

Mast Therapeutics, Inc.  
Form S-1/A  
June 05, 2013  
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As filed with the Securities and Exchange Commission on June 5, 2013

Registration No. 333-188870

**UNITED STATES**  
**SECURITIES AND EXCHANGE COMMISSION**

Washington, D.C. 20549

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

**MAST THERAPEUTICS, INC.**

(Exact name of registrant as specified in its charter)

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**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)

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**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)(2) | Amount of Registration Fee |
|----------------------------------------------------|--------------------------------------------------|----------------------------|
| Common Stock, \$0.001 par value per share          | \$34,500,000                                     | \$4,706(3)                 |

- (1) Estimated solely for the purpose of computing the amount of the registration fee pursuant to Rule 457(o) under the Securities Act of 1933, as amended.
- (2) Includes the offering price of shares that the underwriters have the option to purchase to cover over-allotments, if any.
- (3) \$4,092 of which was paid previously.

**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.**



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**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 5, 2013**

**PRELIMINARY PROSPECTUS**

**Shares**

**Mast Therapeutics, Inc.**

**Common Stock**

**\$ per share**

Mast Therapeutics, Inc. is offering \_\_\_\_\_ shares Trading Symbol: NYSE MKT MSTX  
of common stock.

The last reported sale price of our common stock on  
June 4, 2013 was \$0.70 per share.

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

|                              | <i>Per Share</i> | <i>Total</i> |
|------------------------------|------------------|--------------|
| <b>Public offering price</b> | \$               | \$           |
| <b>Underwriting discount</b> | \$               | \$           |

**Proceeds, before expenses, to us<sup>(1)</sup>** \$ \$

(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 91 of this prospectus.

*The underwriters have a 30-day option to purchase up to additional shares of common stock from us to cover over-allotments, if any.*

The underwriters expect to deliver the shares 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**

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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 91.

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.

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**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



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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 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.

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*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 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**

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.



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**THE OFFERING**

|                                                                                                                                                                                                                                                                    |                                                                                                                                                                                                                                              |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Common stock we are offering                                                                                                                                                                                                                                       | shares                                                                                                                                                                                                                                       |
| Option to purchase additional shares of common stock                                                                                                                                                                                                               | We have granted the underwriters a 30-day option to purchase up to additional shares of common stock from us at the public offering price, less underwriting discounts and commissions, to cover over-allotments, if any.                    |
| Offering price                                                                                                                                                                                                                                                     | \$ per share.                                                                                                                                                                                                                                |
| Common stock outstanding prior to the offering                                                                                                                                                                                                                     | shares.                                                                                                                                                                                                                                      |
| Common stock outstanding after this offering (excluding any shares subject to the underwriters' option to purchase additional shares)                                                                                                                              | shares if we sell all shares being offered in this offering.                                                                                                                                                                                 |
| 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 shares 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

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.

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**RISK FACTORS**

Investment in our stock 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 stock. 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;

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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;

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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, 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 technologies or product candidates, we may be required to relinquish valuable rights and dilute the current and future value of our assets. For



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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.

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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."

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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 the number of shares of our outstanding common stock as of June 4, 2013 and the closing price per share of our common stock on such date, which was \$0.70, we could not raise more than approximately \$6.5 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.

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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 shares outstanding as of June 4, 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.

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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

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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.

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***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 stock and warrant financing. As a result of these ownership changes, we do not expect to be eligible to utilize the NOL carry forwards and research and development tax credits we had accumulated as of November 11, 2011.

We believe the offering described in this prospectus could be deemed an ownership change for purposes of Sections 382 and 383 of the IRC, which may further limit the availability of our NOL carry forwards. Further ownership changes may occur in the future, which could eliminate or restrict our ability to use NOL carry forwards and research and development tax credits generated after November 11, 2011. 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 MST-188 or any of our product candidates on a timely basis, or at all, including due to factors not within our control. For example, the sequester that took effect on March 1, 2013 may result in significant reductions to the FDA's budget, which may lead to slower response times and longer review periods, potentially affecting our ability to progress development of or obtain approval for MST-188.

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*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;

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 significant factor in the time required to complete 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 Food and Drug Administration, or FDA or other regulatory authorities due to a number of factors, including:



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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. Amendments may require us to resubmit protocols to IRBs for reexamination or renegotiate terms with CROs and study sites and investigators, all of which may adversely impact the costs or timing of or our ability to successfully complete a trial.

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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 the 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 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 MST-188's mechanism 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 six prior 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 and the TQT study. 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 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 MST-188. For example, we have licensed to a third party certain rights to ANX-514 in South Korea and have limited control over any nonclinical testing or clinical studies that may be conducted by such third party or a future third-party licensee. If data from investigations of ANX-514 sponsored by a third-party licensee identify a safety or efficacy concern with respect to ANX-514, or the lack of comparable pharmacokinetics between ANX-514 and Taxotere, such data could adversely affect the U.S. regulatory process for ANX-514.

There is significant risk that MST-188 could fail to show anticipated results in nonclinical testing and/or clinical studies and, as a result, we may elect to discontinue its development in a particular indication or in whole. 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.

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*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 MST-188 clinical trial material, we have entered into supply agreements with Pierre Fabre Médicament (PFM) for API and Patheon Inc. for 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 MST-188 progresses, we will need to negotiate agreements for its commercial supply.

If we fail to maintain relationships with our current CMOs, we may not be able to complete development of MST-188 or market it, 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 the 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.

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Currently, we do not anticipate engaging alternative sources to backup our primary sources of clinical trial material and, in the future, we may not engage backup sources for commercial product. 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 PFM, 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 purified poloxamer 188, the API in MST-188, requires application of our proprietary supercritical 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 substantial 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 manufacture it to cGMP requirements applicable to API. The current supplier of our 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 a direct relationship with the supplier of that starting material and, although that third party has extensive, worldwide operations and poloxamer 188 is part of its standard product portfolio, we do not have any control over its production and the 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 PFM 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 PFM-manufactured API 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.

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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 our 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, PFM and Patheon are located in France and Italy, respectively, 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 on-going 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 MST-188 and any other product candidate 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.

If any of our CRO relationships were to terminate, in particular our relationship with Theradex® Systems, Inc., the CRO we engaged to conduct the EPIC study in the U.S., 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.

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### ***Our product candidates may cause undesirable side effects or have other properties that could delay or prevent their 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 function tests 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 function tests, 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. For additional discussion of these risks, see the risk factors above in this section,

Risks Related to Drug Development and Commercialization. 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 in addition to EPIC and the TQT study prior to its review or approval of MST-188 in sickle cell disease. 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 a submitted NDA relating to the data required to be included in marketing applications. For example, despite including in our initial Exelbina 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 Exelbina 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.

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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.

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*Even if we receive regulatory approval for MST-188 or another 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;

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.





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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.***

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

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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.

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*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.

### **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.

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With respect to MST-188, we acquired exclusive rights to a variety of issued patents related to poloxamers and their uses. However, we expect many of the patents will expire prior to our obtaining regulatory approval for MST-188. For exclusivity in sickle cell disease, we expect to rely primarily on the orphan drug designation that the FDA has granted for poloxamer 188 (purified) for the treatment of sickle cell disease, which includes the treatment and prevention of the complications of sickle cell disease. However, the orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review or approval process. MST-188 may not receive the seven-year orphan drug marketing exclusivity if it is not the first poloxamer 188 drug product to obtain FDA marketing approval for the treatment of sickle cell disease. 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 for the treatment of sickle cell disease to be clinically superior to or different from MST-188, the FDA may approve such other product candidate for marketing during MST-188's seven-year exclusivity period.

***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 MST-188 may be difficult to obtain and any issued claims may be limited due to the extent of published literature regarding the use of poloxamer 188.***

We have filed for patent protection covering our proprietary supercritical fluid extraction process, methods of using poloxamers in various clinical settings, and the use of poloxamers in combination therapy. However, these patent applications cover only methods of manufacturing, methods of using MST-188, and combination therapeutic methods; they do not cover the underlying API. Claims covering the API are widely viewed as the strongest form of intellectual property protection for pharmaceutical products, as they apply without regard to how the API is manufactured, used or formulated.

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 obvious.

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. The cost of litigation to uphold the validity and prevent infringement of our patents could be substantial. Furthermore, we cannot provide assurance that others will not independently develop similar technologies or duplicate our technologies or design around the patented aspects of our technologies. We can provide no assurance that our proposed technologies will not infringe patents or rights owned by others, licenses to which might not be available to us.

***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.



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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 adversely affect our rights. Any such proceeding 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 MST-188. Developments by others may render potential application of MST-188 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 MST-188 will face intense competition with respect to each indication in which it is approved. 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 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



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drugs for rare diseases, which may have the effect of increasing the development of agents to treat sickle cell disease, ALI and other indications we may pursue. Legislative action may generate further interest. For instance, in July 2012, the Food and Drug Administration Safety and Innovation Act was signed into law. This Act amended the Federal Food, Drug, and Cosmetic Act in a variety of ways that encourage or facilitate the development of drugs for patients with rare diseases, including by expanding the priority review voucher system to rare pediatric diseases and encouraging the FDA to implement more effective processes for expedited development and review of new medicines intended to address unmet medical needs for serious or life-threatening diseases or conditions using a broad range of surrogate endpoints. 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.

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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. In addition, numerous non-profit or non-commercial foundations and interest groups also 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.

With respect to resuscitation of shock following major trauma, MST-188 could compete with various investigational therapies for hemorrhagic shock, including agents to improve blood flow in the microvasculature, improve oxygenation of ischemic tissues, and/or prevent reperfusion injury. Some organizations with potentially competitive therapies have received funding from the federal government to progress their research and development. To the extent other therapies demonstrate acceptable safety and efficacy and receive regulatory approval prior to MST-188, the need for MST-188 may be diminished. In addition to investigational pharmacologic approaches, new resuscitation protocols are being explored to reduce morbidity and mortality following major hemorrhage and, to the extent they are successful, they may diminish the need for MST-188.

***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;

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.

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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.

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*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;

withdrawal of clinical study participants;

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.

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.

Previously, prior to 2011, we were not in compliance with certain NYSE MKT stockholders' equity continued listing standards. Specifically, we were not in compliance with (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, or (2) Section 1003(a)(iii) of the Company Guide, because we reported stockholders' equity of less than \$6,000,000 and losses from continuing

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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.

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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. However, there is no assurance that we will continue to maintain compliance with such 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," and has traded at under \$1.00 per share for more than twelve consecutive months. 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.

*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 the complete response letter for our Exelbine NDA, which stated that the FDA could not approve it in its present form. Conversely, the market price for our common stock increased over 66% in a 30-day period in June and July 2011 and more than doubled over two trading days in late December 2009. 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;

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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 our executive officers, directors and significant stockholders 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;

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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;

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 and nonclinical studies of MST-188 and regulatory agency decisions affecting that development program.***

We expect announcements of progress with and results of clinical and certain nonclinical 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 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 MST-188 and/or the value of the MST-188 program 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. These 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. Currently, we have effective primary registration statements on Form S-3 under which we may sell and issue more than \$150 million of securities, subject to certain limitations if our public float is less than \$75 million. We also have effective resale registration statements on Form S-3 that register a significant number of shares of our common stock and securities convertible into our common stock that may be sold by us or certain of our stockholders, including an effective resale registration statement for the shares of our common stock that have been and may be issued to the former SynthRx stockholders. Collectively, these registration statements may increase the likelihood of sales by, or the perception of an increased likelihood of sales by, us or our existing stockholders of shares of our common stock.



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***We currently have voting control with respect to approximately 2.8% of our outstanding common stock and we may obtain voting control over a significant additional amount of our outstanding common stock if we issue the milestone-related shares to the former SynthRx stockholders, 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.***

Pursuant to the voting and transfer restriction agreement between us and each of the former principal stockholders of SynthRx, each stockholder party has agreed to vote all shares of our common stock beneficially owned by that party with respect to every action or approval by written consent of our stockholders in such manner as directed by us, except in limited circumstances, and has executed an irrevocable proxy appointing and authorizing us to vote such shares in such manner. If the development of MST-188 achieves each of the milestones set forth in our merger agreement with SynthRx, we will issue an additional 12,478,050 shares of our common stock, which, together with previously issued and outstanding shares held by these former SynthRx stockholders, represent an aggregate approximately 22.5% ownership stake in our company (based on shares outstanding as of June 4, 2013 plus shares issued in connection with achievement of the milestones). As a result of such potential issuances and the voting and transfer restriction agreement, 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 shares are issued, our ability to control a potentially significant block of stockholder votes pursuant to the voting and transfer restriction agreement 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.

***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.

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*If shares of our common or preferred stock available for issuance or shares eligible for future sale were introduced into the market, it could hurt our stock price.*

As of March 31, 2013, there were an aggregate of 46,265,286 shares of our common stock issued and outstanding. That total excludes 4,016,843 shares of our common stock that may be issued upon the exercise of outstanding stock options, 16,488,432 shares of common stock that may be issued upon the exercise of outstanding warrants and 12,728,050 shares of common stock issued or that may be issued to the former stockholders of SynthRx upon the achievement of performance milestones pursuant to the terms of our merger agreement with SynthRx dated February 12, 2011. The exercise of outstanding options and/or warrants or issuance of shares may cause substantial dilution to those who hold shares of common stock prior to such exercises or issuances. In addition, sales of substantial amounts of the common stock in the public market by these holders or perceptions that such sales may take place may lower the common stock's market price.

