more of our outstanding common stock, then following such event, the holders of the warrants will be entitled to receive upon exercise of the warrants the same kind and amount of securities, cash or property which the holders would have received had they exercised the warrants immediately prior to such fundamental transaction. Any successor to us or surviving entity shall assume the obligations under the warrants.

The warrant holders must surrender payment in cash of the aggregate exercise price of the shares being acquired upon exercise of the warrants. If, however, we are unable to offer and sell the shares underlying the warrants pursuant to this prospectus due to the ineffectiveness of the registration statement of which this prospectus is a part, then the warrants may only be exercised on a net or cashless basis. In addition, any time after two years from the date of original issuance of the warrants, a holder may, in its discretion, elect to exercise the warrants on a net or cashless basis. No fractional shares of common stock will be issued in connection with the exercise of a warrant. In lieu of fractional shares, we will pay the holder an amount in cash equal to the fractional amount multiplied by the exercise price.

We do not intend to list the warrants on any securities exchange or automated quotation system.

Subject to applicable laws, the warrants may be offered for sale, sold, transferred or assigned without our consent. Except by virtue of such holder's ownership of shares of our common stock, the holder of a warrant does not have the

rights or privileges of a holder of our common stock, including any voting rights, until the holder exercises the warrant.

S-40

Table of Contents**UNDERWRITING**

We have entered into an underwriting agreement with Cowen and Company, LLC, acting as representative of the several underwriters, with respect to the securities in this offering. Subject to the terms and conditions of the underwriting agreement, we have agreed to issue and sell to the underwriters named below, and each underwriter severally has agreed to purchase, the respective number of units set forth opposite its name below:

Underwriter	Number of Series A Units	Number of Series B Units
Cowen and Company, LLC		

Total

The underwriters are offering the units subject to their acceptance of the units from us and subject to prior sale. The underwriting agreement provides that the obligation of the underwriters to purchase the units offered hereby is subject to certain conditions and that the underwriters are obligated to purchase all of the units offered hereby if they purchase any of the units.

The underwriters initially propose to offer the units directly to the public at the public offering prices set forth on the cover page of this prospectus supplement and to selected dealers at such price less a concession of not more than \$. After this offering, the offering price and other selling terms may be changed by the underwriters. The units are offered subject to receipt and acceptance by the underwriters and to the other conditions of the offering, including the right to reject orders in whole or in part.

The following table summarizes the compensation to be paid to the underwriters by us and the proceeds, before expenses, payable to us, both on a per unit basis and in total:

	Per Series A Unit	Per Series B Unit	Total
Public offering price	\$	\$	\$
Underwriting discounts and commissions	\$	\$	\$
Proceeds, before expenses, to us	\$	\$	\$

The expenses of this offering, not including underwriting discounts and commissions, are estimated to be approximately \$, which includes \$100,000 that we have agreed to reimburse the underwriters for fees incurred by them in connection with this offering.

The public offering price of the Series A units and Series B units and the exercise price and other terms of the warrants and pre-funded warrants were negotiated between us and the underwriters, based on the trading price of our common stock prior to the offering, among other things. Other factors considered in determining the public offering price of the Series A units and the Series B units we are offering and the exercise price and other terms of the warrants and pre-funded warrants include the history and prospects of our company, the stage of development of our business, our business plans for the future and the extent to which they have been implemented, an assessment of our management, general conditions of the securities markets at the time of the offering and such other factors as were

deemed relevant.

Pursuant to the underwriting agreement, we have agreed to indemnify the underwriters against certain liabilities, including liabilities under the Securities Act, or to contribute to payments that the underwriters or such indemnified parties may be required to make in respect of any such liabilities.

We and all of our directors and executive officers have agreed that, subject to certain exceptions, without the prior written consent of Cowen and Company, LLC, we and they will not, (i) during the period ending 90

S-41

Table of Contents

days, subject to an 18-day extension under certain circumstances (subject to clause (ii) below), following the date of this prospectus supplement, offer, pledge, transfer, assign, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant for the sale of, lend or otherwise dispose of any shares of our common stock or any securities convertible into or exchangeable or exercisable for our common stock or file, or cause to be filed, any registration statement under the Securities Act with respect to any of the foregoing, or (ii) during the period ending 30 days following the date of this prospectus supplement, directly or indirectly offer, sell, assign, transfer, pledge, contract to sell, or otherwise dispose of, any shares of Common Stock pursuant to that certain Sales Agreement dated as of February 10, 2014 between us and Cowen and Company, LLC (the ATM Agreement). At any time and without public notice, Cowen and Company, LLC may, in its sole discretion, release some or all of the securities from these lock-up agreements.

The restrictions described above do not apply to certain transactions, including:

with respect to us:

the securities to be sold in this offering
with respect to our directors and executive officers:

the transfer of shares of common stock or any securities convertible into shares of common stock to us upon a vesting event of our securities or upon the exercise of options to purchase our securities, in each case on a cashless or net exercise basis or to cover tax withholding obligations and sales of shares of common stock to cover the exercise price of options and to fund tax obligations arising upon the exercise of options on the vesting of restricted stock.

Our common stock is listed on the NYSE MKT LLC under the symbol MSTX. There is no established public trading market for the warrants and pre-funded warrants, and we do not intend to apply to list the warrants or pre-funded on any national securities exchange. The warrants included in the Series A units are immediately separable from the shares of our common stock being offered as part of the Series A units, and the warrants included in the Series B units are immediately separable from the pre-funded warrants being offered as part of the Series B units.

The underwriters have informed us that they will not engage in over-allotment, stabilizing or syndicate covering transactions in connection with this offering.

Other than the foregoing and the ATM Agreement, the underwriters and certain of their affiliates may in the future provide various investment banking and other financial services for us and our affiliates.

Table of Contents

NOTICE TO INVESTORS

United Kingdom. Each of the underwriters has represented and agreed that:

it has not made or will not make an offer of the securities to the public in the United Kingdom within the meaning of section 102B of the Financial Services and Markets Act 2000, as amended (FSMA), except to legal entities which are authorized or regulated to operate in the financial markets or, if not so authorized or regulated, whose corporate purpose is solely to invest in securities or otherwise in circumstances which do not require the publication by us of a prospectus pursuant to the Prospectus Rules of the Financial Services Authority (FSA);

it has only communicated or caused to be communicated and will only communicate or cause to be communicated an invitation or inducement to engage in investment activity (within the meaning of section 21 of FSMA) to persons who have professional experience in matters relating to investments falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005 or in circumstances in which section 21 of FSMA does not apply to us; and

it has complied with and will comply with all applicable provisions of FSMA with respect to anything done by it in relation to the securities in, from or otherwise involving the United Kingdom.

European Economic Area. In relation to each Member State of the European Economic Area (Iceland, Norway and Lichtenstein in addition to the member states of the European Union) that has implemented the Prospectus Directive (each, a Relevant Member State), each underwriter has represented and agreed that with effect from and including the date on which the Prospectus Directive is implemented in that Relevant Member State, or the Relevant Implementation Date, it has not made and will not make an offer of the securities to the public in that Relevant Member State prior to the publication of a prospectus in relation to the securities that has been approved by the competent authority in that Relevant Member State or, where appropriate, approved in another Relevant Member State and notified to the competent authority in that Relevant Member State, all in accordance with the Prospectus Directive, except that it may, with effect from and including the Relevant Implementation Date, make an offer of the securities to the public in that Relevant Member State at any time:

to legal entities which are authorized or regulated to operate in the financial markets or, if not so authorized or regulated, whose corporate purpose is solely to invest in securities;

to any legal entity which has two or more of (i) an average of at least 250 employees during the last financial year; (ii) a total balance sheet of more than 43,000,000 and (iii) an annual net turnover of more than 50,000,000, as shown in its last annual or consolidated accounts;

in any other circumstances which do not require the publication by the issuer of a prospectus pursuant to Article 3 of the Prospectus Directive.

Each person in a Relevant Member State who receives any communication in respect of, or who acquires any securities under, the offer contemplated in this prospectus will be deemed to have represented, warranted and agreed to and with us and each underwriter that:

it is a qualified investor within the meaning of the law in that Relevant Member State implementing Article 2(1)(e) of the Prospectus Directive; and

in the case of any securities acquired by it as a financial intermediary, as that term is used in Article 3(2) of the Prospectus Directive, (i) the securities acquired by it in the offer have not been acquired on behalf of, nor have they been acquired with a view to their offer or resale to, persons in any Relevant Member State other than qualified investors, as that term is defined in the Prospectus Directive, or in circumstances in which the prior consent of the representative of the underwriters has been given to the offer or resale; or (ii) where securities have been acquired by it on behalf of persons in any Relevant Member State other than qualified investors, the offer of those securities to it is not treated under the Prospectus Directive as having been made to such persons.

S-43

Table of Contents

For the purposes of the provisions in the two immediately preceding paragraphs, the expression an offer of the securities to the public in relation to the securities in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and the securities to be offered so as to enable an investor to decide to purchase or subscribe for the securities, as the same may be varied in that Relevant Member State by any measure implementing the Prospectus Directive in that Relevant Member State, and the expression Prospectus Directive means Directive 2003/71/EC and includes any relevant implementing measure in each Relevant Member State.

Israel. In the State of Israel, the securities offered hereby may not be offered to any person or entity other than the following:

a fund for joint investments in trust, i.e., mutual fund, as such term is defined in the Law for Joint Investments in Trust, 5754-1994, or a management company of such a fund;

a provident fund as defined in the Control of the Financial Services (Provident Funds) Law 5765-2005, or a management company of such a fund;

an insurer, as defined in the Law for Oversight of Insurance Transactions, 5741-1981;

a banking entity or satellite entity, as such terms are defined in the Banking Law (Licensing), 5741-1981, other than a joint services company, acting for its own account or for the account of investors of the type listed in Section 15A(b) of the Securities Law, 1968;

a company that is licensed as a portfolio manager, as such term is defined in Section 8(b) of the Law for the Regulation of Investment Advisors and Portfolio Managers, 5755-1995, acting on its own account or for the account of investors of the type listed in Section 15A(b) of the Securities Law, 1968;

an investment advisor or investment distributor, as such term is defined in Section 7(c) of the Law for the Regulation of Investment Advisors and Portfolio Managers, 5755-1995, acting on its own account;

a member of the Tel Aviv Stock Exchange, acting on its own account or for the account of investors of the type listed in Section 15A(b) of the Securities Law, 1968;

an underwriter fulfilling the conditions of Section 56(c) of the Securities Law, 5728-1968, acting on its own account;

venture capital fund, defined as an entity primarily involved in investments in companies which, at the time of investment, (i) are primarily engaged in research and development or manufacture of new technological

products or processes and (ii) involve above-average risk;

an entity fully owned by investors of the type listed in Section 15A(b) of the Securities Law, 5728-1968;

an entity, other than an entity formed for the purpose of purchasing securities in this offering, in which the shareholders' equity is in excess of NIS 50 million; and

an individual fulfilling the conditions of Section 9 to the supplement to the Law for the Regulation of Investment Advisors and Portfolio Managers, 5755-1995, acting on its own account (for this matter, Section 9 to the supplement shall be referred to as "Investor" as an investor for the meaning of Section 15A(b)(1) of the Securities Law 1968 instead of "eligible client" for the meaning of this law).

