

Mast Therapeutics, Inc.
Form S-1/A
June 13, 2013
Table of Contents

As filed with the Securities and Exchange Commission on June 13, 2013

Registration No. 333-188870

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

AMENDMENT NO. 2
TO
FORM S-1
REGISTRATION STATEMENT
UNDER
THE SECURITIES ACT OF 1933

MAST THERAPEUTICS, INC.

(Exact name of registrant as specified in its charter)

Edgar Filing: Mast Therapeutics, Inc. - Form S-1/A

Delaware
(State or other jurisdiction of
incorporation or organization)

2834
(Primary Standard Industrial
Classification Code Number)
12390 El Camino Real, Suite 150

84-1318182
(I.R.S. Employer
Identification Number)

San Diego, CA 92130

(858) 552-0866

(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

Patrick L. Keran

President and Chief Operating Officer

Mast Therapeutics, Inc.

12390 El Camino Real, Suite 150

San Diego, CA 92130

Telephone: (858) 552-0866

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

With Copies to:

Michael S. Kagnoff, Esq.

DLA Piper LLP (US)

4365 Executive Drive, Suite 1100

San Diego, CA 92121-2133

Tel. 858-677-1400

Fax: 858-677-1477

Michael A. Hedge, Esq.

Jeffrey J. Plumer, Esq.

K&L Gates LLP

1 Park Plaza, Twelfth Floor

Irvine, California 92614

Tel: 949 253-0900

Edgar Filing: Mast Therapeutics, Inc. - Form S-1/A

Approximate date of commencement of proposed sale to the public: As soon as practicable after the effectiveness of this registration statement.

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933 check the following box.

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

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

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

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

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

CALCULATION OF REGISTRATION FEE

Title of Each Class of Securities to be Registered	Proposed Maximum Aggregate Offering Price(1)	Amount of Registration Fee
Common Stock, \$0.001 par value per share(2)(3)		
Common Stock Purchase Warrants(3)		(4)
Shares of Common Stock, \$0.001 par value per share, underlying Common Stock Purchase Warrants(2)		
Total Registration Fee	\$69,000,000	\$9,412(5)

- (1) Estimated solely for the purpose of calculating the amount of registration fee pursuant to Rule 457(o) under the Securities Act.
- (2) Pursuant to Rule 416, the securities being registered hereunder include such indeterminate number of additional shares of common stock as may be issued after the date hereof as a result of stock splits, stock dividends or similar transactions
- (3) Includes shares the underwriters have the option to purchase to cover over-allotments, if any.
- (4) No registration fee required pursuant to Rule 457(g) under the Securities Act.
- (5) \$4,706 of which was previously paid.

The registrant hereby amends this registration statement on such date or dates as may be necessary to delay its effective date until the registrant shall file a further amendment which specifically states that this registration statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933, as amended, or until the registration statement shall become effective on such date as the Securities and Exchange Commission, acting pursuant to said Section 8(a), may determine.

Table of Contents

The information in this prospectus is not complete and may be changed. We may not sell these securities until the registration statement filed with the Securities and Exchange Commission is effective. This prospectus is not an offer to sell these securities and it is not soliciting an offer to buy these securities in any state where the offer or sale is not permitted.

SUBJECT TO COMPLETION, DATED JUNE 13, 2013

PRELIMINARY PROSPECTUS

Units

Mast Therapeutics, Inc.

Shares of Common Stock

Warrants to Purchase up to

Shares of Common Stock

\$ per unit

Mast Therapeutics, Inc. is offering _____ units with each unit consisting of one share of our common stock and a warrant to purchase of a share of our common stock (and the shares of our common stock issuable from time to time upon exercise of the offered warrants).

Each warrant will have an exercise price of \$ _____ per share, will be exercisable upon issuance and will expire _____ years from the date of issuance. The units will not be issued or certificated. The shares of common stock and the warrants are immediately separable and will be issued separately, but will be purchased together in this offering.

The last reported sale price of our common stock on June 12, 2013 was \$0.62 per share.