We have 500,000,000 shares of authorized common stock and we may sell our authorized, but unissued, common stock to satisfy our funding requirements. We are also authorized to issue 1,000,000 shares of preferred stock, without stockholder approval. The preferred stock may have rights that are superior to the rights of the holders of our common stock, at a purchase price then approved by our board of directors. The sale or the proposed sale of substantial amounts of our common or preferred stock in the public markets may adversely affect the market price of our common stock and our stock price. Our stockholders may also experience substantial dilution.

**RISKS RELATED TO THIS OFFERING**

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

Since the price per share of our common stock being offered is substantially higher than the net tangible book value per share of our common stock, you will suffer substantial dilution in the net tangible book value of the common stock you purchase in this offering. Based on an assumed offering price of \$0.70 per share, which was the last reported sale price of our common stock on the NYSE MKT on June 4, 2013, if you purchase shares of common stock in this offering, you will suffer immediate and substantial dilution of approximately \$0.08 per share in the net tangible book value of the common stock. See the section entitled "Dilution" in this prospectus for a more detailed discussion of the dilution you will incur if you purchase common stock in this offering.

*Our management will have broad discretion in the use of the net proceeds from this offering and may not use them effectively.*

Our management will have broad discretion in the application of the net proceeds from this offering and our stockholders will not have the opportunity as part of their investment decision to assess whether the net proceeds are being used appropriately. Because of the number and variability of factors that will determine our use of the net proceeds from this offering, their ultimate use may vary substantially from their currently intended use. The failure by our management to apply these funds effectively could harm our business.

We believe that if the gross proceeds from this offering are approximately \$30 million, the net proceeds will be sufficient to enable us to generate top line data in EPIC. However, it is possible that we may not achieve the progress we currently expect with respect to EPIC, because actual costs and timing of clinical development activities are difficult to predict and subject to substantial risks and delays, as discussed elsewhere in this prospectus, including in this section.

Pending their use, we expect to invest the net proceeds from this offering in short-term, interest-bearing, marketable securities. These investments may not yield a favorable return to our stockholders. See "Use of Proceeds" for a more detailed description of our proposed use of proceeds from this offering. We have broad discretion in the use of the net proceeds from this offering and may not use them effectively.

**SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS**

This prospectus contains 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 (the "Exchange Act"). These statements involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performances or achievements expressed or implied by the forward-looking statements. These forward-looking statements include, but are not limited to, those concerning the following:

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our ability, or that of a future partner, to successfully develop, obtain regulatory approval for and then successfully commercialize MST-188;

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

the potential for us to delay, scale back or discontinue 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 unable to raise sufficient additional capital as needed;

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delays in the commencement or completion of clinical studies or manufacturing and regulatory activities necessary to obtain regulatory approval to commercialize MST-188;

our ability to successfully execute clinical studies and the ability of MST-188 to demonstrate acceptable safety and efficacy in clinical studies;

suspension or termination of a clinical study, including due to patient safety concerns;;

our ability to maintain our relationships with the single-source third-party manufacturers and suppliers for clinical trial material, including the API and the finished drug product, 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 or assist in the conduct of 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;

the potential for the FDA, or another regulatory agency, to require additional nonclinical or clinical studies of MST-188 in sickle cell disease prior to accepting a new drug application for review or granting regulatory approval, even if ongoing or planned studies are successful;

the potential for the FDA, or another regulatory agency, to require additional nonclinical or clinical studies of MST-188 in any indication outside of sickle cell disease prior to our initiation of a phase 2 clinical study in that indication;

the potential that, even if clinical studies of MST-188 in one indication are successful, clinical studies in another indication may not be successful;

the potential for unsuccessful nonclinical or clinical studies in one indication or jurisdiction, or by a future partner that may be outside of our control, to adversely affect opportunities for MST-188 in other indications or jurisdictions;

the potential that we may enter into one or more collaborative arrangements, including partnering and licensing arrangements, for MST-188 or another product candidate, and the terms of any such transactions;

the extent of market acceptance of MST-188 in any indication or jurisdiction in which it receives regulatory approval;

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

competition in the marketplace for our products, if approved;

our ability to protect our intellectual property rights with respect to MST-188 and our MAST platform;

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 commercial success;

undesirable side effects that our product candidates or products may cause;

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

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

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

In some cases, you can identify forward-looking statements by terms such as anticipate, believe, can, continue, could, estimate, expect, may, plan, potential, predict, project, should, will, would or the negative of those terms or other comparable terminology or expressions. Forward-looking statements reflect our current views with respect to future events, are based on assumptions, and are subject to known and unknown risks and uncertainties and other factors. We discuss many of these risks and uncertainties in greater detail under the heading Risk Factors elsewhere in this prospectus. Given these and other risks and uncertainties and other factors, you should not place undue reliance on these forward-looking statements because some or all of them may turn out to be wrong. You should read this prospectus and the other information in this registration statement carefully and completely and with the understanding that our actual future results may be materially different from what we expect. We hereby qualify all of our forward-looking statements by these cautionary statements.

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Forward-looking statements represent our estimates and assumptions only as of the date such forward-looking statements are made. Except as required by law, we assume no obligation to update any forward-looking statements publicly, or to update the reasons actual results could differ materially from those anticipated in any forward-looking statements, even if new information becomes available in the future.

**USE OF PROCEEDS**

We expect to receive net proceeds of approximately \$ \_\_\_\_\_ million from the sale of shares of our common stock in this offering (or \$ \_\_\_\_\_ million if the underwriters exercise their option to purchase additional shares of common stock to cover over-allotments in this offering in full) after deducting underwriting discounts and commissions and estimated offering expenses.

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.

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.

**DILUTION**

Investors in shares of our common stock offered in this offering will experience an immediate dilution in the net tangible book value of their common stock from the public offering price of the common stock. The net tangible book value of our common stock as of March 31, 2013 was approximately \$27.2 million, or approximately \$0.59 per share of common stock. Net tangible book value per share of our common stock is calculated by subtracting our total tangible liabilities from our total tangible assets, and dividing this amount by the number of shares of common stock outstanding.

Dilution per share represents the difference between the public offering price per share of our common stock and the adjusted net tangible book value per share of our common stock included in this offering after giving effect to this offering. After giving effect to the assumed sale of \$30 million of shares of common stock offered in this offering at an assumed offering price of \$0.70 per share, which price was the last reported sale price of our common stock on the NYSE MKT on June 4, 2013, and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us, our net tangible book value as of March 31, 2013 would have been approximately \$54.8 million, or approximately \$0.62 per share of common stock. This change represents an immediate increase in the net tangible book value of \$0.03 per share of common stock to our existing stockholders and an immediate and substantial dilution in net tangible book value of \$0.08 per share of common stock to new investors. The following table illustrates this per share dilution:

|                                                                                                         |         |
|---------------------------------------------------------------------------------------------------------|---------|
| Assumed public offering price per share                                                                 | \$ 0.70 |
| Net tangible book value per share as of March 31, 2013                                                  | \$ 0.59 |
| Increase per share attributable to investors purchasing our common stock in this offering               | \$ 0.03 |
| As adjusted net tangible book value per share as of _____, 2013, after giving effect to this offering   | \$ 0.62 |
| Dilution in net tangible book value per share to investors purchasing our common stock in this offering | \$ 0.08 |

If the underwriters exercise in full their option to purchase \_\_\_\_\_ additional shares of common stock at an assumed public offering price of \$0.70 per share, the pro forma as adjusted net tangible book value after this offering would be \$0.62 per share, representing an increase in net tangible book value of \$0.03 per share to existing stockholders and immediate dilution in net tangible book value of \$0.08 per share to investors purchasing our common stock in this offering at the public offering price.

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The number of shares of our common stock to be outstanding immediately after this offering as shown above assumes that all of the shares 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

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.

To the extent options or warrants outstanding as of March 31, 2013, have been or may be exercised or other shares have been issued, there may be further dilution to investors.

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The following table shows our cash, cash equivalents and short-term investments and capitalization as of March 31, 2013 on an actual basis and on an as adjusted basis to reflect the assumed sale of \$30 million of shares of our common stock in this offering, at an assumed public offering price of \$0.70, which price was the last reported sale price of our common stock on the NYSE MKT on June 4, 2013, after deducting estimated underwriting discounts and commissions and estimated offering expenses.

This table should be read in conjunction with Management's Discussion and Analysis of Financial Condition and Results of Operations and our financial statements and the accompanying notes contained elsewhere in this prospectus.

| <b>As of March 31, 2013</b>                                                                                                                                                           | <b>Actual</b>                           | <b>As Adjusted</b> |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------|--------------------|
|                                                                                                                                                                                       | <b>(in thousands)</b>                   |                    |
|                                                                                                                                                                                       | <b>except share and per share data)</b> |                    |
| Cash, cash equivalents and short-term investments                                                                                                                                     | \$ 32,007                               | \$ 59,682          |
| Stockholders' equity:                                                                                                                                                                 |                                         |                    |
| Common stock, \$0.001 par value; 500,000,000 shares authorized; Actual: 47,719,365 shares issued and 46,265,286 shares outstanding; As Adjusted: shares issued and shares outstanding | \$ 48                                   | \$ 91              |
| Treasury stock, at cost 1,454,079 shares                                                                                                                                              | (1)                                     | (1)                |
| Additional paid-in capital                                                                                                                                                            | 227,048                                 | 254,680            |
| Accumulated other comprehensive loss                                                                                                                                                  | (11)                                    | (11)               |
| Accumulated deficit                                                                                                                                                                   | (190,529)                               | (190,529)          |
| Total stockholders' equity                                                                                                                                                            | 36,555                                  | 64,230             |
| Total capitalization                                                                                                                                                                  | \$ 36,555                               | \$ 64,230          |



**Table of Contents****MARKET PRICE OF OUR COMMON STOCK AND RELATED STOCKHOLDER MATTERS****Market Information**

Our common stock trades under the symbol **MSTX** on the NYSE MKT equities market. During the periods presented in the following table, it traded under the symbol **ANX** on the same market. The following table sets forth the high and low sale prices for our common stock in each full quarterly period within the two most recent fiscal years. On June 4, 2013, the closing price of our common stock reported on the NYSE MKT was \$0.70 per share.

|                                       | 2013    |         | Sales Price<br>2012 |         | 2011    |         |
|---------------------------------------|---------|---------|---------------------|---------|---------|---------|
|                                       | High    | Low     | High                | Low     | High    | Low     |
| First Quarter                         | \$ 0.79 | \$ 0.56 | \$ 0.75             | \$ 0.56 | \$ 3.45 | \$ 1.85 |
| Second Quarter (through June 4, 2013) | \$ 0.76 | \$ 0.63 | \$ 0.70             | \$ 0.45 | \$ 3.25 | \$ 2.08 |
| Third Quarter                         | \$      | \$      | \$ 0.87             | \$ 0.49 | \$ 4.21 | \$ 0.81 |
| Fourth Quarter                        | \$      | \$      | \$ 0.80             | \$ 0.54 | \$ 1.16 | \$ 0.56 |

As of March 31, 2013, we had approximately 148 record holders of our common stock. The number of beneficial owners is substantially greater than the number of record holders because a large portion of our common stock is held of record through brokerage firms in street name.

**DIVIDEND POLICY**

We have never declared or paid any cash dividends on our common stock and do not anticipate declaring or paying any cash dividends on our common stock in the foreseeable future. We expect to retain all available funds and any future earnings to support operations and fund the development and growth of our business. Our board of directors will determine whether we pay and the amount of future dividends (including cash dividends), if any.

In connection with previous preferred stock financings, we have agreed to charter restrictions on our ability to pay cash dividends or distributions on our common stock for so long as any shares of such preferred stock are outstanding, unless we obtain prior written consent from the holders of such preferred stock. Although currently there are no such restrictions on our ability to pay dividends on our common stock, we may agree to similar restrictions in the future.

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**MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS**

*The following discussion and analysis of our financial condition and results of operations should be read in conjunction with the consolidated financial statements and related notes contained elsewhere in this prospectus. In addition to historical information, this discussion and analysis contains forward-looking statements that involve risks, uncertainties, and assumptions. Our actual results could differ materially from those discussed in these forward-looking statements as a result of various factors, including those discussed below, under the headings "Risk Factors" and "Cautionary Note Regarding Forward-Looking Statements" and in other parts of this prospectus.*

**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, our lead product candidate, for diseases and conditions characterized by microcirculatory insufficiency (endothelial dysfunction and/or impaired blood flow).

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 \$5.6 million for the three months ended March 31, 2013. Our cash, cash equivalents and short-term investments were \$32.0 million as of March 31, 2013.

We are focusing our resources on MST-188 and believe that its pharmacologic effects support its development in a wide range of diseases and conditions. Accordingly, we intend to develop MST-188 in multiple clinical indications, both independently and through collaborations. We currently are recruiting patients in EPIC (Evaluation of Purified 188 In Children), a pivotal phase 3 study of MST-188 in sickle cell disease. We also have announced plans to develop MST-188 for complications of arterial disease, initially as an adjunct to thrombolytics in acute limb ischemia, and we intend to initiate a phase 2, clinical proof-of-concept study in acute limb ischemia in late 2013 or early 2014. 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.