Offerees of the securities offered hereby, or the Investors, in the State of Israel shall be required to submit written confirmation that they fall within the scope of one of the above criteria, that they are fully aware of the significance of being an Investor pursuant to such criteria and that they have given their consent, or the Consent. An appeal to an Investor for the Consent shall not be considered a public offering. This prospectus supplement will not be distributed or directed to Investors in the State of Israel who do not fall within one of the above criteria.

Table of Contents

LEGAL MATTERS

The validity of the securities offered hereby will be passed upon for us by DLA Piper LLP (US), San Diego, California. Cowen and Company, LLC is being represented in connection with this offering by LeClairRyan, A Professional Corporation, New York, New York.

EXPERTS

The consolidated financial statements incorporated in this prospectus by reference to the Annual Report on Form 10-K for the year ended December 31, 2013 have been so incorporated in reliance on the report of PricewaterhouseCoopers LLP, an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

WHERE YOU CAN FIND ADDITIONAL INFORMATION

We file annual, quarterly and current reports, proxy statements and other information with the SEC. You may read and copy any reports, statements and other information filed by us at the SEC's Public Reference Room at 100 F Street, N.E., Washington, D.C. 20549. Please call (800) SEC-0330 for further information on the Public Reference Room. The SEC maintains an Internet website that contains reports, proxy and information statements and other information regarding issuers, including us, that file electronically with the SEC. The address for the SEC's website is <http://www.sec.gov>.

We make available, free of charge, through our investor relations website, our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, statements of changes in beneficial ownership of securities and amendments to those reports and statements as soon as reasonably practicable after they are filed with the SEC. The address for our website is <http://www.masttherapeutics.com>. The contents on our website are not part of this prospectus, and the reference to our website does not constitute incorporation by reference into this prospectus of the information contained at that site.

Table of Contents

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to incorporate by reference the information we file with it, which means that we can disclose important information to you by referring you to another document that we have filed separately with the SEC. You should read the information incorporated by reference because it is an important part of this prospectus supplement. We incorporate by reference the following information or documents that we have filed with the SEC (excluding those portions of any Form 8-K that are not deemed filed pursuant to the General Instructions of Form 8-K):

Our Annual Report on Form 10-K for the fiscal year ended December 31, 2013, filed with the SEC on March 26, 2014;

The portions of our definitive proxy statement filed with the SEC on April 29, 2014 in connection with our 2014 annual meeting of stockholders that are incorporated by reference into Part III of our Annual Report on Form 10-K for the fiscal year ended December 31, 2013;

Our Quarterly Report on Form 10-Q for the quarter ended March 31, 2014, filed with the SEC on May 5, 2014, our Quarterly Report on Form 10-Q for the quarter ended June 30, 2014, filed with the SEC on August 11, 2014, and our Quarterly Report on Form 10-Q for the quarter ended September 30, 2014, filed with the SEC on October 31, 2014;

Our Current Reports on Form 8-K filed with the SEC on January 8, 2014, February 10, 2014, February 24, 2014, February 28, 2014, March 21, 2014, March 26, 2014, May 9, 2014, June 5, 2014, June 20, 2014, June 30, 2014, August 14, 2014, September 2, 2014, September 8, 2014, September 9, 2014, and October 7, 2014; and

The description of our common stock contained in our registration statement on Form 8-A filed with the SEC on April 27, 2004 (File No. 001-32157-04755401).

All reports and other documents we subsequently file pursuant to Section 13(a), 13(c), 14 or 15(d) of the Exchange Act prior to the termination of this offering, including all such documents we may file with the SEC after the date of the initial registration statement and prior to the effectiveness of the registration statement, but excluding any information furnished to, rather than filed with, the SEC, will also be incorporated by reference into this prospectus supplement and deemed to be part of this prospectus supplement from the date of the filing of such reports and documents.

Any statement contained in any document incorporated by reference herein shall be deemed to be modified or superseded for purposes of this prospectus supplement to the extent that a statement contained in this prospectus supplement or any additional prospectus supplements modifies or supersedes such statement. Any statement so modified or superseded shall not be deemed, except as so modified or superseded, to constitute a part of this prospectus supplement.

We will provide without charge to each person, including any beneficial owner, to whom this prospectus supplement is delivered, upon written or oral request, a copy of any or all documents that are incorporated by reference into this

prospectus supplement, but not delivered with the prospectus supplement, other than exhibits to such documents unless such exhibits are specifically incorporated by reference into the documents that this prospectus supplement incorporates. You should direct written requests to: Mast Therapeutics, Inc., 12390 El Camino Real, Suite 150, San Diego, California 92130, Attn: Investor Relations, or you may call us at (858) 552-0866.

S-46

Table of Contents

PROSPECTUS

\$150,000,000

Common Stock

Preferred Stock

Debt Securities

Warrants

Units

ADVENTRX PHARMACEUTICALS, INC.

We may, from time to time in one or more offerings, offer and sell up to \$150,000,000 in the aggregate of common stock, preferred stock, debt securities, warrants to purchase common stock, preferred stock or debt securities, or any combination of the foregoing, either individually or as units comprised of one or more of the other securities.

This prospectus provides a general description of the securities we may offer. We will provide the specific terms of the securities offered in one or more supplements to this prospectus. We may also authorize one or more free writing prospectuses to be provided to you in connection with these offerings. The prospectus supplement and any related free writing prospectus may add, update or change information contained in this prospectus. You should read carefully this prospectus, the applicable prospectus supplement and any related free writing prospectus, as well as the documents incorporated by reference before you invest in any of our securities. **This prospectus may not be used to offer or sell any securities unless accompanied by the applicable prospectus supplement.**

Our common stock is listed on the NYSE Amex equities market under the symbol ANX. On March 7, 2012 the last reported sale price for our common stock was \$0.63 per share. The aggregate market value of our outstanding shares of common stock held by non-affiliates is approximately \$29.7 million, based on 47,168,046 outstanding shares held by non-affiliates as of March 5, 2012 and the last reported sale price per share of our common stock on the NYSE Amex equities market on March 7, 2012. We have not offered any securities pursuant to General Instruction I.B.6. of Form S-3 during the prior 12 calendar month period that ends on, and includes, the date of this prospectus.

Investing in our securities involves a high degree of risk. See Risk Factors on page 5 of this prospectus and as updated in the applicable prospectus supplement, any related free writing prospectus and other future filings we make with the Securities and Exchange Commission that are incorporated by reference into this prospectus.

We will sell these securities directly to investors, through agents designated from time to time or to or through underwriters or dealers. For additional information on the methods of sale, you should refer to the section entitled "Plan of Distribution" in this prospectus. If any underwriters

Edgar Filing: Mast Therapeutics, Inc. - Form 424B5

are involved in the sale of any securities with respect to which this prospectus is being delivered, the names of such underwriters and any applicable commissions or discounts will be set forth in a prospectus supplement. The price to the public of such securities and the net proceeds we expect to receive from such sale will also be set forth in a prospectus supplement.

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

The date of this prospectus is May 1, 2012.

Table of Contents

TABLE OF CONTENTS

<u>ABOUT THIS PROSPECTUS</u>	ii
<u>SUMMARY</u>	1
<u>RISK FACTORS</u>	5
<u>SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS</u>	5
<u>RATIO OF EARNINGS TO FIXED CHARGES</u>	7
<u>USE OF PROCEEDS</u>	7
<u>SECURITIES WE MAY OFFER</u>	8
<u>DESCRIPTION OF COMMON STOCK AND PREFERRED STOCK</u>	8
<u>DESCRIPTION OF DEBT SECURITIES</u>	12
<u>DESCRIPTION OF WARRANTS</u>	19
<u>DESCRIPTION OF UNITS</u>	20
<u>LEGAL OWNERSHIP OF SECURITIES</u>	22
<u>PLAN OF DISTRIBUTION</u>	25
<u>LEGAL MATTERS</u>	27
<u>EXPERTS</u>	27
<u>WHERE YOU CAN FIND MORE INFORMATION</u>	27
<u>INCORPORATION OF CERTAIN INFORMATION BY REFERENCE</u>	27

Table of Contents

ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the Securities and Exchange Commission, or the SEC, under the Securities Act of 1933, as amended, or the Securities Act, using a shelf registration process. Under this shelf registration process, we may from time to time sell common stock, preferred stock, debt securities or warrants to purchase common stock, preferred stock or debt securities, or any combination of the foregoing, either individually or as units comprised of one or more of the other securities, in one or more offerings up to a total dollar amount of \$150,000,000. We have provided to you in this prospectus a general description of the securities we may offer. Each time we sell securities under this shelf registration, we will, to the extent required by law, provide a prospectus supplement that will contain specific information about the terms of that offering. We may also authorize one or more free writing prospectuses to be provided to you that may contain material information relating to these offerings. The prospectus supplement and any related free writing prospectus that we may authorize to be provided to you may also add, update or change information contained in this prospectus or in any documents that we have incorporated by reference into this prospectus. To the extent there is a conflict between the information contained in this prospectus and the prospectus supplement or any related free writing prospectus, you should rely on the information in the prospectus supplement or the related free writing prospectus; provided that if any statement in one of these documents is inconsistent with a statement in another document having a later date—for example, a document incorporated by reference in this prospectus or any prospectus supplement or any related free writing prospectus—the statement in the document having the later date modifies or supersedes the earlier statement.

We have not authorized any dealer, agent or other person to give any information or to make any representation other than those contained or incorporated by reference in this prospectus and any accompanying prospectus supplement. You must not rely upon any information or representation not contained or incorporated by reference in this prospectus or an accompanying prospectus supplement, or any related free writing prospectus that we may authorize to be provided to you. This prospectus and the accompanying prospectus supplement, if any, do not constitute an offer to sell or the solicitation of an offer to buy any securities other than the registered securities to which they relate, nor do this prospectus and the accompanying prospectus supplement constitute an offer to sell or the solicitation of an offer to buy securities in any jurisdiction to any person to whom it is unlawful to make such offer or solicitation in such jurisdiction. You should not assume that the information contained in this prospectus, any applicable prospectus supplement or any related free writing prospectus is accurate on any date subsequent to the date set forth on the front of the document or that any information we have incorporated by reference is correct on any date subsequent to the date of the document incorporated by reference (as our business, financial condition, results of operations and prospects may have changed since that date), even though this prospectus, any applicable prospectus supplement or any related free writing prospectus is delivered or securities are sold on a later date.

As permitted by the rules and regulations of the SEC, the registration statement, of which this prospectus forms a part, includes additional information not contained in this prospectus. You may read the registration statement and the other reports we file with the SEC at the SEC's web site or at the SEC's offices described below under the heading [Where You Can Find Additional Information](#).

Trademarks, Trade Names and Service Marks

We own or have rights to use the trademarks, service marks and trade names that we use in conjunction with the operation of our business. Some of the more important trademarks that we own or have rights to use that appear in this prospectus include: Exelbine and SYNTHRAX®, which are registered or trademarked in the United States. Each trademark, trade name or service mark of any other company appearing in this prospectus is, to our knowledge, owned by such other company.

Company References

In this prospectus, unless otherwise specified or the context otherwise requires, references to ADVENTRX Pharmaceuticals, Inc., ADVENTRX, we, us, our and our company refer to ADVENTRX Pharmaceuticals, Inc. and its consolidated subsidiaries.