Trading Symbol: NYSE MKT MSTX

This investment involves risk. See Risk Factors beginning on page 4.

	<i>Per Unit</i>	<i>Total</i>
Public offering price	\$	\$
Underwriting discount	\$	\$
Proceeds, before expenses, to us⁽¹⁾	\$	\$

(1) We have agreed to reimburse the underwriters for fees incurred by it in connection with this offering, up to a maximum of \$150,000. See Underwriting beginning on page 89 of this prospectus.

The underwriters have a 30-day option to purchase up to additional units from us to cover over-allotments, if any.

The underwriters expect to deliver the securities on or about , 2013.

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.

Sole Book-Running Manager

Piper Jaffray

Lead Manager

Canaccord Genuity

The date of this prospectus is , 2013

Table of Contents**TABLE OF CONTENTS**

	Page
<u>Prospectus Summary</u>	1
<u>The Offering</u>	3
<u>Risk Factors</u>	4
<u>Special Note Regarding Forward-Looking Statements</u>	27
<u>Use of Proceeds</u>	29
<u>Dilution</u>	29
<u>Capitalization</u>	31
<u>Market Price of our Common Stock and Related Stockholder Matters</u>	32
<u>Dividend Policy</u>	32
<u>Management's Discussion and Analysis of Financial Condition and Results of Operations</u>	33
<u>Business</u>	45
<u>Management</u>	70
<u>Executive Compensation</u>	75
<u>Certain Relationships and Related Party Transactions</u>	84
<u>Security Ownership Of Certain Beneficial Owners And Management</u>	84
<u>Description of Securities</u>	85
<u>Underwriting</u>	89
<u>Legal Matters</u>	91
<u>Experts</u>	91
<u>Where You Can Find More Information</u>	91
<u>Index to Consolidated Financial Statements</u>	F-1

You should rely only on the information contained in this prospectus. We have not authorized anyone to provide you with different information. If anyone provides you with different or inconsistent information, you should not rely on it. The information contained in this prospectus is accurate only as of the date of this prospectus. Our business, financial condition, results of operations and prospects may have changed since such date. Other than as required under the federal securities laws, we undertake no obligation to publicly update or revise such information, whether as a result of new information, future events or any other reason.

The distribution of this prospectus and the offering of our securities in certain jurisdictions may be restricted by law. This prospectus does not constitute, and may not be used in connection with, an offer or solicitation by anyone in any jurisdiction in which such offer or solicitation is not authorized or in which the person making such offer or solicitation is not qualified to do so to any person to whom it is unlawful to make such offer or solicitation. See the Underwriting section of this prospectus beginning on page 89.

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 included as an exhibit to the registration statement of which this prospectus forms a part 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.

Some of the industry and other data contained in this prospectus may be derived from data from various third-party sources. We have not independently verified any of that information and it may not be accurate or complete and may be subject to change based on various factors, including those discussed under the heading Risk Factors elsewhere in this prospectus.

Table of Contents

PROSPECTUS SUMMARY

This summary highlights information contained elsewhere in this prospectus. This summary does not contain all of the information that you should consider before making an investment decision with respect to our securities. You should read the entire prospectus carefully, including the Risk Factors section beginning on page 4 of this prospectus, our financial statements and related notes appearing at the end of this prospectus, and other information contained in this prospectus, before making an investment decision with respect to our securities. Unless the context indicates otherwise, all references to we, us, our, Mast, or the Company refer to Mast Therapeutics, Inc. and its subsidiaries.

Overview

We are a 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 for diseases and conditions characterized by microcirculatory insufficiency (endothelial dysfunction and/or impaired blood flow).