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

We anticipate that our cash, cash equivalents and short-term investments will be sufficient to fund our operations for at least the next 12 months. However, we have based this estimate on significant assumptions and we could utilize our available financial resources faster than we currently expect. For example, we may pursue development activities for MST-188 in sickle cell disease and multiple other indications at levels or on timelines, or we may incur unexpected expenses, that shorten the period through which our current financial resources will sustain us. We expect to incur significant and increasing losses for the next several years as we advance MST-188 through clinical studies and other development activities and seek regulatory approval to commercialize it. We believe that if the gross proceeds from this offering are approximately \$30 million, the net proceeds 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. In addition, we may seek to expand our product pipeline through acquisition of additional product candidates and/or technologies. We expect that our capital requirements would increase in future periods if we determine to develop MST-188 in indications in addition to those currently planned or expand our product pipeline with new product candidates and/or technologies. For the foreseeable future, we expect to fund our operations through public or private equity and/or debt financings and through collaborations, including licensing arrangements, and other strategic transactions. We also are seeking funding from U.S. government agencies. However, adequate additional financing may not be available to us on acceptable terms, on a timely basis or at all. Our failure to raise capital as and when needed would have a material and adverse effect on our financial condition and ability to pursue our business strategy.

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### **Acquisition of SynthRx**

**Merger Consideration.** In April 2011, we acquired SynthRx, Inc. as a wholly-owned subsidiary through a merger transaction in exchange for shares of our common stock and rights to additional shares of our common stock upon achievement of specified milestones related to MST-188. We also assumed \$0.3 million of SynthRx's transaction expenses. As of the date of this prospectus, we have issued an aggregate of 3,050,851 shares of our common stock to the former SynthRx stockholders, 2,800,851 of which upon completion of the acquisition and 250,000 of which following the dosing of the first patient in the EPIC study, which we considered the First Milestone under the merger agreement. We repurchased 1,454,079 of these shares in December 2012 for \$0.001 per share pursuant to the exercise of a repurchase right triggered as a result of the timing and planned number of patients in the EPIC study. We designated the repurchased shares as treasury stock. We could issue up to an aggregate of 12,478,050 additional shares of our common stock to the former SynthRx stockholders if and when the development of MST-188 achieves certain milestones, with an aggregate of 3,839,400 shares issuable upon the FDA's acceptance for review of a NDA covering the use of purified poloxamer 188 for the treatment of sickle cell crisis in children, which we refer to as the Second Milestone, and 8,638,650 shares issuable upon approval of such NDA by the FDA, which we refer to as the Third Milestone.

**Stockholders' Agreement.** In connection with our acquisition of SynthRx, each of the former principal stockholders of SynthRx entered into a stockholders' voting and transfer restriction agreement with us. This agreement became effective upon completion of the acquisition and will remain in effect until all of the shares of our common stock issued pursuant to the merger agreement to those stockholders and their affiliates have been transferred to non-affiliates. The transfer restriction aspect of the agreement, among other things, limits the amount of shares acquired pursuant to the merger agreement that the stockholder parties and their affiliates, as a group, can sell or transfer to non-affiliates on any trading day to an aggregate number of shares of our common stock of up to 10% of the average daily trading volume of our common stock. The agreement provides, however, that once in any 12-month period, the stockholder parties and their affiliates, as a group, may sell or transfer to non-affiliates up to an aggregate number of such shares of our common stock as is equal to five times the average daily trading volume of our common stock.

**In-License Agreement with CytRx Corporation.** In connection with our acquisition of SynthRx, through a prior license agreement between SynthRx and CytRx Corporation, we have rights to a variety of issued patents related to poloxamers and their uses. The issued patents cover, among other things, poloxamer 188, purified poloxamer 188, methods of treating sickle cell anemia using poloxamer 188 and methods of preparing purified poloxamer 188. Pursuant to this license agreement, we are required to make certain non-refundable and non-creditable milestone payments to CytRx based on the approval of each covered product in a major market, which includes the U.S. The amount of each milestone is in the low single-digit millions, half of which is due on the first commercial sale of the approved product and half of which is payable over time based on a percentage of quarterly net sales. In addition, we would pay a single-digit royalty on net sales of covered products. However, in the event of a sublicense under the specified patents, in lieu of the foregoing milestone and royalty payments, we may elect, in our sole discretion, to pay CytRx an amount equal to 20% of any sublicensing income we receive within 30 days of receipt thereof. Sublicense income includes, without limitation, license fees, royalties, milestone payments, license maintenance fees and strategic alliance payments, whether in cash, equity or other property, with the payment to be in the same form as the payment we receive.

### **Critical Accounting Policies and Significant Judgments and Estimates**

Our discussion and analysis of our financial condition and results of operations included in this prospectus is based upon consolidated financial statements and condensed consolidated financial statements that we have prepared in accordance with U.S. generally accepted accounting principles, or U.S. GAAP. The preparation of these financial statements requires us to make a number of estimates and assumptions that affect the reported amounts of assets, liabilities, revenues and expenses in these financial statements and accompanying notes. On an ongoing basis, we evaluate these estimates and assumptions, including those related to determination of the fair value of contingent consideration, goodwill and acquired in-process research and development, or IPR&D, and recognition of expenses for clinical study accruals and share-based compensation. We base our estimates on historical information, when available, and assumptions believed to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities not readily apparent from other sources. Actual results may differ materially from these estimates under different assumptions or conditions.

We believe the following accounting estimates are those that can have a material impact on our financial condition or operating performance and involve substantial subjectivity and judgment in the application of our accounting policies to account for highly uncertain matters or the susceptibility of such matters to change. The following is not intended to be a comprehensive discussion of all of our significant accounting policies. See the notes accompanying our financial statements contained elsewhere in this prospectus for a summary of all of our significant accounting policies and other disclosures required by U.S. GAAP.

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**Accrued Research and Development Expenses.** As part of the process of preparing our financial statements, we are required to estimate our accrued expenses. This process involves reviewing open contracts and purchase orders, communicating with our personnel to identify services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of the actual cost. Many of our service providers invoice us monthly in arrears for services performed or when contractual milestones are met. We make estimates of our accrued expenses as of each balance sheet date in our financial statements based on facts and circumstances known to us at that time. We periodically confirm the accuracy of our estimates with the service providers and make adjustments, if necessary. The majority of our accrued expenses relate to R&D services and related expenses. Examples of estimated accrued R&D expenses include:

fees paid to contract manufacturing organizations, or CMOs, in connection with process development activities and production of nonclinical and clinical trial material;

fees paid to vendors in connection with nonclinical development activities;

fees paid to consultants for regulatory-related advisory services;

fees paid to contract research organizations, or CROs, in connection with clinical studies; and

fees paid to investigative sites and investigators in connection with clinical studies.

We base our expenses related to CMOs and CROs on our estimates of the services received and efforts expended pursuant to purchase orders or contracts with multiple service providers that we engage to manufacture our clinical trial material and conduct and manage clinical studies on our behalf. The financial terms of our arrangements with our CMOs and CROs are subject to negotiation, vary from contract to contract and may result in uneven payment flows. Payments under some of these contracts depend on factors such as the successful completion of specified process development activities or the successful enrollment of patients and the completion of clinical study milestones. In accruing these service fees, we estimate, as applicable, the time period over which services will be performed (e.g., enrollment of patients, activation of clinical sites, etc.). If the actual timing varies from our estimate, we adjust the accrual accordingly. In addition, there may be instances in which payments made to service providers will exceed the level of services provided and result in a prepayment of R&D expense, which we report as an asset. The actual costs and timing of clinical studies and research-related manufacturing are uncertain and subject to change depending on a number of factors. Differences between actual costs of these services and the estimated costs that we have accrued in a prior period are recorded in the subsequent period in which the actual costs become known to us. Historically, these differences have not resulted in material adjustments, but such differences may occur in the future and have a material impact on our consolidated results of operations or financial position.

**Business Combinations.** We accounted for the acquisition of SynthRx in accordance with Accounting Standards Codification, or ASC, Topic 805, *Business Combinations*, which requires the purchase price to be measured at fair value. The purchase price consisted entirely of shares of our common stock and included contingent consideration, which becomes vested or issuable, as applicable, upon achievement of the First Milestone, the Second Milestone and the Third Milestone, as discussed above under *Acquisition of SynthRx*. We calculated the total purchase price by determining the probability-weighted fair value of the shares of our common stock issued, issued subject to repurchase and issuable to the former SynthRx stockholders as of April 8, 2011, the acquisition date. The probability and timing inputs related to the vesting and issuance events were based on estimates and assumptions regarding development of MST-188, which are highly judgmental due to the inherent unpredictability of drug development, particularly by development-stage companies such as ours. We recognized the estimated fair values as of the acquisition date of the tangible assets and intangible assets acquired, including IPR&D, and liabilities assumed, and we recorded as goodwill the amount equal to the excess of the purchase price over the fair value of the tangible and intangible assets acquired and liabilities assumed.

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The accounting for the acquisition of SynthRx required us to make significant estimates and assumptions, particularly with respect to the fair values of the contingent consideration and acquired IPR&D. We believe the fair values assigned to the contingent consideration and acquired IPR&D were based on reasonable estimates and assumptions given the available facts and circumstances as of the acquisition date. However, these calculations were highly judgmental and it is possible that other professionals, applying reasonable judgment to the same facts and circumstances, could have developed and supported a range of alternative estimated amounts. For instance, we used a discounted cash flow model to determine the fair value of contingent consideration, though other methodologies could have been used. Discounted cash flow models require the use of significant estimates and assumptions, including, but not limited to: the probability of clinical and regulatory success for a product candidate considering its stage of development; the time and resources needed to complete the development and approval of a product candidate, including the inherent difficulties and uncertainties in developing a product candidate, such as obtaining FDA and other regulatory approvals; estimated cash flows projected following the approval of a product candidate in development; the commercial life of the potential approved product and associated risks; and risk associated with uncertainty regarding achievement of the milestone events and, with respect to the First Milestone, the circumstances under which it is achieved. We estimated the time needed to complete the development and approval of MST-188 based on assumptions regarding its stage of development as of the acquisition date and resources needed to complete its development and approval, taking into account the inherent difficulties and uncertainties in developing product candidates in general and MST-188 in particular. Changes to any of these estimates and assumptions could significantly impact the fair values recorded for the assets acquired and liabilities assumed in our acquisition of SynthRx, resulting in significant charges to our operations. In addition, unanticipated events and circumstances may occur which may affect the accuracy or validity of such assumptions, estimates or actual results.

**Asset and Liability for Contingent Consideration.** Our contingent asset and contingent liability are related to our acquisition of SynthRx and the amount of the purchase price, payable in shares of our common stock, subject to repurchase and issuance, respectively, based upon the achievement and circumstances of achievement of the First Milestone. We remeasure the fair value of this contingent consideration as of the end of each fiscal quarter until the arrangements are settled and as of the settlement date. Prior to the period ended December 31, 2012, our determination of the fair values of the contingent asset and contingent liability at each measurement date were based on significant assumptions regarding the timing and design of the EPIC study because up to approximately 75% of the shares we previously issued to the former SynthRx stockholders, or 1,454,079 shares, were subject to repurchase and the number of shares issuable upon achievement of the First Milestone could be reduced by up to 75% (from 1,000,000 to 250,000 shares) based the timing and design of that clinical study. The fair values of the contingent asset and contingent liability are also based on the market price of our common stock. As a proxy, we use the last reported sale price of our common stock on the NYSE MKT equities market on the measurement date (i.e., the last trading day of each quarter or the settlement date, as applicable), which, given the volatility of our stock price, may vary considerably from one measurement date to the next. We believe our estimates and assumptions are reasonable based on available facts and circumstances as of each measurement date. Changes in the fair value of this contingent consideration are recognized in earnings, as transaction-related expenses, until the contingent consideration arrangement is settled. The contingent asset and contingent liability were settled and eliminated in December 2012 and May 2013, respectively. We remeasured the fair value of the contingent asset and contingent liability as of their respective settlement dates and recognized the changes in fair value as transaction-related expenses during the respective periods in which they were settled.

**Goodwill and Acquired IPR&D.** In accordance with ASC Topic 350, *Intangibles – Goodwill and Other*, our goodwill and acquired IPR&D are determined to have indefinite lives and, therefore, are not amortized. Instead, they are tested for impairment annually and between annual tests if we become aware of an event or a change in circumstances that would indicate the carrying value may be impaired. We perform our annual impairment testing on September 30 of each year. Pursuant to Accounting Standards Update, or ASU, No. 2011-08, *Intangibles – Goodwill and Other (Topic 350): Testing Goodwill for Impairment*, and No. 2012-02, *Intangibles – Goodwill and Other (Topic 350): Testing Indefinite-Lived Intangible Assets for Impairment*, we have the option to first assess qualitative factors to determine whether the existence of events or circumstances leads us to determine that it is more likely than not (that is, a likelihood of more than 50%) that our goodwill or our acquired IPR&D is impaired. If we choose to first assess qualitative factors and we determine that it is not more likely than not goodwill or acquired IPR&D is impaired, we are not required to take further action to test for impairment. We also have the option to bypass the qualitative assessment and perform only the quantitative impairment test, which we may choose to do in some periods but not in others. Our determinations as to whether, and, if so, the extent to which, goodwill and acquired IPR&D become impaired are highly judgmental and based on significant assumptions regarding our projected future financial condition and operating results, changes in the manner of our use of the acquired assets, development of MST-188 or our overall business strategy, and regulatory, market and economic environment and trends.