Table of Contents

SUMMARY

This summary highlights selected information from this prospectus and does not contain all of the information that you need to consider in making your investment decision. You should carefully read the entire prospectus, including the section entitled Risk Factors on page 4, the information incorporated herein by reference, including our financial statements, and the exhibits to the registration statement of which this prospectus is a part.

About ADVENTRX Pharmaceuticals, Inc.

We are a biopharmaceutical company focused on developing proprietary product candidates. Our lead product candidate is ANX-188, a rheologic, antithrombotic and cytoprotective agent that improves microvascular blood flow and has potential application in treating a wide range of diseases and conditions, such as complications arising from sickle cell disease. We also are developing ANX-514, a novel, detergent-free formulation of the chemotherapy drug docetaxel.

We are a development-stage company and have not yet marketed or sold any products or generated any significant revenue. We have devoted substantially all of our resources to research and development and to acquisition of our product candidates. We have incurred significant losses since inception and we incurred a loss from operations of \$13.4 million for the year ended December 31, 2011. We had cash, cash equivalents and short-term investments of \$50.7 million at December 31, 2011.

Our company was incorporated in Delaware in December 1995. In October 2000, we merged our wholly-owned subsidiary, Biokeys Acquisition Corp., with and into Biokeys, Inc. and changed our name to Biokeys Pharmaceuticals, Inc. In May 2003, we merged Biokeys, Inc., our wholly owned subsidiary, with and into us and changed our name to ADVENTRX Pharmaceuticals, Inc. In April 2006, we acquired SD Pharmaceuticals, Inc., a Delaware corporation, and, in April 2011, we acquired SynthRx, Inc., a Delaware corporation, each as a wholly-owned subsidiary through a merger transaction.

Our executive offices are located at 12390 El Camino Real, Suite 150, San Diego, California 92130, and our telephone number is (858) 552-0866. Our corporate website is located at www.adventrx.com. We make available free of charge through our website our annual report on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended, or the Exchange Act, as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC. The information contained in, or that can be accessed through, our website is not part of this prospectus or any prospectus supplement.

The Securities We May Offer

We may offer shares of our common stock and preferred stock, various series of debt securities and warrants to purchase any of such securities, either individually or in units, with a total value of up to \$150,000,000 from time to time under this prospectus, together with any applicable prospectus supplement and related free writing prospectus, at prices and on terms to be determined by market conditions at the time of offering. If we issue any debt securities at a discount from their original stated principal amount, then, for purposes of calculating the total dollar amount of all securities issued under this prospectus, we will treat the initial offering price of the debt securities as the total original principal amount of the debt securities. Each time we offer securities under this prospectus, we will provide offerees with a prospectus supplement that will describe the specific amounts, prices and other important terms of the securities being offered, including, to the extent applicable:

Table of Contents

designation or classification;

aggregate principal amount or aggregate offering price;

maturity, if applicable;

original issue discount, if any;

rates and times of payment of interest or dividends, if any;

redemption, conversion, exchange or sinking fund terms, if any;

conversion or exchange prices or rates, if any, and, if applicable, any provisions for changes to or adjustments in the conversion or exchange prices or rates and in the securities or other property receivable upon conversion or exchange;

ranking;

restrictive covenants, if any;

voting or other rights, if any; and

important United States federal income tax considerations.

The prospectus supplement and any related free writing prospectus that we may authorize to be provided to you may also add, update or change information contained in this prospectus or in documents we have incorporated by reference. However, no prospectus supplement or free writing prospectus will offer a security that is not registered and described in this prospectus at the time of the effectiveness of the registration statement of which this prospectus is a part.

We may sell the securities to or through underwriters, dealers or agents or directly to purchasers. We, as well as any agents acting on our behalf, reserve the sole right to accept and to reject in whole or in part any proposed purchase of securities. Each prospectus supplement will set forth the names of any underwriters, dealers or agents involved in the sale of securities described in that prospectus supplement and any applicable fee, commission or discount arrangements with them, details regarding any over-allotment option granted to them, and net proceeds to us. The following is a summary of the securities we may offer with this prospectus.

Common Stock

As of the date of this prospectus, our amended and restated certificate of incorporation, as amended, or our certificate of incorporation, authorizes us to issue 500,000,000 shares of common stock, par value \$0.001 per share. We may offer shares of our common stock either alone or underlying other registered securities convertible into or exercisable for our common stock. Holders of our common stock are entitled to such dividends as our board of directors may declare from time to time out of legally available funds, subject to the preferential rights of the holders of any shares of our preferred stock that are outstanding or that we may issue in the future. Currently, we do not pay any dividends on our common stock. Each holder of our common stock is entitled to one vote per share. In this prospectus, we provide a general description of, among other things, the rights and restrictions that apply to holders of our common stock.

Preferred Stock

As of the date of this prospectus, our certificate of incorporation authorizes us to issue 1,000,000 shares of preferred stock, par value \$0.001 per share, none of which are outstanding. We may issue shares of our preferred stock from time to time, in one or more series. Any authorized and undesignated shares of preferred stock may be issued with such rights and powers as the board of directors may designate. Under our certificate of incorporation, our board of directors has the authority to issue shares of our preferred stock in one or more series

Table of Contents

and to fix or alter the rights, preferences, privileges and restrictions granted to or imposed upon any series of preferred stock. The particular terms of each class or series of preferred stock, including redemption privileges, liquidation preferences, voting rights, dividend rights and/or conversion rights, will be more fully described in the applicable prospectus supplement relating to the preferred stock offered thereby.

The rights, preferences, privileges and restrictions granted to or imposed upon any series of preferred stock that we offer and sell under this prospectus and applicable prospectus supplements will be set forth in a certificate of designation relating to the series. We will file as an exhibit to the registration statement of which this prospectus is a part, or will incorporate by reference from another report that we file with the SEC, the form of any certificate of designation that describes the terms of any series of preferred stock we offer under this prospectus before the issuance of shares of that series of preferred stock. You should read any prospectus supplement and any free writing prospectus that we may authorize to be provided to you related to the series of preferred stock being offered, as well as the complete certificate of designation that contains the terms of the applicable series of preferred stock.

Debt Securities

We may offer general debt obligations, which may be secured or unsecured, senior or subordinated and convertible into shares of our common stock. In this prospectus, we refer to the senior debt securities and the subordinated debt securities together as the debt securities. We may issue debt securities under a note purchase agreement or under an indenture to be entered between us and a trustee; forms of the senior and subordinated indentures are included as an exhibit to the registration statement of which this prospectus is a part. The indentures do not limit the amount of securities that may be issued under it and provides that debt securities may be issued in one or more series. The senior debt securities will have the same rank as all of our other indebtedness that is not subordinated. The subordinated debt securities will be subordinated to our senior debt on terms set forth in the applicable prospectus supplement. In addition, the subordinated debt securities will be effectively subordinated to creditors and preferred stockholders of our subsidiaries. Our board of directors will determine the terms of each series of debt securities being offered. This prospectus contains only general terms and provisions of the debt securities. The applicable prospectus supplement will describe the particular terms of the debt securities offered thereby. You should read any prospectus supplement and any free writing prospectus that we may authorize to be provided to you related to the series of debt securities being offered, as well as the complete note agreements and/or indentures that contain the terms of the debt securities. Forms of indentures have been filed as exhibits to the registration statement of which this prospectus is a part, and supplemental indentures and forms of debt securities containing the terms of debt securities we offer under this prospectus will be filed as exhibits to the registration statement of which this prospectus is a part, or will be incorporated by reference from another report that we file with the SEC.

Warrants

We may offer warrants for the purchase of shares of our common stock or preferred stock or of debt securities. We may issue the warrants by themselves or together with common stock, preferred stock or debt securities, and the warrants may be attached to or separate from any offered securities. Each series of warrants will be issued under a separate warrant agreement to be entered into between us and the investors or a warrant agent. Our board of directors will determine the terms of the warrants. This prospectus contains only general terms and provisions of the warrants. The applicable prospectus supplement will describe the particular terms of the warrants being offered thereby. You should read any prospectus supplement and any free writing prospectus that we may authorize to be provided to you related to the series of warrants being offered, as well as the complete warrant agreements that contain the terms of the warrants. Specific warrant agreements will contain additional important terms and provisions and we will file as an exhibit to the registration statement of which this prospectus is a part, or will incorporate by reference from another report that we file with the SEC, the form of each warrant agreement relating to warrants offered under this prospectus.

Table of Contents

Units

We may offer units consisting of our common stock or preferred stock, debt securities and/or warrants to purchase any of these securities in one or more series. We may evidence each series of units by unit certificates that we will issue under a separate agreement. We may enter into unit agreements with a unit agent. Each unit agent will be a bank or trust company that we select. We will indicate the name and address of the unit agent in the applicable prospectus supplement relating to a particular series of units. This prospectus contains only a summary of certain general features of the units. The applicable prospectus supplement will describe the particular features of the units being offered thereby. You should read any prospectus supplement and any free writing prospectus that we may authorize to be provided to you related to the series of units being offered, as well as the complete unit agreements that contain the terms of the units. Specific unit agreements will contain additional important terms and provisions and we will file as an exhibit to the registration statement of which this prospectus is a part, or will incorporate by reference from another report that we file with the SEC, the form of each unit agreement relating to units offered under this prospectus.

Table of Contents

RISK FACTORS

Investing in our securities involves a high degree of risk. You should carefully consider the risk factors set forth under **Risk Factors** in Item 1A of our annual report on Form 10-K for the year ended December 31, 2011, which is incorporated by reference in this prospectus, together with all other information contained or incorporated by reference in this prospectus, as may be updated by our subsequent filings under the Exchange Act and the risk factors and other information contained in any applicable prospectus supplement and in any related free writing prospectus in connection with a specific offering, before deciding whether to purchase any of the securities being registered pursuant to the registration statement of which this prospectus is a part. Each of the risk factors could adversely affect our business, operating results and financial condition, as well as adversely affect the value of an investment in our securities, and the occurrence of any of these risks might cause you to lose all or part of your investment.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus and the other materials we have filed or will file with the SEC that are incorporated by reference herein contain forward-looking statements within the meaning of Section 27A of the Securities Act and Section 21E of the Exchange Act. All statements, other than statements of historical fact, are statements that could be deemed forward-looking statements, including, but not limited to, statements regarding our business strategy, expectations and plans, our objectives for future operations and our future financial position. When used in this prospectus or in the other materials we have filed or will file with the SEC, the words *believe*, *may*, *could*, *will*, *estimate*, *continue*, *anticipate*, *intend*, *indicate*, *seek*, *should* or *would* and similar expressions are intended to identify forward-looking statements. Among the factors that could cause or contribute to material differences between our actual results and those indicated from the forward-looking statements are risks and uncertainties inherent in our business, including, but not limited to:

our ability, or that of a future partner, to successfully develop and obtain regulatory approval for, and then successfully commercialize our product candidates in the U.S. and/or elsewhere;

our ability to obtain additional funding to develop our product candidates on a timely basis or on acceptable terms, or at all;

the potential for us to delay, reduce or discontinue current and/or planned development activities, partner our product candidates at inopportune times or pursue less expensive but higher-risk development paths if we are unable to raise sufficient additional capital as needed;

delays in the commencement or completion of a clinical study or manufacturing and regulatory activities related to our product candidates;

suspension or termination of a clinical study;

the ability of our product candidates to demonstrate acceptable safety and efficacy in clinical studies;

our ability to maintain our relationships with the single-source third-party manufacturers and suppliers for our product candidates and certain of their component materials and the ability of such manufacturers and suppliers to successfully and consistently meet our manufacturing and supply requirements;

the satisfactory performance of third parties, including contract research organizations, on whom we rely significantly to conduct our nonclinical testing, clinical studies and other aspects of our development programs;

the extent of market acceptance of any of our product candidates for which we receive regulatory approval;

Table of Contents

the extent to which we acquire new technologies and/or product candidates and our ability to integrate them successfully into our operations;

the potential that we may enter into one or more commercial partnerships or other strategic transactions relating to our product candidates, and the terms of any such transactions;

the extent to which we increase our workforce and our ability to attract and retain qualified personnel and manage growth;

competition in the marketplace for our products, if any are approved;

our ability to protect our intellectual rights with respect to our product candidates and proprietary technology;

claims against us for infringing the proprietary rights of third parties;

healthcare reform measures and reimbursement policies that, if not favorable to our products, could hinder or prevent our products' commercial success;

undesirable side effects that our product candidates may cause;

potential product liability exposure and, if successful claims are brought against us, liability for a product or product candidate; and

our ability to maintain compliance with NYSE Amex continued listing standards and maintain the listing of our common stock on the NYSE Amex or another national securities exchange.