We believe the pharmacologic effects of MST-188 support its development in more than one setting and we intend to develop MST-188 in multiple clinical indications, both independently and through collaborations. In January 2013, we initiated EPIC (Evaluation of Purified 188 In Children), a pivotal phase 3 study of MST-188 in sickle cell disease. In February 2013, we announced our plans to develop MST-188 for complications of arterial disease, initially as an adjunct to thrombolytics in acute limb ischemia, and that in late 2013 or early 2014 we intend to initiate a phase 2, clinical proof-of-concept study to evaluate the safety and efficacy of MST-188 in this indication. Additionally, we are conducting or plan to conduct nonclinical studies to investigate the safety and/or efficacy of MST-188 in additional indications, including acute decompensated heart failure and blood transfusion. We also are conducting nonclinical studies that will evaluate the effect of MST-188 on blood coagulation, which may support further development in resuscitation of shock following major trauma. However, even if these nonclinical studies are positive, it is unlikely we will initiate clinical studies in these indications without a strategic collaboration or funding from the U.S. government. We may evaluate MST-188 in other conditions in which its pharmacologic effects may translate into improved clinical outcomes.

Over the past several years, we have changed fundamentally our priorities, personnel and business focus. In 2009, substantially all of the business operations of our company had been suspended and there were only two employees. A restructuring process was implemented that year and, as a result, we now have a substantially new board of directors and management team, which terminated development of our prior reformulated chemotherapeutic programs, raised capital to fund our current strategic direction, acquired MST-188 and focused our resources on its development, and managed substantial internal growth. To reflect this fundamental change in our company, effective March 11, 2013, we changed our name from ADVENTRX Pharmaceuticals, Inc. to Mast Therapeutics, Inc.

We are a development-stage company and have not yet marketed or sold any products or generated any significant revenue.

Business Strategy

Our goal is to be a successful biopharmaceutical company developing novel therapies for serious or life-threatening diseases with significant unmet needs. Near-term activities that underlie our business strategy include the following:

Complete the phase 3 study and seek regulatory approval of MST-188 in sickle cell disease. One of our top priorities is enrolling subjects in our phase 3 study of MST-188 in sickle cell disease. Although predicting the rate of enrollment for EPIC is subject to a number of assumptions and the actual rate may differ materially, we expect to complete enrollment in 2015. If study results are positive, 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 the data from this study.

Develop MST-188 for complications of arterial disease. Data from experimental models demonstrate the potential for MST-188, when used alone or in combination with thrombolytics, to improve outcomes in patients experiencing complications of arterial disease resulting from atherosclerotic and thromboembolic processes. We believe that, based on the similar pathophysiology of atherosclerotic arterial disease (plaque-obstructed arteries reducing the flow of blood to tissue), an agent that is effective in one form of occlusive arterial disease also may be effective in its other manifestations. Our strategy in arterial disease is first to demonstrate the utility of MST-188 in patients with acute limb ischemia, or ALI, an advanced

Edgar Filing: Mast Therapeutics, Inc. - Form S-1/A

form of atherosclerosis, where we believe the potential to demonstrate a treatment effect is greatest. By generating clinical proof-of-concept data in ALI, we believe we increase development and partnering opportunities in other forms of occlusive arterial disease. Our near-term goals include obtaining orphan drug designation for MST-188 for ALI, submitting to FDA a protocol for our planned phase 2, clinical proof-of-concept study in ALI, and initiating the phase 2 study in late 2013 or

Table of Contents

early 2014. With relatively modest investment, we expect to generate clinical proof-of-concept data in a relatively short period of time. We plan to leverage the data generated in the planned phase 2 study in ALI to find a partner to develop MST-188 in larger market indications within arterial disease, such as ischemic stroke.

Secure funding from the U.S. government to develop MST-188 for resuscitation of shock following major trauma, or other conditions of interest to the U.S. military. The potential clinical benefits of MST-188 in hemorrhagic shock are suggested by the results of a variety of experimental models, including statistically significant improvements in survival. If the survival advantage observed in experimental models can be demonstrated in clinical studies, it would represent a multi-billion dollar opportunity and a significant benefit to both civilian and military populations. We plan to conduct additional nonclinical studies this year to support the development of MST-188 in resuscitation of shock following major trauma. We also plan to seek funding from the U.S. government to conduct a dose-finding, phase 2, clinical proof-of-concept study in that indication, the protocol for which already has been developed in collaboration with a leading university in the research and care of trauma patients.