**Property and Equipment, Net.** Property and equipment are stated at cost, less accumulated depreciation. Property and equipment are depreciated using the straight-line method over the estimated useful lives of the assets, which is generally three to five years. Leasehold improvements are amortized over the economic life of the asset or the lease term, whichever is shorter. Repairs and maintenance are expensed as incurred.

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In accordance with ASC Topic 360-10, *Property, Plant and Equipment* Overall, we test for recoverability of long-lived assets, including property and equipment, if events or changes in circumstances indicate that the carrying amount for the assets may not be recoverable. If our assessment indicates impairment, we measure the impairment loss as the amount by which the carrying amount exceeds fair value of the assets. Fair value determinations are based on an undiscounted cash flow model, or independent appraisals, as appropriate.

**Share-based Compensation Expenses.** We account for share-based compensation awards granted to employees, including non-employee members of our board of directors, in accordance with ASC Topic 718, *Compensation – Stock Compensation*. Compensation expense for all share-based awards is based on the estimated fair value of the award on its date of grant and recognized on a straight-line basis over its vesting period. As share-based compensation expense is based on awards ultimately expected to vest, it is reduced for estimated forfeitures. We estimate forfeitures at the time of grant based on the expected forfeiture rate for our unvested stock options which is based in large part on our historical forfeiture rates, but also on assumptions believed to be reasonable under the circumstances. We revise our estimates in subsequent periods if actual forfeitures differ from those estimates. Although share-based compensation expense can be significant to our consolidated financial statements, it is not related to the payment of any cash by us.

We estimate the grant date fair value of a stock option award using the Black-Scholes option-pricing model, or Black-Scholes model. In determining the grant date fair value of a stock option award under the Black-Scholes model, we must make a number of assumptions, including the term of the award, the volatility of the price of our common stock over the term of the award, the risk-free interest rate and estimated forfeiture rate. Changes in these or other assumptions could have a material impact on the compensation expense we recognize.

## **Results of Operations Overview**

We operate our business and evaluate our company on the basis of a single reportable segment, which is the business of developing therapies for serious or life-threatening diseases.

## **Revenue**

We have not generated any revenue from product sales to date, and we do not expect to generate revenue from product sales until such time, if any, that we have obtained approval from a regulatory agency to sell one or more of our product candidates, which we cannot predict with certainty will occur.

## **Operating Expenses**

**Research and Development Expenses.** We maintain and evaluate our R&D expenses by the type of cost incurred rather than by project. We do this primarily because we outsource a substantial portion of our work and our R&D personnel and consultants work across multiple programs rather than dedicating their time to one particular program. We began maintaining such expenses by type on January 1, 2005. We categorize our R&D expenses as external clinical study fees and expenses, external nonclinical study fees and expenses, personnel costs and share-based compensation expense. The major components of our external clinical study fees and expenses are fees and expenses related to CROs and clinical study investigative sites and investigators. The major components of our external nonclinical study fees and expenses are fees and expenses related to preclinical studies and other nonclinical testing, research-related manufacturing, including process development activities, quality assurance and regulatory affairs services. Research-related manufacturing expenses include costs associated with purchasing API, conducting process development activities, producing clinical trial material, producing material for stability testing to support regulatory filings, related labeling, testing and release, packaging and storing services and related consulting fees. Impairment losses on R&D-related manufacturing equipment are also considered research-related manufacturing expenses. Personnel costs relate to employee salaries, benefits and related costs.

A general understanding of drug development is critical to understanding our results of operations and, particularly, our R&D expenses. Drug development in the U.S. and most countries throughout the world is a process that includes several steps defined by the FDA and similar regulatory authorities in foreign countries. The FDA approval processes relating to new drug products differ depending on the nature of the particular product candidate for which approval is sought. With respect to any product candidate with active ingredients not previously approved by the FDA, a prospective drug product manufacturer is required to submit an NDA that includes complete reports of pre-clinical, clinical and laboratory studies and extensive manufacturing information to demonstrate the product candidate's safety and effectiveness. Generally, a new drug application, or NDA, must be supported by at least phase 1, 2 and 3 clinical studies, with each study typically more expensive and lengthy than the previous study.



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Future expenditures on R&D programs are subject to many uncertainties, including the number of clinical studies required to be conducted for each development program and whether we will develop a product candidate with a partner or independently. At this time, due to such uncertainties and the risks inherent in drug product development and the associated regulatory process, we cannot estimate with any reasonable certainty the duration of or costs to complete our R&D programs, or whether or when or to what extent revenues will be generated from the commercialization and sale of any of our product candidates. The duration and costs of our R&D programs, in particular those associated with clinical studies and research-related manufacturing, can vary significantly among programs as a result of a variety of factors, including:

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 included and the rate of site approval in each clinical 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 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 availability and cost of comparative agents used in clinical studies;

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

the cost, requirements, timing of and the ability to secure regulatory approvals.

We regularly evaluate the prospects of our R&D programs, including in response to available scientific, nonclinical and clinical data, our assessments of a product candidate's market potential and our available resources, and make determinations as to which programs to pursue and how much funding to direct to each one.

We expect our R&D expenses to increase as we continue EPIC, our phase 3 clinical study of MST-188, and initiate and conduct additional studies of MST-188 in sickle cell disease and other indications, as well as perform additional manufacturing process development activities and manufacture additional clinical trial material. As a result, we expect our R&D expenses to increase significantly in 2013 relative to 2012.

While many of our R&D expenses are transacted in U.S. dollars, certain expenses are required to be paid in foreign currencies and expose us to transaction gains and losses that could result from changes in foreign currency exchange rates. In particular, we may be obligated to pay in foreign currencies for the services of third-party manufacturers of and component suppliers for our product candidates. Our exposure to currency risk may increase in connection with the manufacture of product for commercial sale, if and as we obtain the regulatory approvals necessary to market our product candidates. We include realized gains and losses from foreign currency transactions in operations as incurred.



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*Selling, General and Administrative Expenses.* Selling, general and administrative, or SG&A, expenses consist primarily of salaries, benefits and related costs for personnel in executive, finance and accounting, legal and market research functions, and professional and consulting fees for accounting, legal, investor relations, business development, market research, human resources and information technology services. Other SG&A expenses include facility lease and insurance costs.

We expect SG&A expenses in 2013 to remain consistent relative to 2012.

*Transaction-Related Expenses.* Transaction-related expenses consist of legal, accounting, financial and business development advisory fees associated with the evaluation of potential acquisition targets and execution of acquisition transactions, including our acquisition of SynthRx. Transaction-related expenses also include any changes in the fair value of the contingent consideration related to our acquisition of SynthRx, which we remeasure as of the end of each quarter until the contingent arrangement is settled.

*Interest and Other Income/(Expense).* Interest and other income/(expense) includes interest income, interest expense, unrealized gains and losses due to changes in the exchange rates on assets and liabilities denominated in foreign currencies, realized gains and losses from foreign currency transactions and other non-operating gains and losses.

**Table of Contents****Results of Operations****Comparison of Three Months Ended March 31, 2013 and 2012**

**Revenue.** We recognized no revenue for the three months ended March 31, 2013 and 2012.

**R&D Expenses.** Our R&D expenses for the three months ended March 31, 2013 consisted primarily of external costs associated with the EPIC study and the thorough QT/QTc, or TQT, clinical study of MST-188 and research-related manufacturing expenses related to MST-188. The following table summarizes our consolidated R&D expenses by type for each of the periods listed and their respective percent of our total R&D expenses for such periods:

|                                              | Three months ended March 31, |             |                     |             | January 1, 2005 through |
|----------------------------------------------|------------------------------|-------------|---------------------|-------------|-------------------------|
|                                              | 2013                         | %           | 2012                | %           | March 31, 2013          |
| External clinical study fees and expenses    | \$ 2,308,102                 | 67%         | \$ 251,050          | 11%         | \$ 28,405,601           |
| External nonclinical study fees and expenses | 547,351                      | 16%         | 1,547,895           | 70%         | 36,703,388              |
| Personnel costs                              | 550,331                      | 16%         | 385,808             | 18%         | 13,904,777              |
| Share-based compensation expense             | 37,128                       | 1%          | 25,701              | 1%          | 3,012,349               |
| <b>Total</b>                                 | <b>\$ 3,442,912</b>          | <b>100%</b> | <b>\$ 2,210,454</b> | <b>100%</b> | <b>\$ 82,026,115</b>    |

R&D expenses increased by \$1.2 million, or approximately 55.8%, to \$3.4 million for the three months ended March 31, 2013, compared to \$2.2 million for the same period in 2012. This increase was due primarily to a \$2.0 million increase in external clinical study fees and expenses and a \$0.2 million in personnel costs, offset by a \$1.0 million decrease in external nonclinical study fees and expenses. The increase in external clinical study fees and expenses was related primarily to the EPIC and TQT clinical studies, which were initiated during the three months ended March 31, 2013. The increase in personnel costs was related primarily to increased headcount. The \$1.0 million decrease in external nonclinical study fees and expenses resulted primarily from a decrease in research-related manufacturing activities for ANX-514, which we discontinued during 2012.

**Selling, General and Administrative Expenses.** SG&A expenses increased by \$0.1 million, or approximately 3.3%, to \$2.1 million for the three months ended March 31, 2013, compared to \$2.0 million for the same period in 2012. This increase resulted primarily from an increase in personnel costs related to increased headcount.

**Transaction-Related Expenses.** Transaction-related expenses were \$27,500 for the three months ended March 31, 2013, compared to (\$114,388) for the same period in 2012. We recognized transaction-related expenses for the three months ended March 31, 2013 due to changes in the fair value at March 31, 2013 relative to December 31, 2012, of the contingent liability related to the consideration for our acquisition of SynthRx. The increase in the fair value of the contingent liability was due to the increase in our stock price at March 28, 2013 (\$0.68 per share), the last trading day of the three months ended March 31, 2013, relative to December 31, 2012 (\$0.57 per share). We recognized transaction-related expenses for the three months ended March 31, 2012 due to changes in the fair values at March 31, 2012 relative to December 31, 2011, of the contingent asset and contingent liability related to the consideration for our acquisition of SynthRx.

**Interest Income.** Interest income amounted to \$14,416 for the three months ended March 31, 2013, compared to \$18,668 for the same period in 2012. The decrease in interest income for the three months ended March 31, 2013 was attributable primarily to lower cash balances.

**Net Loss.** Net loss was \$5.6 million, or \$0.12 per share, for the three months ended March 31, 2013, compared to net loss of \$4.2 million, or \$0.09 per share, for the same period in 2012.

**Comparison of 2012 and 2011**

**Revenue.** We recognized no revenue for the years ended December 31, 2012 and December 31, 2011.

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**Operating Expenses.** The following table illustrates the types of operating expenses we incurred in 2012 and 2011 and their respective percent of our total operating costs for those periods:

|                                     | Operating Expenses |             |
|-------------------------------------|--------------------|-------------|
|                                     | Years Ended        |             |
|                                     | December 31,       |             |
|                                     | 2012               | 2011        |
| Research and development            | 52%                | 43%         |
| Selling, general and administrative | 48%                | 54%         |
| Transaction-related expenses        | 0%                 | 3%          |
| Depreciation and amortization       | 0%                 | 0%          |
| <b>Total operating expenses</b>     | <b>100%</b>        | <b>100%</b> |

**R&D Expenses.** In 2012, our most significant R&D expenses were third-party fees and expenses that related primarily to generating MST-188 clinical trial material and preparing for the EPIC study. These expenses consisted primarily of costs associated with research-related manufacturing, clinical study-related consulting and study set-up services, and regulatory affairs- and quality assurance-related consulting services. In 2011, our most significant R&D expenses were third-party fees and expenses that related primarily to the Exelbine and ANX-514 programs. These expenses consisted primarily of costs associated with research-related manufacturing and regulatory affairs- and quality assurance-related consulting services.

The following table summarizes our consolidated R&D expenses by type for each of the periods listed and their respective percent of our total R&D expenses for 2012 and 2011:

|                                              | Years Ended December 31, |             |                     |             | January 1, 2005<br>through |
|----------------------------------------------|--------------------------|-------------|---------------------|-------------|----------------------------|
|                                              | 2012                     |             | 2011                |             | December 31,               |
|                                              |                          | %           |                     | %           | 2012                       |
| External clinical study fees and expenses    | \$ 1,328,201             | 16%         | \$ 751,236          | 13%         | \$ 26,097,499              |
| External nonclinical study fees and expenses | 4,688,770                | 58%         | 4,212,596           | 73%         | 36,156,037                 |
| Personnel costs                              | 1,993,405                | 25%         | 817,045             | 14%         | 13,354,446                 |
| Share-based compensation expense             | 77,776                   | 1%          | (22,540)            | 0%          | 2,975,221                  |
| <b>Total</b>                                 | <b>\$ 8,088,152</b>      | <b>100%</b> | <b>\$ 5,758,337</b> | <b>100%</b> | <b>\$ 78,583,203</b>       |

R&D expenses increased by \$2.3 million, or 40.5%, to \$8.1 million for the year ended December 31, 2012, compared to \$5.8 million for the year ended December 31, 2011. The increase in R&D expenses in 2012 compared to 2011 was due to a \$1.2 million increase in personnel costs, a \$0.6 million increase in external clinical study fees and expenses, and a \$0.5 million increase in external nonclinical study fees and expenses. The increase in personnel costs resulted primarily from additional clinical and research-related manufacturing staff hired in 2012, including relocation and recruitment costs for our new Chief Medical Officer. The increase in external clinical study fees and expenses was related primarily to a \$0.8 million increase in clinical consulting and phase 3 study planning expenses for MST-188, offset by a \$0.2 million decrease in clinical consulting expenses for ANX-514 and Exelbine. The increase in external nonclinical study fees and expenses was related primarily to a \$2.0 million increase in research-related manufacturing activities and regulatory affairs-related consulting expenses for MST-188 and a \$0.7 million increase in research-related manufacturing activities for ANX-514, offset by a \$2.2 million decrease in commercial-readiness manufacturing activities for Exelbine. The increase in research-related manufacturing expenses for ANX-514 resulted from recognition of an impairment loss of \$0.4 million on equipment used to manufacture clinical trial material and \$0.3 million of other expenses related to the discontinuation of ANX-514 manufacturing activities.