Additional factors that could cause or contribute to such differences include, but are not limited to, those discussed in this prospectus, and in particular, the risks discussed under the heading "Risk Factors" in this prospectus and those discussed in other documents we file with the SEC and incorporate herein. Except as required by law, we do not intend to update these forward-looking statements publicly or to update the reasons actual results could differ materially from those anticipated in these forward-looking statements, even if new information becomes available in the future. In light of these risks, uncertainties and assumptions, the forward-looking events and circumstances discussed in this prospectus and in the documents incorporated in this prospectus may not occur and actual results could differ materially and adversely from those anticipated or implied in the forward-looking statements. Accordingly, readers are cautioned not to place undue reliance on such forward-looking statements.

Table of Contents**RATIO OF EARNINGS TO FIXED CHARGES**

The following table sets forth, for the periods presented, our ratio of earnings to fixed charges and our ratio of earnings to combined fixed charges and preferred stock dividends. For purposes of computing the ratio of earnings to fixed charges and the ratio of earnings to combined fixed charges and preferred stock dividends, earnings consist of net loss plus fixed charges. Fixed charges consist of interest expense and an estimate of the interest component of rent expense. In each of the periods presented, earnings were insufficient to cover fixed charges and combined fixed charges and deemed dividends on preferred stock and the extent of such deficiencies in each period is shown below.

	Year Ended December 31,				
	2011	2010	2009	2008	2007
Ratio of earnings to fixed charges	\$	\$	\$	\$	\$
Deficiency of earnings available to cover fixed charges	\$ (13,259,931)	\$ (8,450,922)	\$ (11,325,058)	\$ (26,647,493)	\$ (22,142,040)
Ratio of earnings to combined fixed charges and preferred stock dividends	\$	\$	\$	\$	\$
Deficiency of earnings available to cover combined fixed charges and preferred stock dividends	\$ (13,259,931)	\$ (14,090,718)	\$ (16,191,945)	\$ (26,647,493)	\$ (22,142,040)

USE OF PROCEEDS

Except as described in any prospectus supplement and any free writing prospectus in connection with a specific offering, we currently intend to use the net proceeds from the sale of the securities offered under this prospectus to fund continued development of our product candidates, including clinical studies, nonclinical testing and research-related manufacturing activities, to pursue regulatory approval for our product candidates and, potentially, to commercialize product candidates that receive regulatory approval, and for general corporate purposes, including working capital. We may also use a portion of the net proceeds to acquire or invest in technologies, product candidates, products and/or businesses that we believe will enhance the value of our company, although we have no current commitments or agreements with respect to any such transactions as of the date of this prospectus. We have not determined the amount of net proceeds to be used specifically for the foregoing purposes. As a result, our management will have broad discretion in the allocation of the net proceeds and investors will be relying on the judgment of our management regarding the application of the proceeds of any sale of the securities. Pending use of the net proceeds, we intend to invest the proceeds in short-term, investment-grade, interest-bearing instruments.

Each time we offer securities under this prospectus, we will describe the intended use of the net proceeds from that offering in the applicable prospectus supplement. The actual amount of net proceeds we spend on a particular use will depend on many factors, including, our future capital expenditures, the amount of cash required by our operations, and our future revenue growth, if any. Therefore, we will retain broad discretion in the use of the net proceeds.

Table of Contents

SECURITIES WE MAY OFFER

We may offer shares of common stock, shares of preferred stock, debt securities or warrants to purchase common stock, preferred stock or debt securities, or any combination of the foregoing, either individually or as units comprised of one or more of the other securities. We may offer up to \$150,000,000 of securities under this prospectus. If securities are offered as units, we will describe the terms of the units in a prospectus supplement.

DESCRIPTION OF COMMON STOCK AND PREFERRED STOCK

The following description of our common stock and preferred stock, together with any additional information we include in any applicable prospectus supplement or any related free writing prospectus, summarizes the material terms and provisions of our common stock and the preferred stock that we may offer under this prospectus. While the terms we have summarized below will apply generally to any future common stock or preferred stock that we may offer, we will describe the particular terms of any class or series of these securities in more detail in the applicable prospectus supplement. For the complete terms of our common stock and preferred stock, please refer to our certificate of incorporation and our amended and restated bylaws, or bylaws, that are incorporated by reference into the registration statement of which this prospectus is a part or may be incorporated by reference in this prospectus or any applicable prospectus supplement. The terms of these securities may also be affected by Delaware General Corporation Law. The summary below and that contained in any applicable prospectus supplement or any related free writing prospectus are qualified in their entirety by reference to our certificate of incorporation and bylaws, as in effect at the time of any offering of securities under this prospectus.

Common Stock

As of the date of this prospectus, our certificate of incorporation authorizes us to issue 500,000,000 shares of common stock, par value \$0.001 per share, of which 47,715,709 shares were issued and outstanding as of March 5, 2012. Additional shares of authorized common stock may be issued, as authorized by our board of directors from time to time, without stockholder approval, except as may be required by applicable securities exchange requirements. The holders of common stock possess exclusive voting rights in us, except to the extent our board of directors specifies voting power with respect to any other class of securities issued in the future. Each holder of our common stock is entitled to one vote for each share held of record on each matter submitted to a vote of stockholders, including the election of directors. Stockholders do not have any right to cumulate votes in the election of directors.

Subject to preferences that may be granted to the holders of preferred stock, each holder of our common stock is entitled to share ratably in distributions to stockholders and to receive ratably such dividends as may be declared by our board of directors out of funds legally available therefor. In the event of our liquidation, dissolution or winding up, the holders of our common stock will be entitled to receive, after payment of all of our debts and liabilities and of all sums to which holders of any preferred stock may be entitled, the distribution of any of our remaining assets. Holders of our common stock have no conversion, exchange, sinking fund, redemption or appraisal rights (other than such as may be determined by our board of directors in its sole discretion) and have no preemptive rights to subscribe for any of our securities.

All of the outstanding shares of our common stock are fully paid and non-assessable. The shares of common stock offered by this prospectus or upon the conversion of any preferred stock or debt securities or exercise of any warrants offered pursuant to this prospectus, when issued and paid for, will also be, fully paid and non-assessable.

Table of Contents

Securities Exchange Listing

Our common stock is listed on the NYSE Amex under the symbol ANX.

Transfer Agent and Registrar

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

Preferred Stock

As of the date of this prospectus, our certificate of incorporation authorizes us to issue 1,000,000 shares of preferred stock, par value \$0.001 per share, none of which are outstanding. Pursuant to our certificate of incorporation, our board of directors has the authority to provide for the issuance, in one or more series, of our authorized preferred stock and to fix or alter the rights, preferences, privileges and restrictions granted to or imposed upon any series of our preferred stock. The rights, privileges, preferences and restrictions of any such series of our preferred stock may be subordinated to, pari passu with (including, without limitation, inclusion in provisions with respect to liquidation and acquisition preferences, redemption or approval of matters by vote or written consent), or senior to any of those of any present or future class or series of preferred stock or common stock. Our board of directors is also expressly authorized to increase or decrease the number of shares of any series prior or subsequent to the issue of that series, but not below the number of shares of such series then outstanding. The issuance of preferred stock may have the effect of decreasing the market price of our common stock and may adversely affect the voting power of holders of our common stock and reduce the likelihood that holders of our common stock will receive dividend payments and payments upon liquidation.

The particular terms of each class or series of preferred stock that we may offer under this prospectus, including redemption privileges, liquidation preferences, voting rights, dividend rights and/or conversion rights, will be more fully described in the applicable prospectus supplement relating to the preferred stock offered thereby.

The rights, preferences, privileges and restrictions of any series of preferred stock we may offer under this prospectus will be set forth in the certificate of designation relating to that series of preferred stock. We will file as an exhibit to the registration statement of which this prospectus is a part, or will incorporate by reference from another report we file with the SEC, the form of any certificate of designation that describes the terms of the series of preferred stock we may offer before the issuance of the related series of preferred stock. The applicable prospectus supplement will specify the particular terms of any series of preferred stock we may offer, including, but not limited to:

the distinctive designation and the maximum number of shares in the series;

the number of shares we are offering and purchase price per share;

the liquidation preference, if any;

the terms on which dividends, if any, will be paid;

the voting rights, if any, on the shares of the series;

the terms and conditions, if any, on which the shares of the series shall be convertible into, or exchangeable for, shares of any other class or classes of capital stock;

the terms on which the shares may be redeemed, if at all;

any listing of the preferred stock on any securities exchange or market;

a discussion of any material or special United States federal income tax considerations applicable to the preferred stock; and

Table of Contents

any or all other preferences, rights, restrictions, including restrictions on transferability, and qualifications of shares of the series.

The description of preferred stock above and the description of the terms of a particular series of preferred stock in any applicable prospectus supplement are not complete. You should refer to any applicable certificate of designation for complete information.

The General Corporate Law of the State of Delaware, the state of our incorporation, provides that the holders of preferred stock will have the right to vote separately as a class on any proposal involving fundamental changes in the rights of holders of that preferred stock. This right is in addition to any voting rights that may be provided for in the applicable certificate of designation.

Anti-Takeover Effects of Provisions of our Charter Documents and Delaware Law

Provisions of Delaware General Corporation Law, or the DGCL, and our certificate of incorporation and bylaws could make it more difficult to acquire us by means of a tender offer, a proxy contest or otherwise, or to remove incumbent officers and directors. These provisions, summarized below, are expected to discourage certain types of coercive takeover practices and takeover bids that our board of directors may consider inadequate and to encourage persons seeking to acquire control of us to first negotiate with our board of directors. We believe that the benefits of increased protection of our ability to negotiate with the proponent of an unfriendly or unsolicited proposal to acquire or restructure us outweigh the disadvantages of discouraging takeover or acquisition proposals because, among other things, negotiation of these proposals could result in an improvement of their terms. This summary does not purport to be complete and is qualified in its entirety by reference to the corporate law of Delaware and our certificate of incorporation and bylaws.