Establish partnerships to accelerate the development of MST-188 in multiple jurisdictions and indications. We are focused on developing MST-188 in the U.S. and plan to seek partners to develop and commercialize MST-188 outside of the U.S. Collaborating with companies with country-specific development, regulatory and commercial expertise will enhance the overall value of MST-188 and allow us to remain focused on our core competencies, which are in U.S. markets. In addition, establishing partnerships outside of the U.S., whether on an indication or product basis, will help fund development of MST-188 in sickle cell disease, ALI and other indications within the U.S.

Risk Factors

Our business is subject to numerous risks and uncertainties. As a development-stage biopharmaceutical company, we face many risks inherent in our business and our industry generally, including the risks and uncertainties described below. You should carefully consider all of the information set forth in this prospectus and, in particular, the information under the heading **Risk Factors**, prior to making an investment in our securities.

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

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.

We believe that if the gross proceeds from this offering are approximately \$30 million, the net proceeds from this offering (excluding any proceeds from the exercise of warrants issued pursuant to this offering), will be sufficient to enable us to generate top line data in EPIC; however, we do not anticipate that such capital alone will be sufficient to fund our operations through the successful development and commercialization of MST-188. Any capital-raising transaction we are able to complete in the future may result in dilution to our existing stockholders, require us to relinquish significant rights or restrict our operations.

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.

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

Corporate Information

Edgar Filing: Mast Therapeutics, Inc. - Form S-1/A

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

Common stock we are offering	shares, plus shares of our common stock underlying the warrants offered in this offering.
Warrants we are offering	Warrants to purchase up to shares of common stock. Each warrant will have an exercise price of \$ per share, will be exercisable upon issuance and will expire years from the date of issuance. This prospectus also relates to the offering of the shares of common stock issuable upon exercise of the warrants. The warrants will not be listed on any national securities exchange or other nationally recognized trading system, including the NYSE MKT.
Option to purchase additional units	We have granted the underwriters a 30-day option to purchase up to additional units from us at the public offering price, less underwriting discounts and commissions, to cover over-allotments, if any.
Offering price	\$ per unit.
Common stock outstanding after this offering (excluding any shares subject to the underwriters option to purchase additional units)	shares if we sell all shares being offered in this offering, or shares of our common stock if the warrants offered in this offering are issued and exercised in full.
Use of proceeds	We currently intend to use the net proceeds from this offering primarily to fund EPIC, our phase 3 clinical study of MST-188 in sickle cell disease, and for working capital and general corporate purposes. See Use of Proceeds on page 29.
Risk factors	See Risk Factors beginning on page 4 and other information included in this prospectus for a discussion of factors you should carefully consider before deciding to invest in our securities.
NYSE MKT symbol	MSTX
The number of shares of our common stock to be outstanding immediately after this offering as shown above assumes that all of the units offered hereby are sold and is based on 46,265,286 shares of common stock outstanding as of March 31, 2013, and excludes:	

16,488,432 shares of our common stock issuable upon exercise of outstanding warrants, with a weighted-average exercise price of \$1.79 per share;

250,000 shares of common stock issued after March 31, 2013 to the former stockholders of SynthRx pursuant to the terms of our merger agreement with SynthRx dated February 12, 2011;

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

4,016,843 shares of our common stock issuable upon exercise of outstanding options, with a weighted-average exercise price of \$2.12 per share; and

Edgar Filing: Mast Therapeutics, Inc. - Form S-1/A

789,207 shares and 246,945 shares of our common stock available for future grants under our Amended and Restated 2008 Omnibus Incentive Plan and 2005 Employee Stock Purchase Plan, respectively.

Unless otherwise indicated, all information in this prospectus assumes:

that the underwriters do not exercise their option to purchase up to additional shares of our common stock to cover over-allotments, if any; and

no options, warrants or shares of common stock were issued after March 31, 2013, and no outstanding options or warrants were exercised after March 31, 2013.