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***Selling, General and Administrative Expenses.*** In 2012 and 2011, our SG&A expenses consisted primarily of consulting fees for finance, accounting, human resources, facilities, internal systems support, business development, commercialization, market research and investor relations functions services, salaries, benefits and related personnel costs for employees and share-based compensation expense.

SG&A expenses increased by \$0.3 million, or 4.6%, to \$7.5 million for the year ended December 31, 2012, compared to \$7.2 million for the year ended December 31, 2011. This increase resulted from a \$0.7 million increase in personnel costs, mainly due to additional staff hired in 2012, and a \$0.5 million increase in share-based compensation expense, offset by a \$0.9 million decrease in consulting fees and legal expenses. The decrease in consulting fees and legal expenses was due primarily to cost-savings realized by discontinuation of activities related to Exelbine and ANX-514.

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**Transaction-Related Expenses.** Transaction-related expenses were negative, (\$0.1) million, for the year ended December 31, 2012, compared to \$0.4 million for the year ended December 31, 2011. We recognized transaction-related expenses for the year ended December 31, 2012 due to changes in the fair values of our contingent asset and contingent liability at December 13, 2012 and December 31, 2012, respectively, compared to December 31, 2011. The contingent asset and contingent liability both relate to contingent consideration for the SynthRx acquisition. The contingent asset was settled on December 13, 2012 by our repurchase of 1,454,079 shares of our common stock from the former SynthRx stockholders, and we remeasured its fair value as of that date. The contingent liability was not settled before the end of the year and, consequently, we remeasured its fair value as of December 31, 2012. The changes in the fair values of the contingent asset and contingent liability were due to updated estimates regarding the probability and circumstances of achievement of the First Milestone and the differences in our stock price at December 13, 2012 (\$0.61 per share) and December 31, 2012 (\$0.57 per share) relative to December 30, 2011 (\$0.59 per share), which was the last trading day of 2011.

Transaction-related expenses for the year ended December 31, 2011 consisted of \$1.9 million related to legal, accounting, financial and business development advisory fees associated with the evaluation of potential acquisition targets, including SynthRx, and the execution of our acquisition of SynthRx, offset by a net \$1.5 million reduction in the fair value of contingent consideration that resulted from changes in the fair values of the contingent asset and contingent liability at December 31, 2011 relative to April 8, 2011, the acquisition date. Those changes in fair value were due to our significantly lower stock price at December 30, 2011 (\$0.59 per share) relative to April 8, 2011 (\$2.34 per share) and updated estimates regarding the probability and circumstances of achievement of the First Milestone.

**Interest and Other Income/(Expense).** Interest income amounted to \$74,000 for 2012, compared to \$66,000 for 2011. The increase in interest income of \$8,000 for 2012 was attributable primarily to higher interest rates on invested balances in 2012 as compared to 2011. Other expense was (\$5,000) in 2012, compared to other income of \$71,000 in 2011. The other income in 2011 was primarily attributable to insurance proceeds.

**Net Loss.** Net loss was \$15.6 million, or \$0.33 per share (basic and diluted), for the year ended December 31, 2012, compared to a net loss of \$13.3 million, or \$0.47 per share (basic and diluted), for the year ended December 31, 2011.

## **Liquidity and Capital Resources**

We have a history of annual losses from operations and we anticipate that we will continue to incur losses for at least the next several years. For the three months ended March 31, 2013, we incurred a loss from operations of \$5.6 million. For the years ended December 31, 2012 and 2011, we incurred losses from operations of \$15.6 million and \$13.4 million, respectively. Our cash, cash equivalents and short-term investments were \$32.0 million as of March 31, 2013 and \$36.5 million as of December 31, 2012. Our short-term investments at March 31, 2013 consisted entirely of FDIC-insured certificates of deposit.

We historically have funded our operations principally through proceeds from sales of our equity securities. We did not conduct any capital-raising transaction during the three months ended March 31, 2013 or in fiscal year 2012. In 2011, we raised an aggregate of \$36.6 million in net proceeds through the following equity financings:

In January 2011, we completed a registered direct equity financing involving the issuance of units consisting of 8,184,556 shares of our common stock, 5-year warrants to purchase up to an aggregate of 2,046,139 shares of our common stock and 1-year warrants to purchase up to an aggregate of 2,046,139 shares of our common stock. The gross proceeds of this financing were \$22.5 million, and we received \$21.0 million in net proceeds after deducting the fees and expenses of our placement agent and our other offering expenses. The 1-year warrants expired unexercised in January 2012. We may receive up to \$5.6 million of additional proceeds from the exercise of the 5-year warrants. The exercise price of the warrants is \$2.75 per share, and, subject to certain beneficial ownership limitations, the 5-year warrants are exercisable any time on or before January 11, 2016.

In November 2011, we completed an underwritten public offering of 21,250,000 shares of our common stock and warrants exercisable for up to 10,625,000 additional shares of our common stock. These securities were offered and sold to the public in multiples of a fixed combination consisting of one share and a warrant to purchase up to 0.5 of a share of our common stock. The gross proceeds from this financing were \$17.0 million, and we received \$15.6 million in net proceeds after deducting the underwriting commissions and our other offering expenses. We may receive up to \$11.7 million of additional proceeds from the exercise of the warrants issued to investors in this financing. The exercise price of the warrants is \$1.10 per share, and, subject to certain beneficial ownership limitations, the 5-year warrants are

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exercisable any time on or before November 16, 2016.

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In addition to potential proceeds from exercise of the warrants described above, we may receive up to \$0.8 million and \$6.6 million from the exercise of warrants issued in the registered direct equity financings we completed in October 2009 and May 2010, respectively; however, the exercise of these warrants is subject to certain beneficial ownership limitations. In addition, the exercise prices of these warrants are \$3.67 and \$3.65, respectively, and, in comparison, the closing sale price of our common stock on March 28, 2013, the last trading day of the three months ended March 31, 2013, was \$0.68 per share and we do not expect the holders of the warrants to exercise them unless and until our common stock trades at or above the exercise price of their warrants. For additional information regarding outstanding warrants to purchase our common stock, see Note 12, Warrants, of the Notes to the Condensed Consolidated Financial Statements (Unaudited) contained at the end of this prospectus.

For further discussion of our 2011 equity financings, see Note 8, Capital Stock and Warrants, of the Notes to Consolidated Financial Statements for the fiscal year ended December 31, 2012, contained at the end of this prospectus.

For a discussion of our liquidity and capital resources outlook, see Management Outlook below.

Analysis of our 2012 versus 2011 cash flow from operating, investing and financing activities is provided below.

|                                                   | December 31,<br>2012 | Decrease<br>During 2012 | December 31,<br>2011 |
|---------------------------------------------------|----------------------|-------------------------|----------------------|
| Cash, cash equivalents and short-term investments | \$ 36,511,402        | \$ (14,192,242)         | \$ 50,703,644        |
| Net working capital                               | \$ 34,602,996        | \$ (14,720,196)         | \$ 49,323,192        |

|                                           | Year Ended<br>December 31,<br>2012 | Change<br>Between<br>Periods | Year Ended<br>December 31,<br>2011 |
|-------------------------------------------|------------------------------------|------------------------------|------------------------------------|
| Net cash used in operating activities     | \$ (13,918,868)                    | \$ (451,914)                 | \$ (13,466,954)                    |
| Net cash used in investing activities     | \$ (7,165,175)                     | \$ 378,801                   | \$ (7,543,976)                     |
| Net cash provided by financing activities | \$ 740                             | \$ (36,603,470)              | \$ 36,604,210                      |

**Operating activities.** Net cash used in operating activities was \$4.5 million for the three months ended March 31, 2013 and for the same period in 2012. While net cash used in operating activities for the three months ended March 31, 2013 was consistent with the amount used in the same period in 2012, the net loss for the three months ended March 31, 2013 was \$1.4 million greater than the net loss for the same period in 2012. The higher net loss for the three months ended March 31, 2013 was offset by a \$1.1 million increase in accounts payable and accrued liabilities, a \$0.2 million decrease in prepaid expenses and other assets and a \$0.1 million loss on the change in fair value of contingent consideration related to our acquisition of SynthRx. The \$1.1 million increase in accounts payable and accrued liabilities was related primarily to fees and expenses of the TQT and EPIC clinical studies.

Net cash used in operating activities was \$13.9 million in 2012, compared to \$13.5 million in 2011. The increase in cash used in operating activities in 2012 was due primarily to a higher net loss in 2012 as compared to 2011 (\$2.3 million), which was attributable primarily to increases in our R&D expenses in connection with MST-188 development activities, and an increase in prepaids and other assets (\$0.5 million), offset by a decrease in the gain on the change in fair value of contingent consideration related to our SynthRx acquisition (\$1.4 million), increased share-based compensation expense (\$0.6 million), and a write-off of manufacturing equipment related to the discontinuation of ANX-514 manufacturing activities (\$0.4 million). The gain on the change in fair value of contingent consideration was greater in 2011 compared to 2012 primarily due to a significantly greater stock price difference on the 2011 fair value measurement dates compared to 2012 fair value measurement dates. For 2011, the closing sales price of our common stock was \$0.59 per share on December 30, 2011 compared to \$2.34 per share on April 8, 2011. For 2012, the closing sales price of our common stock was \$0.61 per share on December 13, 2012 and \$0.57 per share on December 31, 2012 compared to \$0.59 per share on December 30, 2011.

**Investing activities.** Net cash provided by investing activities was \$3.4 million for the three months ended March 31, 2013 compared to net cash used in investing activities of \$4.1 million for the same period in 2012. The difference was due primarily to an increase of \$5.0 million in proceeds from maturities of certificates of deposits, a decrease of \$2.3 million in purchases of certificates of deposit and a decrease of \$0.2 million in purchases of property and equipment.

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Net cash used in investing activities was \$7.2 million in 2012, compared to \$7.5 million in 2011. The difference was due primarily to an increase of \$8.7 million in purchases of certificates of deposit, offset by \$8.9 million in maturities and sales of certificates of deposits.

**Financing activities.** There was no cash used in or provided by financing activities during the three months ended March 31, 2013 or 2012.



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Net cash provided by financing activities was \$740 in 2012, compared to \$36.6 million in 2011. The cash provided by financing activities in 2011 consisted primarily of proceeds from the issuance of our equity securities in the financing transactions we completed during that year.

### **Management Outlook**

We anticipate that our cash, cash equivalents and short-term investments as of March 31, 2013 will be sufficient to fund our currently planned level of operations for at least the next 12 months. However, our estimate of the period of time through which our current financial resources will be adequate to support our operations is a forward-looking statement based on significant assumptions that involve a number of risks and uncertainties and actual results could differ materially. Factors that will affect our future funding requirements include, but are not limited to: the progress of our clinical and nonclinical studies of MST-188, particularly the EPIC study; the number and nature of indications and jurisdictions in which we pursue development and regulatory approval of MST-188, and the extent to which we do so independently or through collaborations or other strategic transactions; the rate of progress and costs of development and regulatory approval activities associated with MST-188, including expenses related to initiating and conducting clinical studies and research-related manufacturing expenses; the extent to which we increase our workforce; the extent to which we seek to commercialize and sell MST-188, if approved, independently or through collaborations or other strategic transactions; the extent of commercial success of any of our product candidates for which we receive regulatory approval; the costs and timing of establishing commercial manufacturing supply arrangements for our product candidates and establishing or acquiring sales and distribution capabilities for any approved products; and the extent to which we seek to expand our product pipeline and execute on transactions intended to do so.

We are focusing our resources almost exclusively on the development of MST-188. Earlier this year, we initiated the EPIC study and one of our top priorities is to enroll subjects in that study. In addition to the approximately 40 sites that we plan to open in the U.S., we are engaging another CRO to expand EPIC by opening approximately 30 sites outside of the U.S., beginning in the fourth quarter of 2013. Accordingly, we expect to enroll 388 subjects from a total of approximately 70 medical centers. 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. We currently estimate that external clinical study fees and expenses for EPIC, including preliminary estimates for the cost of opening sites and enrolling subjects outside of the U.S., will be approximately \$20 million.

In January 2013, we initiated a TQT study of MST-188 in healthy volunteers to evaluate its effect on cardiac ventricular repolarization, specifically the QT-interval, and we expect to announce results in the third quarter of 2013. We estimate that external clinical study fees and expenses for the TQT study will be approximately \$2 million. In addition, in the fourth quarter of 2013, we plan to initiate a sub-study within EPIC to evaluate the effect of MST-188 on microvascular blood flow (mBF) and tissue oxygen saturation (StO<sub>2</sub>). This sub-study will be conducted at select EPIC sites using non-invasive devices to measure mBF and StO<sub>2</sub> and we plan to enroll approximately 30 patients in the sub-study.