Certificate of Incorporation and Bylaws

Preferred Stock. Under our certificate of incorporation, our board of directors has the power to authorize the issuance of up to 1,000,000 shares of preferred stock, all of which are currently undesignated, and to determine the price, rights, preferences, privileges and restrictions, including voting rights, of those shares without further vote or action by our stockholders. The issuance of preferred stock may:

delay, defer or prevent a change in control;

discourage bids for our common stock at a premium over the market price of our common stock;

adversely affect the voting and other rights of the holders of our common stock; and

discourage acquisition proposals or tender offers for our shares and, as a consequence, inhibit fluctuations in the market price of our shares that could result from actual or rumored takeover attempts.

Advance Notice Requirement. Stockholder nominations of individuals for election to our board of directors and stockholder proposals of other matters to be brought before an annual meeting of our stockholders must comply with the advance notice procedures set forth in our bylaws. Generally, to be timely, such notice must be received at our principal executive offices no later than the date specified in our proxy statement released to stockholders in connection with the preceding year's annual meeting of stockholders, which date shall be not earlier than the 120th day, nor later than the close of business on the 90th day, prior to the first anniversary of the date of the preceding year's annual meeting of stockholders.

Special Meeting Requirements. Our bylaws provide that special meetings of our stockholders may be called only at the request of our board of directors, president (unless there is a chief executive officer who is not the president, in which case a special meeting may be called at any time by the chief executive officer and not the president) or chair of the board of directors. Only such business shall be considered at a special meeting as shall have been stated in the notice for such meeting.

Table of Contents

No Cumulative Voting. Our certificate of incorporation does not include a provision for cumulative voting for directors.

Indemnification. Our certificate of incorporation and bylaws provide that we will indemnify our officers and directors against losses as they incur in investigations and legal proceedings resulting from their services to us, which may include service in connection with takeover defense measures.

Removal of Directors. Our bylaws provide that the affirmative vote of the holders of at least 75% of our voting stock then outstanding is required to remove our directors, either with or without cause.

Authorized but Unissued Shares. Our authorized but unissued shares of common stock and preferred stock will be available for future issuance without stockholder approval. We may use additional shares for a variety of purposes, including future public offerings to raise additional capital, to fund acquisitions and as employee compensation. The existence of authorized but unissued shares of common stock and preferred stock could render more difficult or discourage an attempt to obtain control of us by means of a proxy contest, tender offer, merger or otherwise.

Delaware Anti-Takeover Statute.

We are subject to Section 203 of the DGCL, an anti-takeover law. In general, Section 203 prohibits, with some exceptions, a publicly held Delaware corporation from engaging in a business combination with any interested stockholder for a period of three years following the date that stockholder became an interested stockholder, unless:

prior to that date, the board of directors of the corporation approved either the business combination or the transaction that resulted in the stockholder becoming an interested stockholder;

upon consummation of the transaction that 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 number of shares of voting stock outstanding (but not the voting stock owned by the interested stockholder) those shares owned by persons who are directors and officers and by excluding employee stock plans in which employee participants do not have the right to determine whether shares held subject to the plan will be tendered in a tender or exchange offer; or

on or subsequent to that date, the business combination is approved by the board of directors of the corporation and authorized at an annual or special meeting of stockholders, and not by written consent, by the affirmative vote of at least 66-2/3% of the outstanding voting stock that is not owned by the interested stockholder.

Section 203 defines business combination to include any of the following:

any merger or consolidation involving the corporation and the interested stockholder;

any sale, transfer, pledge or other disposition of 10% or more of the assets of the corporation involving the interested stockholder;

subject to certain exceptions, any transaction that results in the issuance or transfer by the corporation of any stock of the corporation to the interested stockholder;

any transaction involving the corporation that has the effect of increasing the proportionate share of the stock of any class or series of the corporation beneficially owned by the interested stockholder; or

the receipt by the interested stockholder of the benefit of any loans, advances, guarantees, pledges or other financial benefits provided by or through the corporation.

Table of Contents

In general, Section 203 defines an interested stockholder as any person who, together with the person's affiliates and associates, beneficially owns, or within three years prior to the determination of interested stockholder status did beneficially own, 15% or more of the outstanding voting stock of the corporation.

The above provisions may deter a hostile takeover or delay a change in control of management or us.

DESCRIPTION OF DEBT SECURITIES

General

The debt securities that we may issue may constitute debentures, notes, bonds or other evidences of indebtedness of our company, to be issued in one or more series, which may include senior debt securities, subordinated debt securities and senior subordinated debt securities. The particular terms of any series of debt securities we may offer, including the extent to which the general terms set forth below may be applicable to a particular series, will be described in a prospectus supplement relating to such series.

Debt securities that we may issue may be issued under a senior indenture between us and a trustee, or a subordinated indenture between us and a trustee (collectively, the indentures). We have filed forms of the indentures as exhibits to the registration statement of which this prospectus is a part. Supplemental indentures and forms of debt securities containing the terms of the debt securities being offered will be filed as exhibits to the registration statement of which this prospectus is a part or will be incorporated by reference from reports that we file with the SEC.

THE FOLLOWING DESCRIPTION IS A SUMMARY OF THE MATERIAL PROVISIONS OF THE INDENTURES. IT DOES NOT RESTATE THE INDENTURES IN THEIR ENTIRETY. THE INDENTURES ARE GOVERNED BY THE TRUST INDENTURE ACT OF 1939. THE TERMS OF THE DEBT SECURITIES INCLUDE THOSE STATED IN THE INDENTURES AND THOSE MADE PART OF THE INDENTURES BY REFERENCE TO THE TRUST INDENTURE ACT. WE URGE YOU TO READ THE INDENTURES BECAUSE THEY, AND NOT THIS DESCRIPTION, DEFINE YOUR RIGHTS AS A HOLDER OF THE DEBT SECURITIES. EXCEPT AS WE MAY OTHERWISE INDICATE, THE TERMS OF THE SENIOR INDENTURE AND THE SUBORDINATED INDENTURE ARE IDENTICAL.

The indentures contain no covenant or provision which affords debt holders protection in the event of a highly leveraged transaction.

Information You Will Find in the Prospectus Supplement

The indentures provide that we may issue debt securities from time to time in one or more series by resolution of our board of directors or by means of a supplemental indenture, and that we may denominate the debt securities and make them payable in foreign currencies. The indentures do not limit the aggregate principal amount of debt securities that can be issued thereunder. We may specify a maximum aggregate principal amount for the debt securities of any series. We will describe in the applicable prospectus supplement the terms of the series of debt securities being offered, including:

the title;

the principal amount being offered, and if a series, the total amount authorized and the total amount outstanding;

any limit on the amount that may be issued;

whether or not we will issue the series of debt securities in global form, and, if so, the terms and who the depository will be;

Table of Contents

the maturity date;

whether and under what circumstances, if any, we will pay additional amounts on any debt securities held by a person who is not a United States person for tax purposes, and whether we can redeem the debt securities if we have to pay such additional amounts;

the annual interest rate, which may be fixed or variable, or the method for determining the rate and the date interest will begin to accrue, the dates interest will be payable and the regular record dates for interest payment dates or the method for determining such dates;

whether or not the debt securities will be secured or unsecured, and the terms of any secured debt;

the terms of the subordination of any series of subordinated debt;

the place where payments will be payable;

restrictions on transfer, sale or other assignment, if any;

our right, if any, to defer payment of interest and the maximum length of any such deferral period;

the date, if any, after which, and the price at which, we may, at our option, redeem the series of debt securities pursuant to any optional or provisional redemption provisions and the terms of those redemption provisions;

the date, if any, on which, and the price at which we are obligated, pursuant to any mandatory sinking fund or analogous fund provisions or otherwise, to redeem, or at the holder's option, to purchase, the series of debt securities and the currency or currency unit in which the debt securities are payable;

whether the indenture will restrict our ability or the ability of our subsidiaries to:

incur additional indebtedness;

issue additional securities;

create liens;

pay dividends or make distributions in respect of our capital stock or the capital stock of our subsidiaries, or redeem capital stock;

Edgar Filing: Mast Therapeutics, Inc. - Form 424B5

place restrictions on our subsidiaries ability to pay dividends, make distributions or transfer assets;

make investments or other restricted payments;

sell or otherwise dispose of assets;

enter into sale-leaseback transactions;

engage in transactions with stockholders or affiliates;

issue or sell stock of our subsidiaries;

effect a consolidation or merger;

whether the indenture will require us to maintain any interest coverage, fixed charge, cash flow-based, asset-based or other financial ratios;

a discussion of certain material or special United States federal income tax considerations applicable to the debt securities;

information describing any book-entry features;

provisions for a sinking fund purchase or other analogous fund, if any;

Table of Contents

the applicability of the provisions in the indenture on discharge;

whether the debt securities are to be offered at a price such that they will be deemed to be offered at an original issue discount as defined in paragraph (a) of Section 1273 of the Internal Revenue Code of 1986, as amended;

the denominations in which we will issue the series of debt securities, if other than denominations of \$1,000 and any integral multiple thereof;

the currency of payment of debt securities if other than U.S. dollars and the manner of determining the equivalent amount in U.S. dollars; and

any other specific terms, preferences, rights or limitations of, or restrictions on, the debt securities, including any additional events of default or covenants provided with respect to the debt securities, and any terms that may be required by us or advisable under applicable laws or regulations.

Conversion or Exchange Rights

We will set forth in the applicable prospectus supplement the terms on which a series of debt securities may be convertible into or exchangeable for our common stock, our preferred stock or other securities (including securities of a third-party). We will include provisions as to whether conversion or exchange is mandatory, at the option of the holder or at our option. We may include provisions pursuant to which the number of shares of our common stock, our preferred stock or other securities (including securities of a third-party) that the holders of the series of debt securities receive would be subject to adjustment.

Consolidation, Merger or Sale

Unless we provide otherwise in the prospectus supplement applicable to a particular series of debt securities, the indentures will not contain any covenant that restricts our ability to merge or consolidate, or sell, convey, transfer or otherwise dispose of all or substantially all of our assets. However, any successor to or acquirer of such assets must assume all of our obligations under the indentures or the debt securities, as appropriate. If the debt securities are convertible into or exchangeable for our other securities or securities of other entities, the person with whom we consolidate or merge or to whom we sell all of our property must make provisions for the conversion of the debt securities into securities that the holders of the debt securities would have received if they had converted the debt securities before the consolidation, merger or sale.

Events of Default under the Indentures

Unless otherwise indicated in the applicable prospectus supplement, the following will be events of default under the indentures with respect to each series of debt securities issued under the indenture:

if we fail to pay interest when due and payable and our failure continues for 90 days and the time for payment has not been extended;

if we fail to pay the principal, premium or sinking fund payment, if any, when due and payable at maturity, upon redemption or repurchase or otherwise, and the time for payment has not been extended;

if we fail to observe or perform any other covenant contained in the debt securities or the indentures, other than a covenant specifically relating to another series of debt securities, and our failure continues for 90 days after we receive notice from the trustee or we and the trustee receive notice from the holders of at least 25% in aggregate principal amount of the outstanding

debt securities of the applicable series; and

if specified events of bankruptcy, insolvency or reorganization occur.

Table of Contents

We will describe in each applicable prospectus supplement any additional events of default relating to the relevant series of debt securities.

If an event of default with respect to debt securities of any series occurs and is continuing, other than an event of default specified in the last bullet point above, the trustee or the holders of at least 25% in aggregate principal amount of the outstanding debt securities of that series, by notice to us in writing, and to the trustee if notice is given by such holders, may declare the unpaid principal, premium, if any, and accrued interest, if any, due and payable immediately. If an event of default specified in the last bullet point above occurs with respect to us, the unpaid principal, premium, if any, and accrued interest, if any, of each issue of debt securities then outstanding shall be due and payable without any notice or other action on the part of the trustee or any holder.