Table of Contents

RISK FACTORS

Investment in our securities involves a high degree of risk. Our business, operating results, growth prospects and financial condition are subject to various risks, many of which are not exclusively within our control, that may cause actual performance to differ materially from historical or projected future performance. We urge you to consider carefully the risks described below, together with the other information in this prospectus and our other public filings, before making investment decisions regarding our securities. Each of these risk factors, as well as additional risks not presently known to us or that we currently deem immaterial, could adversely affect our business, operating results, growth prospects or financial condition, as well as the trading price of our common stock, in which case you may lose all or part of your investment.

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 development-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. We have accumulated net losses totaling approximately \$192.8 million as of March 31, 2013, and we expect to continue to incur substantial operating losses for the next several years as we advance MST-188, our lead product candidate, through clinical studies and other development activities and seek approval from the FDA to commercialize it. 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 MST-188 or another product candidate 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 on the success of MST-188 and this product candidate may not receive regulatory approval or be successfully commercialized.

We currently have no products for sale and we are focusing our resources almost exclusively 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, including successful completion of EPIC, our ongoing phase 3 clinical study in sickle cell disease, and significant manufacturing 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 EPIC, or in other clinical studies we initiate in sickle cell disease or other indications or, 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.

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;

Edgar Filing: Mast Therapeutics, Inc. - Form S-1/A

the number of patients who participate in each clinical study;

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

Table of Contents

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.

If our estimated future expenditures on our development programs increased more than our current expectations, we would need to seek additional capital or reduce other expenditures. We may not be able to raise capital as and when needed or reduce other expenditures to offset an increase in expenditures on our development programs, which could have a material adverse effect on our financial condition and ability to pursue our business.

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 short-term investments, which were approximately \$32.0 million as of March 31, 2013, 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 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. We may also seek to 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.

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

Edgar Filing: Mast Therapeutics, Inc. - Form S-1/A

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 could involve covenants that 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.

Table of Contents

For particular development programs, such as development of MST-188 for resuscitation of shock 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 drug research and development funding. For example, on March 1, 2013, automatic, across-the-board federal budget cuts, known as sequestration, went into effect, which could significantly reduce funding for drug research and development programs and reduce the likelihood of our receipt of government funding in the future. 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, which likely would have a material adverse effect on our financial condition and prospects.

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, including the continued volatility of U.S. and international equity markets, may adversely impact our ability to raise additional capital. Our failure to raise capital as and when 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 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, current SEC rules and regulations. Under current SEC rules and regulations, we must meet certain requirements to use a Form S-3 registration statement to 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 of 1933, as amended, or the Securities Act, or under a Form S-1 registration statement, such as this offering and which we have done in the past, 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."

Table of Contents

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 46,515,286 shares of our outstanding common stock as of June 12, 2013 and the closing price per share of our common stock on such date, which was \$0.62, we could not raise more than approximately \$5.7 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 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 MST-188, partner it 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 our development of MST-188 or other 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.

Table of Contents***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 MST-188 or another product candidate 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 to employees of stock options we provide 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 with or without notice. If we cannot attract and retain skilled personnel, as needed, we may not achieve our development and other goals.

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.

Although we are focused on developing MST-188, from time to time, we may evaluate pipeline expansion opportunities 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 develop MST-188 or any other product candidate. 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, given our recent market capitalization, such dilution could be substantial. For example, in addition to the 1,596,772 outstanding shares we have issued to SynthRx's former stockholders as consideration for our acquisition of SynthRx that are outstanding, we could issue up to an aggregate of 12,478,050 additional shares of our common stock to such persons upon achievement of milestones related to the development and regulatory approval of MST-188 for the treatment of sickle cell crisis in children. If those milestones are achieved, the number of shares issued and outstanding in connection with the SynthRx acquisition would, in the aggregate, represent an approximately 23.9% ownership stake in our company (based on 46,515,286 shares outstanding as of June 12, 2013 plus shares issued in connection with achievement of the milestones). The issuance of shares in connection with other 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.

Table of Contents

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 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

Edgar Filing: Mast Therapeutics, Inc. - Form S-1/A

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.

Table of Contents

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. We have identified several ownership changes within the meaning of IRC Section 382, with the most recent as a result of our November 2011 common