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. We plan to submit a protocol for our planned phase 2, clinical proof-of-concept study in acute limb ischemia to the FDA in the third quarter of 2013, and, depending in part upon FDA input, we expect to initiate the study in late 2013 or early 2014. We anticipate that the study will enroll approximately 60 patients and we estimate that external clinical study fees and expenses for the study will be approximately \$2 million.

We intend to evaluate MST-188 in other conditions in which we believe its pharmacologic effects may translate into improved clinical outcomes, including resuscitation of shock following major trauma, acute decompensated heart failure and blood transfusion. We plan to conduct a number of nonclinical studies of MST-188 to further assess its efficacy, safety and tolerability in sickle cell disease and other indications, including an experimental model of heart failure that we expect to begin in the third quarter of 2013 and six-month toxicology studies that we expect to begin later this year. However, unless we secure U.S. government or other third-party funding for development of MST-188 in a particular indication, other than as described above, we do not plan to initiate additional clinical studies in 2013.

In March 2013, we announced that we intend to evaluate opportunities for strategic alliances for MST-188 and had engaged a financial advisor to identify potential partners and advise us in potential transaction discussions. We believe that the European Commission's recent designation of MST-188 as an orphan medicinal product for the treatment of sickle cell disease will enhance its appeal in Europe.

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Although we anticipate that our cash, cash equivalents and short-term investments as of March 31, 2013 will be sufficient to fund our operations for at least the next 12 months, we do not anticipate that such capital alone will be sufficient to fund our operations through the successful development and commercialization of MST-188. In addition, our capital requirements likely will increase in future periods as we pursue development of MST-188 in additional indications, both those identified above and potentially other indications that we have not yet identified, or if we were to expand our product pipeline through acquisition of new product candidates and/or technologies. For the foreseeable future, we expect to fund our operations through public or private equity and/or debt financings and through collaborations, including licensing arrangements, and other strategic transactions. We also are seeking funding from U.S. government agencies. Even though we were able to raise significant funds in the recent past through equity financings, adequate additional financing may not be available to us in the future on acceptable terms, on a timely basis or at all. It is difficult to secure funding from the U.S. government without an existing relationship with a federal agency, which we do not have, which difficulty is increased based on current and anticipated constraints on federal spending. Our failure to raise capital as and when needed would have a material and adverse effect on our financial condition and ability to pursue our business strategy.

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**BUSINESS**

**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. In particular, in the third quarter of 2013, we plan to initiate a study of MST-188 in an experimental model of heart failure. 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 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 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 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.

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*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.

### **The MAST Platform**

The MAST platform describes the repository of both proprietary (to us) and non-proprietary poloxamer-related data, know-how and other information that has been developed over the course of several decades by numerous sponsors, most recently by our company. It reflects the accumulated knowledge of over 100 pharmacology studies, more than 15 clinical studies in multiple indications in which over 2,500 subjects have been exposed to both purified and non-purified poloxamer 188, and over two decades of experience manufacturing and purifying poloxamers. This knowledge, and those aspects that are proprietary to us in particular, provide us with unique insight into the mechanism of action of, and areas of potential clinical benefit with, MST-188.

The MAST platform provides us with several key benefits as we develop MST-188. In particular, we believe it:

*Accelerates development of MST-188 in new indications, at reduced cost.* Proof-of-concept in pharmacologic studies or experimental models has been demonstrated in a wide range of diseases and conditions and, for most new indications we plan to pursue, we believe we will not need to re-conduct many of the preclinical activities that consume substantial time and resources in drug development (e.g., IND-enabling toxicology, pharmacokinetic, absorption/distribution/metabolism /excretion studies). Further, we already have evaluated MST-188 in healthy volunteers and a study to evaluate its effect on cardiac ventricular repolarization is underway. Furthermore, we already have successfully manufactured clinical trial material. As a result, we expect to move MST-188 directly into phase 2 studies and generate clinical proof-of-concept data in new indications in relatively short time frames with relatively modest investment. By leveraging already-completed pre-clinical and phase 1 clinical activities, we can focus on later-stage, higher-value activities, as well as save time and money (both in terms of the costs to conduct these activities and by maintaining a more streamlined infrastructure).

*Provides broad-based, indication-agnostic exclusivity for MST-188.* We have filed for patent protection and continue to develop patent positions that we expect will provide exclusivity around the use of MST-188 in new indications and in combination with other therapies. In addition, the MAST platform allows us to augment our proprietary position around broadly-applicable, indication-agnostic activities that we believe will provide additional barriers to entry for MST-188 competitors. For example, for macromolecules such as MST-188, acceptance criteria for starting materials and in-process and release specifications are critical to the quality of drug product. Without these proprietary specifications, we believe competitors will be unable to manufacture products that are equivalent to MST-188 in the manner that regulatory agencies will require and, therefore, will be required to invest in and take the time to conduct clinical studies to demonstrate the safety and efficacy of their follow-on products. We also are evaluating the use of proprietary analytical standards and bioanalytical assays to further augment our control over product quality, as well as developing our own proprietary process for manufacturing API starting material, which we expect would further enhance our proprietary position around MST-188 without regard to indication.

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*Increases partnering interest in and value of MST-188.* We believe that we increase our ability to attract collaborators by pursuing multiple development programs within the MST-188 franchise and, if advantageous, partnering different indications in different jurisdictions. We intend to structure all partnering transactions, whether indication- or product-based and whether regional or global, to ensure that we realize the financial benefit of the development, regulatory and commercial success of MST-188, regardless of the partnered indication, including through milestones, accelerating tiered royalties and, possibly, contingent value rights.

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*Reduces our overall risk profile.* Pursuing multiple development programs reduces the risk associated with any one program, assuming MST-188 has an acceptable safety profile in each indication. Importantly, this diversification can be achieved without the costs typically associated with product pipeline expansion. By leveraging the MAST platform to move MST-188 directly into phase 2 studies, we expect to be able to expand into new indications without the time, expense and distraction needed to identify, negotiate and acquire new product candidates.

### **MST-188**

We are leveraging the MAST platform to develop MST-188. MST-188 is formulated using a purified form of poloxamer 188. Substantial research has demonstrated that poloxamer 188, the active ingredient in MST-188, has cytoprotective and hemorheologic properties and inhibits inflammatory processes and thrombosis. As described below, purified poloxamer 188 was designed to preserve the activity but eliminate certain impurities and other substances that we believe were the cause of the acute renal dysfunction observed in clinical studies of non-purified poloxamer 188 conducted by a prior sponsor.

#### ***Composition and Proposed Mechanism of Action***

The active ingredient in MST-188 is poloxamer 188, a nonionic, block copolymer comprised of a central linear chain of hydrophobic polyoxypropylene flanked on both sides by linear hydrophilic polyoxyethylene chains. The activity of MST-188 is not based on specific receptor/ligand binding interactions, which are the mechanistic bases for most drugs. Rather, its binding activity and pharmacologic effects are driven by hydrophobic adhesive interactions.

The cell membrane is comprised predominantly of lipids and proteins. The fundamental structure of the cell membrane is a phospholipid bilayer that forms a fluid, yet stable, selectively-permeable barrier between the aqueous environments of both the cell interior and exterior. The exterior surface of healthy cell membranes normally is hydrophilic, comprised of the polar head groups of lipid molecules that bury their hydrophobic tails in the interior of the bilayer. When a cell membrane is damaged, the interior hydrophobic regions of the lipid bilayer become exposed.

The cell membrane serves many functions, but one of its primary roles is to regulate the passage of ions and large molecules into and out of the cell and, in particular, to maintain critical transmembrane ion concentrations. Damaged cell membranes result in increased diffusion of ions between the intracellular and extracellular environments. The integrity of a cell membrane can be compromised by chemical agents (e.g., air pollutants, free radicals, poisons), physical trauma (e.g., electric shock, frostbite, radiation, thermal burns, hypovolemia) and disease. Cells have evolved endogenous mechanisms for membrane repair, but membrane injury can exceed the cell's natural repair capacity. If the damage is not repaired, cell ion pumps become overwhelmed and subsequently deplete the cell's energy stores, leading to cell death.

After intravenous administration, the MST-188 hydrophobic polyoxypropylene core is believed to adhere to hydrophobic domains on cell membranes, which, as described above, become exposed when the membrane is damaged. At sites of adhesion, it physically occupies the available area, minimizing or preventing other hydrophobic adhesive interactions, while displacing water and causing lipid molecules to pack more tightly, effectively sealing the damaged area and arresting unchecked transport of ions across the membrane. MST-188 does not bond covalently with the cell membrane and the adhesive interaction is reversible. If the phospholipid density is restored, the physical adhesion may be reversed and MST-188 dislodges from the cell membrane and returns to circulation. While MST-188 adheres specifically to hydrophobic domains, these domains may be widespread in sick or injured patients. As a result, MST-188's activity broadly targets hydrophobic domains, without regard to the cause of the underlying damage, and, as described below, simultaneously may resolve multiple pathophysiologic processes. At the same time, MST-188 has demonstrated little or no affinity for hydrophilic domains and, thus, does not adhere to healthy cells.

#### ***Pharmacodynamics***

MST-188 is believed to exert multiple pharmacologic effects as a result of its adhesion to hydrophobic domains. First, it protects cells by interrupting the pathological cascade associated with cell membrane dysfunction and the resulting diffusion of ions across the membrane. This cytoprotective effect provides time for the cell's natural repair mechanisms to restore the cell to normal functioning, of importance during reperfusion, when viable but damaged cells may not survive the oxidative stress resulting from the reintroduction of oxygenated blood.

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Second, MST-188 improves blood flow, particularly in the microcirculation where the vast majority of oxygen and nutrient exchange occurs, thereby improving tissue perfusion (and reperfusion following ischemia). It impedes the aggregation of red blood cells, or RBCs, by inhibiting the fibrin/fibrinogen cross-bridges that form between RBCs, causing them to aggregate. Since RBCs traverse microcapillaries in single file, the presence in the circulation of RBC aggregates can significantly impair microvascular blood flow. Inhibiting RBC aggregation also reduces blood viscosity, allowing it to flow more readily, particularly in the low shear environment of the microcirculation. The anti-inflammatory and anti-thrombotic/pro-fibrinolytic properties described below also contribute to improved blood flow.

Third, MST-188 inhibits adhesion of circulating blood cells to the endothelium by competing for and physically occupying hydrophobic domains on vessel walls, which has anti-inflammatory effects. Endothelial cells line the interior surface of blood vessels, provide a smooth surface for the flow of blood and regulate the movement of water and dissolved materials between the blood and tissues. The initial step in the inflammatory cascade is adhesion of white blood cells to the endothelium. By blocking adhesive interactions between white blood cells and the vessel wall, MST-188 helps prevent an inflammatory process from beginning.

Fourth, MST-188 helps reduce the pro-thrombotic state that may result from disease or injury. A thrombus, or blood clot, results from aggregation of platelets and clotting factors. Platelet activation, triggered by damage to a vessel wall, causes a cascade of further platelet activation eventually leading to formation of a thrombus. Disease or injury may cause this normal response to turn pathologic, leading to thrombosis, where the thrombus grows to the point of obstructing the flow of blood through the occluded vessel. Studies suggest that MST-188 inhibits weak platelet-activation stimuli (e.g., shear activation of platelets) and release of adenosine di-phosphate from RBCs, minimizing the self-perpetuating response that leads to thrombosis. However, MST-188 does not inhibit strong platelet-activation stimuli (e.g., platelet/receptor interactions directly at the endothelium). Accordingly, we believe MST-188 does not negatively affect normal hemostatic function, which is supported by data from multiple nonclinical studies. Further, MST-188 facilitates fibrinolysis, the body's natural process of dissolving a thrombus. MST-188 adheres to fibrin monomers during clot formation, making them larger and more readily degraded by plasmin, the endogenous fibrinolytic enzyme that dissolves formed clots.

### ***Clinical Application***

We believe the pharmacodynamic properties of MST-188 (cytoprotective, hemorheologic, anti-inflammatory, anti-thrombotic/pro-fibrinolytic) enable it simultaneously to address, or prevent activation of, multiple biochemical pathways that can result in microcirculatory insufficiency, principally characterized by endothelial dysfunction and impaired blood flow. The microcirculation is responsible for the delivery of blood through the smallest blood vessels (arterioles and capillaries) embedded within tissues. A healthy endothelium is critical to a functional microcirculation. Without the regular delivery of blood and transfer of oxygen to tissue from the microcirculation, individual cells (in both the endothelium and tissue) are unable to maintain aerobic metabolism and, through a series of complex and interrelated events, eventually die. If the microcirculatory insufficiency continues, the patient will suffer tissue necrosis, organ damage and, eventually, death.

The potential clinical benefit of MST-188 is greatest in diseases where improving microcirculatory insufficiency is central to improving clinical outcomes. This includes a wide range of seemingly unrelated diseases and conditions. Poloxamer 188 has shown effectiveness in experimental models of stroke, hemorrhagic shock, acute decompensated heart failure, muscular dystrophy, bypass surgery, deep hypothermic circulatory arrest, spinal cord injury, amniotic fluid embolism, acute ischemic bowel disease and burns.