The holders of a majority in principal amount of the outstanding debt securities of an affected series may waive any default or event of default with respect to the series and its consequences, except defaults or events of default regarding payment of principal, premium, if any, or interest, unless we have cured the default or event of default in accordance with the indenture. Any waiver shall cure the default or event of default.

Subject to the terms of the indentures, if an event of default under an indenture shall occur and be continuing, the trustee will be under no obligation to exercise any of its rights or powers under such indenture at the request or direction of any of the holders of the applicable series of debt securities, unless such holders have offered the trustee reasonable indemnity or security satisfactory to it against any loss, liability or expense. The holders of a majority in principal amount of the outstanding debt securities of any series will have the right to direct the time, method and place of conducting any proceeding for any remedy available to the trustee, or exercising any trust or power conferred on the trustee, with respect to the debt securities of that series, provided that:

the direction so given by the holder is not in conflict with any law or the applicable indenture; and

subject to its duties under the Trust Indenture Act, the trustee need not take any action that might involve it in personal liability or might be unduly prejudicial to the holders not involved in the proceeding.

The indentures provide that if an event of default has occurred and is continuing, the trustee will be required in the exercise of its powers to use the degree of care that a prudent person would use in the conduct of its own affairs. The trustee, however, may refuse to follow any direction that conflicts with law or the indenture, or that the trustee determines is unduly prejudicial to the rights of any other holder of the relevant series of debt securities, or that would involve the trustee in personal liability. Prior to taking any action under the indentures, the trustee will be entitled to indemnification against all costs, expenses and liabilities that would be incurred by taking or not taking such action.

A holder of the debt securities of any series will have the right to institute a proceeding under the indentures or to appoint a receiver or trustee, or to seek other remedies only if:

the holder has given written notice to the trustee of a continuing event of default with respect to that series;

the holders of at least 25% in aggregate principal amount of the outstanding debt securities of that series have made written request, and such holders have offered reasonable indemnity to the trustee or security satisfactory to it against any loss, liability or expense or to be incurred in compliance with instituting the proceeding as trustee; and

the trustee does not institute the proceeding, and does not receive from the holders of a majority in aggregate principal amount of the outstanding debt securities of that series other conflicting directions within 90 days after the notice, request and offer.

Table of Contents

These limitations do not apply to a suit instituted by a holder of debt securities if we default in the payment of the principal, premium, if any, or interest on, the debt securities, or other defaults that may be specified in the applicable prospectus supplement.

We will periodically file statements with the trustee regarding our compliance with specified covenants in the indentures.

The indentures provide that if a default occurs and is continuing and is actually known to a responsible officer of the trustee, the trustee must mail to each holder notice of the default within the earlier of 90 days after it occurs and 30 days after it is known by a responsible officer of the trustee or written notice of it is received by the trustee, unless such default has been cured or waived. Except in the case of a default in the payment of principal or premium of or interest on any debt security or certain other defaults specified in an indenture, the trustee shall be protected in withholding such notice if and so long as the board of directors, the executive committee or a trust committee of directors, or responsible officers of the trustee, in good faith determine that withholding notice is in the best interests of holders of the relevant series of debt securities.

Modification of Indenture; Waiver

Subject to the terms of the indenture for any series of debt securities that we may issue, we and the trustee may change an indenture without the consent of any holders with respect to the following specific matters:

to fix any ambiguity, defect or inconsistency in the indenture;

to comply with the provisions described above under **Description of Debt Securities – Consolidation, Merger or Sale** ;

to comply with any requirements of the SEC in connection with the qualification of any indenture under the Trust Indenture Act;

to add to, delete from or revise the conditions, limitations, and restrictions on the authorized amount, terms, or purposes of issue, authentication and delivery of debt securities, as set forth in the indenture;

to provide for the issuance of and establish the form and terms and conditions of the debt securities of any series as provided under **Description of Debt Securities – General**, to establish the form of any certifications required to be furnished pursuant to the terms of the indenture or any series of debt securities, or to add to the rights of the holders of any series of debt securities;

to evidence and provide for the acceptance of appointment hereunder by a successor trustee;

to provide for uncertificated debt securities and to make all appropriate changes for such purpose;

to add to our covenants such new covenants, restrictions, conditions or provisions for the benefit of the holders, to make the occurrence, or the occurrence and the continuance, of a default in any such additional covenants, restrictions, conditions or provisions an event of default or to surrender any right or power conferred to us in the indenture; or

to change anything that does not adversely affect the interests of any holder of debt securities of any series in any material respect.

Edgar Filing: Mast Therapeutics, Inc. - Form 424B5

In addition, under the indentures, the rights of holders of a series of debt securities may be changed by us and the trustee with the written consent of the holders of at least a majority in aggregate principal amount of the outstanding debt securities of each series that is affected. However, subject to the terms of the indenture for any series of debt securities that we may issue or otherwise provided in the prospectus supplement applicable to a particular series of debt securities, we and the trustee may only make the following changes with the consent of each holder of any outstanding debt securities affected:

Table of Contents

extending the stated maturity of the series of debt securities;

reducing the principal amount, reducing the rate of or extending the time of payment of interest, or reducing any premium payable upon the redemption or repurchase of any debt securities; or

reducing the percentage of debt securities, the holders of which are required to consent to any amendment, supplement, modification or waiver.

Discharge

Each indenture provides that, subject to the terms of the indenture and any limitation otherwise provided in the prospectus supplement applicable to a particular series of debt securities, we can elect to be discharged from our obligations with respect to one or more series of debt securities, except for specified obligations, including obligations to:

register the transfer or exchange of debt securities of the series;

replace stolen, lost or mutilated debt securities of the series;

maintain paying agencies;

hold monies for payment in trust;

recover excess money held by the trustee;

compensate and indemnify the trustee; and

appoint any successor trustee.

In order to exercise our rights to be discharged, we must deposit with the trustee money or government obligations sufficient to pay all the principal of, any premium and interest on, the debt securities of the series on the dates payments are due.

Form, Exchange and Transfer

We will issue the debt securities of each series only in fully registered form without coupons and, unless we otherwise specify in the applicable prospectus supplement, in denominations of \$1,000 and any integral multiple thereof. The indentures provide that we may issue debt securities of a series in temporary or permanent global form and as book-entry securities that will be deposited with, or on behalf of, The Depository Trust Company or another depository named by us and identified in a prospectus supplement with respect to that series. See **Legal Ownership of Securities** below for a further description of the terms relating to any book-entry securities.

At the option of the holder, subject to the terms of the indentures and the limitations applicable to global securities described in the applicable prospectus supplement, the holder of the debt securities of any series can exchange the debt securities for other debt securities of the same series, in any authorized denomination and of like tenor and aggregate principal amount.

Subject to the terms of the indentures and the limitations applicable to global securities set forth in the applicable prospectus supplement, holders of the debt securities may present the debt securities for exchange or for registration of transfer, duly endorsed or with the form of transfer

Edgar Filing: Mast Therapeutics, Inc. - Form 424B5

endorsed thereon duly executed if so required by us or the security registrar, at the office of the security registrar or at the office of any transfer agent designated by us for this purpose. Unless otherwise provided in the debt securities that the holder presents for transfer or exchange, we will make no service charge for any registration of transfer or exchange, but we may require payment of any taxes or other governmental charges.

Table of Contents

We will name in the applicable prospectus supplement the security registrar, and any transfer agent in addition to the security registrar, that we initially designate for any debt securities. We may at any time designate additional transfer agents or rescind the designation of any transfer agent or approve a change in the office through which any transfer agent acts, except that we will be required to maintain a transfer agent in each place of payment for the debt securities of each series.

If we elect to redeem the debt securities of any series, we will not be required to:

issue, register the transfer of, or exchange any debt securities of that series during a period beginning at the opening of business 15 days before the day of mailing of a notice of redemption of any debt securities that may be selected for redemption and ending at the close of business on the day of the mailing; or

register the transfer of or exchange any debt securities so selected for redemption, in whole or in part, except the unredeemed portion of any debt securities we are redeeming in part.

Information Concerning the Trustee

The trustee, other than during the occurrence and continuance of an event of default under an indenture, undertakes to perform only those duties as are specifically set forth in the applicable indenture and is under no obligation to exercise any of the powers given it by the indentures at the request of any holder of debt securities unless it is offered reasonable security and indemnity against the costs, expenses and liabilities that it might incur. However, upon an event of default under an indenture, the trustee must use the same degree of care as a prudent person would exercise or use in the conduct of his or her own affairs.

Payment and Paying Agents

Unless we otherwise indicate in the applicable prospectus supplement, we will make payment of the interest on any debt securities on any interest payment date to the person in whose name the debt securities, or one or more predecessor securities, are registered at the close of business on the regular record date for the interest.

We will pay principal of and any premium and interest on the debt securities of a particular series at the office of the paying agents designated by us, except that unless we otherwise indicate in the applicable prospectus supplement, we will make interest payments by check that we will mail to the holder or by wire transfer to certain holders. Unless we otherwise indicate in the applicable prospectus supplement, we will designate the corporate trust office of the trustee as our sole paying agent for payments with respect to debt securities of each series. We will name in the applicable prospectus supplement any other paying agents that we initially designate for the debt securities of a particular series. We will maintain a paying agent in each place of payment for the debt securities of a particular series.

All money we pay to a paying agent or the trustee for the payment of the principal of or any premium or interest on any debt securities that remains unclaimed at the end of two years after such principal, premium or interest has become due and payable will be repaid to us, and the holder of the debt security thereafter may look only to us for payment thereof.

Governing Law

The indentures and the debt securities will be governed by and construed in accordance with the laws of the State of New York, except to the extent that the Trust Indenture Act is applicable.

Table of Contents

Ranking Debt Securities

The subordinated debt securities will be unsecured and will be subordinate and junior in priority of payment to certain other indebtedness to the extent described in a prospectus supplement. The subordinated indenture does not limit the amount of subordinated debt securities that we may issue. It also does not limit us from issuing any other secured or unsecured debt.

The senior debt securities will be unsecured and will rank equally in right of payment to all our other senior unsecured debt. The senior indenture does not limit the amount of senior debt securities that we may issue. It also does not limit us from issuing any other secured or unsecured debt.

Existing Debt

As of March 8, 2012 the Company had no existing subordinated debt and no secured debt.

DESCRIPTION OF WARRANTS

We may issue warrants for the purchase of common stock, preferred stock or debt securities. Warrants may be offered independently or together with common stock, preferred stock or debt securities offered by any prospectus supplement and may be attached to or separate from those securities. While the terms we have summarized below will apply generally to any warrants that we may offer under this prospectus, we will describe in particular the terms of any series of warrants that we may offer in more detail in the applicable prospectus supplement and any related free writing prospectus. The terms of any warrants offered under a prospectus supplement may differ from the terms described below.

We will file as an exhibit to the registration statement of which this prospectus is a part, or will incorporate by reference from another report that we file with the SEC, the form of warrant agreement, which may include a form of warrant certificate, that describes the terms of the of the particular series of warrants we may offer before the issuance of the related series of warrants. We may issue the warrants under a warrant agreement that we will enter into with a warrant agent to be selected by us. The warrant agent will act solely as our agent in connection with the warrants and will not assume any obligation or relationship of agency or trust for or with any registered holders of warrants or beneficial owners of warrants. The following summary of material provisions of the warrants and warrant agreements are subject to, and qualified in their entirety by reference to, all the provisions of the warrant agreement and warrant certificate applicable to a particular series of warrants. We urge you to read the applicable prospectus supplement and any related free writing prospectus, as well as the complete warrant agreements and warrant certificates that contain the terms of the warrants.

The particular terms of any issue of warrants will be described in the prospectus supplement relating to the issue. Those terms may include:

the title of such warrants;

the aggregate number of such warrants;

the price or prices at which such warrants will be issued;

the currency or currencies (including composite currencies) in which the price of such warrants may be payable;

the terms of the securities purchasable upon exercise of such warrants and the procedures and conditions relating to the exercise of such warrants;

the price at which the securities purchasable upon exercise of such warrants may be purchased;

Table of Contents

the date on which the right to exercise such warrants will commence and the date on which such right shall expire;

any provisions for adjustment of the number or amount of securities receivable upon exercise of the warrants or the exercise price of the warrants;

if applicable, the minimum or maximum amount of such warrants that may be exercised at any one time;

if applicable, the designation and terms of the securities with which such warrants are issued and the number of such warrants issued with each such security;

if applicable, the date on and after which such warrants and the related securities will be separately transferable;

information with respect to book-entry procedures, if any;

the terms of any rights to redeem or call the warrants;

United States federal income tax consequences of holding or exercising the warrants, if material; and

any other terms of such warrants, including terms, procedures and limitations relating to the exchange or exercise of such warrants.

Each warrant will entitle its holder to purchase the principal amount of debt securities or the number of shares of preferred stock or common stock at the exercise price set forth in, or calculable as set forth in, the applicable prospectus supplement. Unless we otherwise specify in the applicable prospectus supplement, holders of the warrants may exercise the warrants at any time up to the specified time on the expiration date that we set forth in the applicable prospectus supplement. After the close of business on the expiration date, unexercised warrants will become void.

We will specify the place or places where, and the manner in which, warrants may be exercised in the warrant agreement or warrant certificate and applicable prospectus supplement. Upon receipt of payment and the warrant certificate properly completed and duly executed at the corporate trust office of the warrant agent or any other office indicated in the applicable prospectus supplement, we will, as soon as practicable, issue and deliver the purchased securities. If less than all of the warrants represented by the warrant certificate are exercised, a new warrant certificate will be issued for the remaining amount of warrants. If we so indicate in the applicable prospectus supplement, holders of the warrants may surrender securities as all or part of the exercise price for warrants.

Prior to the exercise of any warrants to purchase common stock, preferred stock or debt securities, holders of the warrants will not have any of the rights of holders of the common stock, preferred stock or debt securities purchasable upon exercise, including (i) in the case of warrants for the purchase of common stock or preferred stock, the right to vote or to receive any payments of dividends or payments upon our liquidation, dissolution or winding up on the common stock or preferred stock purchasable upon exercise, if any; or (ii) in the case of warrants for the purchase of debt securities, the right to receive payments of principal of, any premium or interest on the debt securities purchasable upon exercise or to enforce covenants in the applicable indenture.

DESCRIPTION OF UNITS

The following description, together with the additional information we may include in any applicable prospectus supplement, summarizes the material terms and provisions of the units that we may offer under this prospectus. While the terms we have summarized below will apply generally to any units that we may offer under this prospectus, we will describe the particular terms of any series of units in more detail in the applicable

Table of Contents

prospectus supplement and any related free writing prospectus. The terms of any units offered under a prospectus supplement may differ from the terms described below. However, no prospectus supplement will fundamentally change the terms that are set forth in this prospectus or offer a security that is not registered and described in this prospectus at the time of its effectiveness.

We will file as an exhibit to the registration statement of which this prospectus is a part, or will incorporate by reference from another report we file with the SEC, the form of unit agreement that describes the terms of the series of units we offer under this prospectus, and any supplemental agreements, before the issuance of the related series of units. The following summaries of material terms and provisions of the units are subject to, and qualified in their entirety by reference to, all the provisions of the unit agreement and any supplemental agreements applicable to a particular series of units. We urge you to read the applicable prospectus supplement and any related free writing prospectus, as well as the complete unit agreement and any supplemental agreements that contain the terms of the units.

General

We may issue units comprised of one or more debt securities, shares of common stock, shares of preferred stock and warrants in any combination. Each unit 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.

We will describe in the applicable prospectus supplement the terms of the series of units, including, but not limited to:

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 that differ from those described below; and

any provisions for the issuance, payment, settlement, transfer or exchange of the units or of the securities comprising the units.

The provisions described in this section, as well as those described under [Description of Common Stock and Preferred Stock](#), [Description of Debt Securities](#) and [Description of Warrants](#) will apply to each unit and to any common stock, preferred stock, debt security or warrant included in each unit, respectively.

Issuance in Series

We may issue units in such amounts and in numerous distinct series as we determine.

Enforceability of Rights by Holders of Units

Each unit agent will act solely as our agent under the applicable unit agreement and will not assume any obligation or relationship of agency or trust with any holder of any unit. A single bank or trust company may act as unit agent for more than one series of units. A unit agent will have no duty or responsibility in case of any default by us under the applicable unit agreement or unit, including any duty or responsibility to initiate any proceedings at law or otherwise, or to make any demand upon us. Any holder of a unit may, without the consent of the related unit agent or the holder of any other unit, enforce by appropriate legal action its rights as holder under any security included in the unit.

We, the unit agents and any of their agents may treat the registered holder of any unit certificate as an absolute owner of the units evidenced by that certificate for any purpose and as the person entitled to exercise the rights attaching to the units so requested, despite any notice to the contrary.

Table of Contents

LEGAL OWNERSHIP OF SECURITIES

We can issue securities in registered form or in the form of one or more global securities. We describe global securities in greater detail below. We refer to those persons who have securities registered in their own names on the books that we or any applicable trustee or depository or warrant agent maintain for this purpose as the holders of those securities. These persons are the legal holders of the securities. We refer to those persons who, indirectly through others, own beneficial interests in securities that are not registered in their own names, as indirect holders of those securities. As we discuss below, indirect holders are not legal holders, and investors in securities issued in book-entry form or in street name will be indirect holders.

Book-Entry Holders

We may issue securities in book-entry form only, as we will specify in the applicable prospectus supplement. This means securities may be represented by one or more global securities registered in the name of a financial institution that holds them as depository on behalf of other financial institutions that participate in the depository's book-entry system. These participating institutions, which are referred to as participants, in turn, hold beneficial interests in the securities on behalf of themselves or their customers.

Only the person in whose name a security is registered is recognized as the holder of that security. Global securities will be registered in the name of the depository. Consequently, for global securities, we will recognize only the depository as the holder of the securities, and we will make all payments on the securities to the depository. The depository passes along the payments it receives to its participants, which in turn pass the payments along to their customers who are the beneficial owners. The depository and its participants do so under agreements they have made with one another or with their customers; they are not obligated to do so under the terms of the securities.

As a result, investors in a global security will not own securities directly. Instead, they will own beneficial interests in a global security, through a bank, broker or other financial institution that participates in the depository's book-entry system or holds an interest through a participant. As long as the securities are issued in global form, investors will be indirect holders, and not legal holders, of the securities.

Street Name Holders

We may terminate a global security or issue securities that are not issued in global form. In these cases, investors may choose to hold their securities in their own names or in street name. Securities held by an investor in street name would be registered in the name of a bank, broker or other financial institution that the investor chooses, and the investor would hold only a beneficial interest in those securities through an account he or she maintains at that institution.

For securities held in street name, we or any applicable trustee or depository will recognize only the intermediary banks, brokers and other financial institutions in whose names the securities are registered as the holders of those securities, and we or any such trustee or depository will make all payments on those securities to them. These institutions pass along the payments they receive to their customers who are the beneficial owners, but only because they agree to do so in their customer agreements or because they are legally required to do so. Investors who hold securities in street name will be indirect holders, not legal holders, of those securities.

Legal Holders

Our obligations, as well as the obligations of any applicable trustee or third party employed by us or a trustee, run only to the legal holders of the securities. We do not have obligations to investors who hold beneficial interests in global securities, in street name or by any other indirect means. This will be the case whether an investor chooses to be an indirect holder of a security or has no choice because we are issuing the securities only in global form.

Table of Contents

For example, once we make a payment or give a notice to the legal holder, we have no further responsibility for the payment or notice even if that holder is required, under agreements with its participants or customers or by law, to pass it along to the indirect holders but does not do so. Similarly, we may want to obtain the approval of the legal holders to amend an indenture, to relieve us of the consequences of a default or of our obligation to comply with a particular provision of an indenture, or for other purposes. In such an event, we would seek approval only from the legal holders, and not the indirect holders, of the securities. Whether and how the legal holders contact the indirect holders is up to the legal holders.

Special Considerations for Indirect Holders

If you hold securities through a bank, broker or other financial institution, either in book-entry form because the securities are represented by one or more global securities or in street name, you should check with your own institution to find out:

how it handles securities payments and notices;

whether it imposes fees or charges;

how it would handle a request for the legal holders' consent, if ever required;

whether and how you can instruct it to send you securities registered in your own name so you can be a legal holder, if that is permitted in the future;

how it would exercise rights under the securities if there were a default or other event triggering the need for legal holders to act to protect their interests; and

if the securities are in book-entry form, how the depository's rules and procedures will affect these matters.

Global Securities

A global security is a security that represents one or any other number of individual securities held by a depository. Generally, all securities represented by the same global securities will have the same terms.

Each security issued in book-entry form will be represented by a global security that we issue to, deposit with and register in the name of a financial institution or its nominee that we select. The financial institution that we select for this purpose is called the depository. Unless we specify otherwise in the applicable prospectus supplement, The Depository Trust Company, New York, New York, known as DTC, will be the depository for all securities issued in book-entry form.

A global security may not be transferred to or registered in the name of anyone other than the depository, its nominee or a successor depository, unless special termination situations arise. We describe those situations below under "Special Situations When A Global Security Will Be Terminated." As a result of these arrangements, the depository, or its nominee, will be the sole registered owner and legal holder of all securities represented by a global security, and investors will be permitted to own only beneficial interests in a global security. Beneficial interests must be held by means of an account with a broker, bank or other financial institution that in turn has an account with the depository or with another institution that does. Thus, an investor whose security is represented by a global security will not be a legal holder of the security, but only an indirect holder of a beneficial interest in the global security.

If the prospectus supplement for a particular security indicates that the security will be issued as a global security, then the security will be represented by a global security at all times unless and until the global security is terminated. If termination occurs, we may issue the securities through another book-entry clearing system or decide that the securities may no longer be held through any book-entry clearing system.

Table of Contents

Special Considerations For Global Securities

As an indirect holder, an investor's rights relating to a global security will be governed by the account rules of the investor's financial institution and of the depository, as well as general laws relating to securities transfers. We do not recognize an indirect holder as a holder of securities and instead deal only with the depository that holds the global security.