### ***Safety***

As described above under Composition and Mechanism of Action, MST-188 has little or no affinity for undamaged, hydrophilic domains and, thus, has little or no interaction with healthy cells and tissues. In addition, the carbon/oxygen ether bonds that comprise the poloxamer backbone are not susceptible to biologically relevant metabolic pathways in humans. Following administration, essentially all of the drug is recovered, unchanged, in the urine. A small amount is recovered in fecal biliary excretion, presumably following uptake by the reticuloendothelial system. The lack of metabolization and elimination by normal excretion pathways reduces concern over active metabolites driving unintended toxicities.

The safety of poloxamer 188 (both purified and non-purified) has been evaluated in more than 15 clinical studies in multiple indications in which over 2,500 subjects have received active drug. In these studies, poloxamer 188 was generally well-tolerated, with the exception of renal toxicities associated with the non-purified form of poloxamer 188; in particular, in a 2,950-patient, randomized, controlled study in acute myocardial infarction conducted by Burroughs Wellcome (now, GlaxoSmithKline), which we refer to as the CORE study. In contrast, as discussed below, no clinically significant elevations in serum creatinine have been observed in patients treated with purified poloxamer 188.



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### ***Purified Poloxamer 188***

The therapeutic potential of non-purified poloxamer 188 is limited by toxicities associated with low molecular weight substances (e.g., di-block polymers, oligomers, glycols, aldehydes) generated during the chemical process by which the poloxamer is synthesized. We believe these substances were primarily responsible for the acute renal dysfunction observed in prior clinical studies of non-purified poloxamer 188, including the CORE study, and are a principal reason why clinical development of non-purified poloxamer 188 was discontinued by Burroughs Wellcome.

To address the renal toxicity associated with non-purified poloxamer 188, a proprietary manufacturing and purification process was developed to remove certain low molecular weight substances present in non-purified poloxamer 188. In nonclinical studies, compared to the non-purified version, purified poloxamer 188 resulted in less accumulation in kidney tissue, lower levels of serum creatinine, less vacuolization of proximal tubular epithelium, and more rapid recovery from vacuolar lesions. In addition, no difference was observed in the efficacy of purified poloxamer 188 compared to non-purified poloxamer 188.

Data from six clinical studies of purified poloxamer 188, including a 255-patient, phase 3 study in sickle cell disease, demonstrate that purified poloxamer 188 was generally well-tolerated. Transient elevations in liver function tests have been observed, though in each case levels returned to baseline during the follow-up period, except in subjects whose liver function tests had been elevated at baseline. In particular, in contrast to the acute renal dysfunction observed with non-purified poloxamer 188, no clinically significant elevations in serum creatinine were observed in patients treated with purified poloxamer 188. We are developing MST-188 using the purified form of poloxamer 188.

### **Sickle Cell Disease**

#### ***Overview***

Sickle cell disease is an inherited genetic disorder that affects millions of people worldwide. It is the most common inherited blood disorder in the U.S., where it is estimated to affect approximately 90,000 to 100,000 people, including approximately 1 in 500 African American births. More than \$1.0 billion is spent annually in the U.S. to treat patients with sickle cell disease.

Sickle cell disease is characterized by the sickling of red blood cells, which normally are disc-shaped, deformable and move easily through the microvasculature carrying oxygen from the lungs to the rest of the body. Sickled, or crescent-shaped, red blood cells, on the other hand, are rigid and sticky and tend to adhere to each other and the walls of blood vessels (the vascular endothelium).

The hallmark of the disease is recurring episodes of severe pain commonly known as crisis or vaso-occlusive crisis. Vaso-occlusive crisis occurs when the proportion of sickled cells rises, leading to obstruction of small blood vessels and reduced blood flow to organs and bone marrow. This obstruction results in intense pain and tissue damage, including necrosis (tissue death). The frequency, severity and duration of these acute crises can vary considerably. Frequency may range from infrequent to more than monthly and duration is typically four to five days, but may last a week or longer. Over a lifetime, the accumulated burden of damaged tissue frequently results in the loss of vital organ function and a greatly reduced lifespan. The average age of death of a patient with sickle cell disease is under 40 years.

In addition to vaso-occlusive crises, sickle cell patients can suffer many additional complications, including: acute chest syndrome, a respiratory distress syndrome that may arise in the course of an acute crisis; stroke, including silent stroke, which can result from a progressive narrowing of blood vessels, preventing oxygen from reaching the brain; pulmonary hypertension and heart failure; kidney dysfunction and chronic renal failure; bone necrosis of the hip and other major joints; frequent infections due to loss of splenic function and decreased immune function; leg ulcers; blindness; increased rate of complications from pregnancy; and chronic deep muscle and bone pain, even in the absence of acute vaso-occlusive pain.

#### ***Significant Unmet Need***

We estimate that, in the U.S., sickle cell disease results in approximately 100,000 hospitalizations and, in addition, approximately 69,000 emergency department treat-and-release encounters each year. Further, although the number is difficult to measure, we estimate that the number of untreated vaso-occlusive crisis events is substantial and in the hundreds of thousands in the U.S. each year. If MST-188 is approved and as people with sickle cell disease are made aware of the new therapy, we believe that people who would otherwise suffer through a crisis at home may seek treatment.

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We are not aware of any currently available therapeutic agents with demonstrated efficacy in shortening the duration or reducing the severity of an ongoing vaso-occlusive crisis. For patients experiencing a vaso-occlusive crisis, treatment typically consists of hydration, oxygenation and analgesia for pain, usually using narcotics. By improving microvascular blood flow and reducing tissue ischemia, MST-188 has the potential to reduce the severity and shorten the duration of vaso-occlusive crisis and improve patient outcomes.

### *Clinical Development*

#### Overview

MST-188 currently is being evaluated in a phase 3 study in sickle cell disease. In prior-sponsor clinical studies, MST-188 was administered to 211 patients with sickle cell disease over four studies, three of which were for vaso-occlusive crisis, including a 255-patient phase 3 study; the fourth study involved patients with acute chest syndrome. Encouraging results in early clinical studies warranted continued development.

In these studies, MST-188 was generally well-tolerated. Based on an integrated analysis of all four studies, the majority of adverse events reported were mild or moderate. The most common adverse events (incidence >20%) were fever, bilirubinemia direct, pruritus, vomiting, nausea, constipation, headache, tachycardia, pain, weight loss, bilirubinemia, and anemia. The tolerability of MST-188 did not change significantly with increasing exposure (increasing dose and/or duration). The safety profile was similar in children (ages 18 and younger) compared to adults.

#### Ongoing and Planned Clinical Studies

*Phase 3 Study; EPIC (Evaluation of Purified 188 In Children).* In January 2013, we initiated EPIC, a randomized, double-blind, two-arm, placebo-controlled, phase 3 study of MST-188 in patients with sickle cell disease. We considered the study initiated when we opened the first clinical site in the study and we consider a site open when all of the following have been completed: we and the site have signed an agreement regarding the conduct of the study at the site, which agreement includes the budget and compensation for activities related to conducting the study; the site has received approval from its IRB to participate in the study; we have conducted a site initiation visit involving our personnel and key personnel from the site who will be involved in the study; and MST-188 clinical trial material for use in the study has been delivered to the site. Even after a site is open, however, it typically must complete a variety of internal procedures before it is ready to enroll patients in a study.

The primary objective of EPIC is to demonstrate that MST-188 reduces the duration of vaso-occlusive crisis, with the duration of crisis measured from the time a patient is randomized to the time at which the patient receives the last dose of parenteral opioid analgesic for the treatment of vaso-occlusive crisis prior to hospital discharge. A total of 388 patients, ages 8 to 17, who have sickle cell disease and are experiencing acute pain typical of vaso-occlusive crisis will be enrolled. Using a two-sided alpha of 0.05, the study has approximately 90% power to detect a 16-hour difference between treatment arms. Secondary endpoints will compare the rate of re-hospitalization for vaso-occlusive crisis within 14 days of initial discharge from the hospital and the occurrence of acute chest syndrome within 120 hours of randomization.

We expect to enroll subjects from approximately 40 sites in the U.S. and 30 sites outside the U.S. In mid-March, the first open site in EPIC was ready to enroll patients. The first patient was dosed in May 2013. As of June 4, 2013, we had opened 14 sites and nine of these sites had completed their internal procedures. In addition, five patients had pre-consented to participate in the study. While predicting the rate of enrollment in any clinical study, including EPIC, is subject to a number of assumptions and the actual enrollment rate may differ materially from our estimates, we expect to complete enrollment in 2015. We anticipate enrollment in 2013 will be slow, after accounting for the time needed to open sites, for open sites to complete their internal procedures, and to create awareness of the study among potential participants. In particular, during the early stages of EPIC (i.e., during 2013), most potential participants and their parents (or other guardian) will first be introduced to the study in the emergency department during an ongoing crisis episode, a difficult environment in which to evaluate the benefits and risks of participating in a clinical study. However, over time, as our study outreach and awareness activities reach a broader portion of potential participants, and as investigators introduce the study to their patients during regular check-up visits and patients pre-consent to participate in the study, we expect the rate of enrollment to increase.

*EPIC Sub-Study.* It is generally believed that the long-term morbidity and mortality associated with sickle cell disease is the consequence of a lifetime of repeated vaso-occlusive events and the ensuing ischemia and end-organ damage. We believe decreased microvascular blood flow, or mBF, results in decreased tissue oxygenation and is the physiologic mechanism through which sickle cell disease induces both immediate and long-term clinical events. While the cumulative effect of vaso-occlusive episodes may lead to premature end-organ failure and death, the incremental effect of an individual episode on organ damage may not present clinically and may not be measurable with current technology. However, it is possible to measure changes in underlying pathophysiology, such as mBF. As such, we believe the effect of MST-188 on mBF may be relevant in assessing long-term outcomes for sickle cell patients and that mBF, alone or in combination with measures of tissue oxygenation, may be reasonably likely to predict clinical benefit in sickle cell disease. In the fourth quarter of 2013, we plan to initiate a

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sub-study within EPIC to evaluate the effect of MST-188 on mBF, as well as tissue oxygen saturation, or StO<sub>2</sub>. This sub-study will be conducted at select EPIC sites using non-invasive devices to measure mBF and StO<sub>2</sub> and we plan to enroll approximately 30 patients.

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*TQT Study.* In January 2013, we also initiated a thorough QT/QTc study, or TQT study, of MST-188 to evaluate the effect of therapeutic and supra-therapeutic doses of MST-188 on cardiac ventricular repolarization, specifically the QT-interval. The FDA typically requires an assessment of cardiac repolarization for new drugs having systemic bioavailability. The study is a single-center, four-period, four-way cross-over, placebo- and positive-controlled, double-blind, randomized trial. Dosing is completed and we expect to announce study results in the third quarter of 2013.

### Prior-Sponsor Studies in Sickle Cell Disease

*Phase 3 Study in Vaso-Occlusive Crisis.* A 255-subject, randomized, double-blind, placebo-controlled study of MST-188 in patients with sickle cell disease experiencing vaso-occlusive crisis was conducted in 1998-1999. Signs of efficacy were observed in the primary endpoint, duration of crisis, but it did not reach statistical significance. An 8-hour decrease in the duration of crisis (approximately 132 hours in the MST-188 group compared to approximately 140 hours in the control group ( $p=0.072$ )) was observed in the intent-to-treat population ( $n=249$ ). Notably, *post hoc* analyses identified a statistically significant and greater treatment effect in patients under 16 years of age. Among patients under 16 years of age ( $n=73$ ), there was a 21.6-hour decrease in the duration of vaso-occlusive crisis in the MST-188 group compared to the placebo group ( $p=0.010$ ).

A potentially significant limitation of the prior phase 3 study is that it did not follow subjects until hospital discharge; rather, subjects were followed for 168 hours from randomization and any subject whose crisis had not resolved by 168 hours was, for purposes of determining that patient's duration of crisis, attributed a duration of exactly 168 hours. This truncation had a potentially significant effect on the duration of crisis reported in the prior phase 3 study, particularly because a substantial number of subjects did not achieve crisis resolution within 168 hours. However, a responder's analysis, which analyzes the proportion of subjects who had achieved crisis resolution at 168 hours (without attribution), would not be affected by this truncation and may provide a more accurate picture of the MST-188 treatment effect in this setting. In a *post-hoc* responder's analysis, in the intent-to-treat population ( $n=249$ ), over 50% of subjects receiving MST-188 achieved crisis resolution within 168 hours, compared to 37% in the control group ( $p=0.02$ ). Likewise, in the under-16 age group, over 60% of the MST-188 group achieved crisis resolution within 168 hours, compared to under 28% of the control group ( $p=0.009$ ).

Notably, the prior phase 3 study was the first large, interventional study in sickle cell disease. We believe features of the study's design and the study enrolling fewer than the originally-planned number of patients, which was 350 patients, may have further diluted the treatment effect observed in the study, or its significance. In addition to avoiding arbitrary observation periods (e.g., 168 hours), which will allow us to minimize the truncation effect described above, other lessons that we learned from the prior phase 3 study include: simplifying the primary endpoint, to minimize protocol violations and left censored data; avoiding subjective endpoints, which increase variability; standardizing pain management practices across study sites; increasing homogeneity in terms of cumulative disease burden; controlling the duration of crisis prior to randomization; and limiting the heterogeneity of sickle cell disease genotypes.