If securities are issued only as global securities, an investor should be aware of the following:

an investor cannot cause the securities to be registered in his or her name, and cannot obtain non-global certificates for his or her interest in the securities, except in the special situations we describe below;

an investor will be an indirect holder and must look to his or her own bank or broker for payments on the securities and protection of his or her legal rights relating to the securities, as we describe above;

an investor may not be able to sell interests in the securities to some insurance companies and to other institutions that are required by law to own their securities in non-book-entry form;

an investor may not be able to pledge his or her interest in the global security in circumstances where certificates representing the securities must be delivered to the lender or other beneficiary of the pledge in order for the pledge to be effective;

the depository's policies, which may change from time to time, will govern payments, transfers, exchanges and other matters relating to an investor's interest in the global security. We and any applicable trustee have no responsibility for any aspect of the depository's actions or for its records of ownership interests in the global security. We and the trustee also do not supervise the depository in any way;

the depository may, and we understand that DTC will, require that those who purchase and sell interests in the global security within its book-entry system use immediately available funds, and your broker or bank may require you to do so as well; and

financial institutions that participate in the depository's book-entry system, and through which an investor holds its interest in the global security, may also have their own policies affecting payments, notices and other matters relating to the securities. There may be more than one financial intermediary in the chain of ownership for an investor. We do not monitor and are not responsible for the actions of any of those intermediaries.

Special Situations When a Global Security Will Be Terminated

In a few special situations described below, a global security will terminate and interests in it will be exchanged for physical certificates representing those interests. After that exchange, the choice of whether to hold securities directly or in street name will be up to the investor. Investors must consult their own banks or brokers to find out how to have their interests in securities transferred to their own names, so that they will be direct holders. We have described the rights of holders and street name investors above.

A global security will terminate when the following special situations occur:

if the depository notifies us that it is unwilling, unable or no longer qualified to continue as depository for that global security and we do not appoint another institution to act as depository within 90 days;

if we notify any applicable trustee that we wish to terminate that global security; or

if an event of default has occurred with regard to securities represented by that global security and has not been cured or waived.

Table of Contents

The applicable prospectus supplement may also list additional situations for terminating a global security that would apply only to the particular series of securities covered by the prospectus supplement. When a global security terminates, the depositary, and neither we nor any applicable trustee, is responsible for deciding the names of the institutions that will be the initial direct holders.

PLAN OF DISTRIBUTION

We may sell the securities to or through underwriters or dealers, through agents, or directly to one or more purchasers. A prospectus supplement or supplements (and any related free writing prospectus that we may authorize to be provided to you) will describe the terms of the offering of the securities, including, to the extent applicable:

the name or names of any agents or underwriters;

the purchase price of the securities being offered and the proceeds we will receive from the sale;

any over-allotment options under which underwriters may purchase additional securities from us;

any agency fees or underwriting discounts and/or commissions and other items constituting agents' or underwriters' compensation;

any public offering price;

any discounts or concessions allowed or reallocated or paid to dealers; and

any securities exchanges or markets on which such securities may be listed.

We may distribute the securities from time to time in one or more transactions at:

fixed price or prices, which may be changed from time to time;

market prices prevailing at the time of sale;

prices related to such prevailing market prices; or

negotiated prices.

Agents

We may designate agents who agree to use their reasonable efforts to solicit purchases of our securities for the period of their appointment or to sell our securities on a continuing basis. We will name any agent involved in the offering and sale of securities and we will describe any fees or commissions we will pay the agent in the applicable prospectus supplement.

Underwriters

If we use underwriters for a sale of securities, the underwriters will acquire the securities for their own account. The underwriters may resell the securities in one or more transactions, including negotiated transactions, at a fixed public offering price or at varying prices determined at the time of sale. The obligations of the underwriters to purchase the securities will be subject to the conditions set forth in the applicable underwriting agreement. Subject to certain conditions, the underwriters will be obligated to purchase all the securities of the series offered if they purchase any of the securities of that series. We may change from time to time any public offering price and any discounts or concessions the underwriters allow or reallow or pay to dealers. We may use underwriters with whom we have a material relationship. We will describe the nature of any such relationship in any applicable prospectus supplement naming any such underwriter. Only underwriters we name in the prospectus supplement are underwriters of the securities offered by the prospectus supplement.

Table of Contents

We may provide agents and underwriters with indemnification against civil liabilities related to offerings under this prospectus, including liabilities under the Securities Act, or contribution with respect to payments that the agents or underwriters may make with respect to these liabilities.

Direct Sales

We may also sell securities directly to one or more purchasers without using underwriters or agents. Underwriters, dealers and agents that participate in the distribution of the securities may be underwriters as defined in the Securities Act, and any discounts or commissions they receive from us and any profit on their resale of the securities may be treated as underwriting discounts and commissions under the Securities Act. We will identify in the applicable prospectus supplement any underwriters, dealers or agents and will describe their compensation. We may have agreements with the underwriters, dealers and agents to indemnify them against specified civil liabilities, including liabilities under the Securities Act. Underwriters, dealers and agents may engage in transactions with or perform services for us in the ordinary course of their businesses.

Trading Markets and Listing of Securities

Unless otherwise specified in the applicable prospectus supplement, each class or series of securities will be a new issue with no established trading market, other than our common stock, which is currently listed on the NYSE Amex. We may elect to list any other class or series of securities on any exchange or market, but we are not obligated to do so. It is possible that one or more underwriters may make a market in a class or series of securities, but the underwriters will not be obligated to do so and may discontinue any market making at any time without notice. We cannot give any assurance as to the liquidity of the trading market for any of the securities.

Stabilization Activities

Any underwriter may engage in overallotment, stabilizing transactions, short covering transactions and penalty bids in accordance with Regulation M under the Exchange Act. Overallotment involves sales in excess of the offering size, which create a short position. Stabilizing transactions permit bids to purchase the underlying security so long as the stabilizing bids do not exceed a specified maximum. Short covering transactions involve purchases of the securities in the open market after the distribution is completed to cover short positions. Penalty bids permit the underwriters to reclaim a selling concession from a dealer when the securities originally sold by the dealer are purchased in a covering transaction to cover short positions. Those activities may cause the price of the securities to be higher than it would otherwise be. If commenced, the underwriters may discontinue any of these activities at any time.

Passive Market Making

Any underwriters who are qualified market makers on the NYSE Amex may engage in passive market making transactions in the securities on the NYSE Amex in accordance with Rule 103 of Regulation M, during the business day prior to the pricing of the offering, before the commencement of offers or sales of the securities. Passive market makers must comply with applicable volume and price limitations and must be identified as passive market makers. In general, a passive market maker must display its bid at a price not in excess of the highest independent bid for such security. If all independent bids are lowered below the passive market maker's bid, however, the passive market maker's bid must then be lowered when certain purchase limits are exceeded.

Compensation Cap

In compliance with the guidelines of the Financial Regulatory Authority, or FINRA, the maximum aggregate value of all compensation to be received by any FINRA member or independent broker-dealer will not exceed 8% of the gross proceeds from the sale of securities pursuant to this prospectus and any applicable prospectus supplement.

Table of Contents

LEGAL MATTERS

The validity of the securities being offered by this prospectus will be passed upon for us by DLA Piper LLP (US), San Diego, California. If the validity of any securities is also passed upon by counsel any underwriters, dealers or agents, that counsel will be named in the prospectus supplement relating to that specific offering.

EXPERTS

The consolidated financial statements as of December 31, 2011 and for the year ended December 31, 2011 and cumulatively for the period from January 1, 2011 to December 31, 2011 and management's assessment of the effectiveness of internal control over financial reporting (which is included in Management's Report on Internal Control over Financial Reporting) as of December 31, 2011 incorporated in this prospectus by reference to the annual report on Form 10-K for the year ended December 31, 2011 have been incorporated in reliance upon the report of PricewaterhouseCoopers LLP, an independent registered public accounting firm, given on the authority of such firm as an expert in accounting and auditing.

The consolidated balance sheet of ADVENTRX Pharmaceuticals, Inc. and its subsidiaries as of December 31, 2010, and the related consolidated statements of operations, stockholders' equity (deficit) and comprehensive loss and cash flows for the year then ended and for the period from January 1, 2002 through December 31, 2010 are incorporated by reference herein and in the registration statement in reliance upon the report of J.H. Cohn LLP, an independent registered public accounting firm, given on the authority of such firm as an expert in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and current reports, proxy statements and other information electronically with the SEC. You may read and copy these reports, proxy statements and other information at the SEC's public reference room at 100 F Street, N.E., Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for more information about the operation of the public reference room. You can request copies of these documents by writing to the SEC and paying a fee for the copying costs. The SEC also maintains an Internet site that contains reports, proxy and information statements, and other information regarding issuers that file electronically with the SEC, including us. The SEC's Internet site can be found at <http://www.sec.gov>. In addition, we make available on or through our Internet site copies of these reports as soon as reasonably practicable after we electronically file or furnish them to the SEC. Our Internet site can be found at <http://www.adventrx.com>.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

We are allowed to incorporate by reference information contained in documents that we file with the SEC. This means that we can disclose important information to you by referring you to those documents and that the information in this prospectus is not complete. You should read the information incorporated by reference for more detail. We incorporate by reference in two ways. First, we list below certain documents that we have already filed with the SEC. The information in these documents is considered part of this prospectus. Second, the information in documents that we file in the future will update and supersede the information currently in, and be incorporated by reference in, this prospectus.

We incorporate by reference into this prospectus the documents listed below, any filings we make with the SEC pursuant to Section 13(a), 13(c), 14 or 15(d) of the Exchange Act after the date of the initial registration statement of which this prospectus is a part and prior to the effectiveness of the registration statement, and any

Table of Contents

filings we make with the SEC pursuant to Section 13(a), 13(c), 14 or 15(d) of the Exchange Act from the date of this prospectus until the termination of this offering (in each case, except for the information furnished under Item 2.02 or Item 7.01 in any current report on Form 8-K and Form 8-K/A):

our annual report on Form 10-K for the year ended December 31, 2011 filed with the SEC on March 8, 2012;

our current reports on Form 8-K filed with the SEC on January 23, 2012 (File No. 001-32157-12539625), February 27, 2012 (File No. 001-32157-12642097) and March 8, 2012; and

the description of our common stock contained in our registration statement on Form 8-A filed with the SEC on April 27, 2004 (File No. 001-32157-041020580).

We will provide each person, including any beneficial owner, to whom a prospectus is delivered, a copy of any or all of the information that has been incorporated by reference into this prospectus but not delivered with this prospectus upon written or oral request at no cost to the requester. Requests should be directed to: ADVENTRX Pharmaceuticals, Inc., 12390 El Camino Real, Suite 150, San Diego, CA 92130, Attn: Investor Relations, telephone: (858) 552-0866.

This prospectus is part of a registration statement on Form S-3 that we filed with the SEC. That registration statement contains more information than this prospectus regarding us and our common stock, including certain exhibits and schedules. You can obtain a copy of the registration statement from the SEC at the address listed above or from the SEC's Internet website.

You should rely only on the information provided in and incorporated by reference into this prospectus or any prospectus supplement. We have not authorized anyone else to provide you with different information. You should not assume that the information in this prospectus or any prospectus supplement is accurate as of any date other than the date on the front cover of these documents.

Table of Contents

Series A Units consisting of Common Stock and Warrants

Series B Units consisting of Pre-Funded Warrants and Warrants

(**Shares of Common Stock Underlying the Pre-Funded Warrants**)

(**Shares of Common Stock Underlying the Warrants**)

Prospectus Supplement

Sole Book-Running Manager

Cowen and Company

, 2014