In terms of safety, no clinically significant differences in the overall incidence of adverse events or adverse events defined as serious were observed between the MST-188 and placebo groups. Notably, there were no clinically significant changes in renal function following treatment with MST-188 compared to placebo. The MST-188 arm was associated with transient elevations of liver function tests (total and direct bilirubin, AST (aspartate aminotransferase), and ALT (alanine aminotransferase)), each of which returned to its respective baseline level by the day-35 follow-up visit, except in patients whose liver function tests had been elevated at baseline. Adverse events with a greater than 5% increased incidence in the MST-188 group compared to the placebo group and their incidences for MST-188 and placebo patients, respectively, were as follows: bilirubinemia direct (54% vs. 37%), bilirubinemia (21% vs. 13%), ALT increased (12% vs. 2%), thrombocytopenia (25% vs. 16%), nausea (41% vs. 34%), vomiting (36% vs. 28%), weight loss (28% vs. 15%), and urticaria (6% vs. 0%). Serious adverse events were reported for 23% and 22% of the patients in the MST-188 and placebo groups, respectively. Six patients in the MST-188 group discontinued treatment due to adverse events that included fever, bilirubinemia, tachycardia, pruritus, anemia, embolus, thrombocytopenia, acute chest syndrome, hypoxia, and dyspepsia. One patient in the MST-188 group died due to cardiopulmonary arrest, which was considered secondary to a fat embolism based on autopsy. The study investigator believed the underlying cause of death was due to sickle cell disease and not to treatment with MST-188.

*Phase 1 Study in Vaso-Occlusive Crisis.* A phase 1, multicenter study was conducted to evaluate the safety and pharmacokinetics of MST-188 in patients with sickle cell disease experiencing vaso-occlusive crisis. The study enrolled 17 adults (ages 19 and older) and 15 received study drug but two discontinued prior to completing the full dose due to breakthrough crisis pain and a problem with the IV line administration, respectively. The most common adverse events (incidence >20%) were vomiting, nausea, headache, bilirubinemia, fever, anemia, and abdominal pain. Serious adverse events were reported in six patients. The serious adverse events experienced by five of the six patients were considered unrelated to study drug. The serious adverse events experienced by the sixth patient were nausea, vomiting, and abdominal pain that were considered possibly related to study drug. No clinically significant changes in renal function were observed.

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*Repeat Exposure Study in Vaso-Occlusive Crisis.* An open-label, multicenter study was conducted to evaluate the safety of repeat exposure of MST-188 in patients with sickle cell disease experiencing vaso-occlusive crisis. The study enrolled 28 patients, 16 of whom were children (ages 18 and younger). MST-188 was administered as a treatment for up to six episodes of vaso-occlusive crisis within a period of one year from enrollment. Seventeen patients received two or more exposures and one patient received six exposures. The most common adverse events (incidence >20%) were fever, pruritis, bilirubinemia direct, constipation, nausea, vomiting, tachycardia, abdominal pain, headache, thrombocytopenia, ALT increase, urine abnormality, jaundice, and dyspnea. Serious adverse events were reported in five patients. One study patient died sixteen days after the completion of treatment. The cause of this patient's death is not known, but the study investigator attributed it to sickle cell disease and considered it to be unrelated to study treatment. Two other subjects discontinued treatment due to adverse events. No clinically significant changes in renal function were observed.

*Acute Chest Syndrome.* A dose-escalating, multicenter study was conducted to evaluate the safety and pharmacokinetics of MST-188 in patients with sickle cell disease experiencing acute chest syndrome. The study enrolled 43 patients who were under 65 years of age and 42 received study drug. The median age of the patients was 19 years (range of 1 to 38 years). Patients were randomized to one of five dose groups and MST-188 was administered as a continuous, two-stage, intravenous infusion over 24 hours. All patients received a loading dose of 200 mg/kg given over one hour, followed by one of the following maintenance doses: 40 mg/kg/hr, 60 mg/kg/hr, 80 mg/kg/hr, 100 mg/kg/hr or 120 mg/kg/hr given over 23 hours. Secretory phospholipase A2 (sPLA<sub>2</sub>) was measured as an efficacy biomarker. sPLA<sub>2</sub> has been shown in clinical studies to correlate with the onset and resolution of acute chest syndrome. Among the 34 patients who had elevated sPLA<sub>2</sub> levels at baseline, levels returned to steady-state levels by the end of the 24-hour infusion period and remained at steady-state through follow-up. All doses appeared equally effective.

Notably, while the mean duration of hospitalization in a 538-subject, 30-center study of patients with sickle cell disease experiencing acute chest syndrome published in the *New England Journal of Medicine* (2000) was 12.8 days for patients older than 19 years (n=128) and 9.9 days for patients 19 years and younger (n=409), in the dose-escalating study of MST-188 in acute chest syndrome, the mean duration of hospitalization of patients older than 19 years (n=14) was 7.2 days for patients in the low dose groups (maintenance doses of 40, 60 or 80 mg/kg/hr, n=10) and 6.3 days for patients in the high dose groups (maintenance doses of 100 or 120 mg/kg/hr, n=4) and the mean duration of hospitalization of patients 19 years and younger (n=27) was 7.9 days for patients in the low dose groups (n=20) and 4.1 days for patients in the high dose groups (n=7).

In terms of safety, MST-188 was generally well-tolerated at all dose levels. The most common adverse events (incidence of >20%) were fever, pain, tachycardia, constipation, vomiting, bilirubinemia, bilirubinemia-direct, weight loss and rhinitis. Serious adverse events were reported in eight patients (19%), and two patients had serious adverse events considered related to study treatment (abnormal gait, bilirubinemia and bilirubinemia-direct), but no patients discontinued treatment due to adverse events. One patient died during the study due to acute respiratory distress syndrome. That patient had a cardiac arrest and was resuscitated, but developed acute respiratory distress syndrome and died on day 8 post-treatment. The study investigator considered the patient's death unlikely to be attributable to the study drug. Importantly, results from the renal function test did not reveal any pattern or dose-related effects suggestive of renal dysfunction across the range of doses studied.

*Phase 2 Study of Non-Purified P188 in Vaso-Occlusive Crisis.* Prior to development of purified poloxamer 188, non-purified poloxamer 188 was evaluated in a phase 1 study in patients with sickle cell disease (n=7) and a randomized, double-blind, placebo-controlled, multicenter phase 2 study in patients with sickle cell disease experiencing vaso-occlusive crisis. The phase 2 study enrolled 50 patients ages 15 and older, with 28 randomized to receive non-purified poloxamer 188 and 22 to receive placebo. Study medication was administered as a continuous, two-stage, intravenous infusion over 48 hours. In the efficacy analyses, three subgroups of patients were considered: subgroup 1 (n=49) was the intent-to-treat population, subgroup 2 (n=45) excluded patients with a study drug infusion duration of less than 24 hours, and subgroup 3 (n=31) excluded patients who did not receive the full dose of study drug or for whom the end-of-painful episode time was estimated. Safety data were analyzed in all 50 patients. The primary endpoint in this study was duration of crisis and secondary endpoints were pain intensity, total analgesic use, and days of hospitalization. Median duration of crisis was reduced in the non-purified poloxamer 188 group compared to the control group by 13 hours in subgroup 1 (67 vs 80 hours, p=0.147), by 28 hours in subgroup 2 (60 vs 88 hours, p=0.097), and by 36 hours in subgroup 3 (44 vs 80 hours, p=0.020). Duration of hospitalization was reduced in the non-purified poloxamer 188 group compared to the control group by one day in subgroup 1 (5 vs 6 days, p=0.298), by two days in subgroup 2 (5 vs 7 days, p=0.261), and by two days in subgroup 3 (5 vs 7 days, p=0.145). Total analgesic use (measured by morphine equivalent units, or MEU) was reduced in the non-purified poloxamer 188 group compared to the control group by 102 mg in subgroup 1 (median MEU of 57 mg vs 159 mg, p=0.055), by 120 mg in subgroup 2 (median MEU of 49 mg vs 169 mg, p=0.037), and by 111 mg in subgroup 3 (median MEU of 34 mg vs 145 mg, p=0.014). Parenteral analgesic use was reduced in the non-purified poloxamer 188 group compared to the control group by 102 mg in subgroup 1 (median MEU of 47 mg vs 149 mg, p=0.075), by 110 mg in subgroup 2 (median MEU of 40 mg vs 150 mg, p=0.048), and by 106 mg in subgroup 3 (median MEU of 27 mg vs 133 mg, p=0.014).

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In terms of safety, non-purified poloxamer 188 was generally well-tolerated. Adverse events were similar in both groups and most were either mild or moderate in intensity. The most common adverse events (incidence >5%) were headache, nausea, injection site pain, abdominal pain, vomiting and constipation. One adverse event was considered serious and attributable to study medication – a subject in the non-purified poloxamer 188 with mild underlying renal dysfunction (baseline creatinine 1.5 mg/dL) had a transient increase in serum creatinine concentration during infusion (peak concentration = 2.7 mg/dL). No treatment was required and his creatinine returned to baseline by the time of the follow-up assessment.

### **Arterial Disease**

#### ***Introduction***

As discussed more fully below, data from experimental models demonstrate the potential of MST-188 to improve outcomes in patients experiencing complications of arterial disease. For these indications, we believe MST-188 may be useful as a stand-alone agent or as an adjunct to thrombolytics. We plan first to demonstrate its potential in acute limb ischemia, a complication of peripheral arterial disease. Ultimately, we plan to leverage the clinical data generated in ALI studies to find a partner to develop MST-188 in larger market indications within arterial disease, such as ischemic stroke.

#### ***Overview***

Arterial disease resulting from atherosclerotic and thromboembolic processes is associated with significant morbidity and mortality. It is a common circulatory problem in which plaque-obstructed arteries reduce the flow of blood to tissues. Atherosclerosis occurs with advanced age, smoking, hypertension, diabetes and dyslipidemia.

Peripheral arterial disease, or PAD, refers to disease affecting arteries outside the brain and heart and often refers to blockage of arteries in the lower extremities. Progression of PAD is associated with ongoing obstruction, or occlusion, of the peripheral arteries, which can occur slowly over time or may lead to a sudden, acute occlusion. Acute limb ischemia, or ALI, is a sudden decrease in perfusion of a limb, typically in the legs, that often threatens viability of the limb. The condition is considered acute if clinical presentation occurs within approximately two weeks after symptom onset. Critical limb ischemia, or CLI, occurs after chronic and severe lack of blood flow to an artery that leads to leg pain while resting, ulcers and gangrene. In contrast to CLI, in which collateral blood vessels may circumvent an occluded artery, ALI rapidly threatens limb viability because there is insufficient time for new blood-vessel growth to compensate for loss of perfusion.

#### ***Significant Unmet Need***

There are an estimated 8 to 12 million people with PAD in the United States. This prevalence is expected to increase, not only in the U.S., but throughout the world, as the population ages, cigarette smoking persists, and the prevalence of diabetes mellitus and obesity grows. Acute limb ischemia is an orphan disease within PAD with significant unmet needs. Despite urgent revascularization with thrombotic agents or surgery, for patients presenting with ALI, the 30-day amputation rate is 10% to 30% and the mortality rate is 15% to 20%.

Timely restoration of blood flow is central to the treatment of acute events associated with arterial disease. Current treatment options for ALI include revascularization with thrombolytics, endovascular treatment, open surgery, or various combinations of these approaches. The principal goal is to restore blood flow and tissue perfusion as rapidly as possible – rapid restoration of tissue perfusion is critical to regaining clinical function.

Current treatments focus on dissolution of the blood clots and improving blood flow in large arteries. However, these approaches may not improve flow in the microcirculation, where the vast majority of oxygen and nutrient transport occurs. In addition, while restoration of blood flow is required for limb salvage, the reintroduction of blood flow can initiate reactive hyperemia, leading to reperfusion injury. Existing treatments are not effective at reducing reperfusion injury. Many patients also suffer re-thrombosis/re-stenosis, in which new clots form in a previously treated blood vessel.

A pharmacologic agent that simultaneously can address the limitations of current treatment options is needed to improve clinical outcomes. We believe the mechanistic activities of MST-188 to shorten time to thrombolysis, reduce re-thrombosis and, independent of these, improve blood flow, as well as protect tissues from reperfusion injury, will have utility in treating acute complications of thrombotic arterial disease. These activities have been demonstrated in experimental and clinical studies, as discussed below.



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### ***Nonclinical Data***

#### **Effect on thrombolysis, blood flow and re-thrombosis/re-stenosis**

The effectiveness of thrombolytic therapy is limited by the time required to achieve thrombolysis, or dissolution of the occluding clot, the extent of blood flow following thrombolysis and the time to and incidence of re-thrombosis.

To assess whether poloxamer 188 improves these outcomes, it was evaluated in an experimental femoral artery thrombolysis model. Tissue plasminogen activator, or tPA, was administered either in combination with saline (control) or poloxamer 188. The time to restoration of flow, or reperfusion, and the extent of flow following reperfusion were measured using a calibrated electromagnetic flow probe. Treatment with poloxamer 188 resulted in a 38% shorter time-to-reperfusion, compared to tPA plus saline ( $26 \pm 3$  minutes v.  $42 \pm 6$  minutes, respectively) ( $p < 0.04$ ). Blood flow following reperfusion was also significantly increased (by 28%) over tPA plus saline ( $p < 0.02$ ) and the time to re-occlusion was also significantly prolonged ( $50 \pm 13$  min vs.  $22 \pm 2$  min) ( $p < 0.04$ ).

#### **Effect on reperfusion injury**

Reperfusion injury is the paradoxical damage to tissues caused by the restoration of blood flow following a period of ischemia. It is believed to result from activation of inflammatory and oxidative processes upon ischemia-injured cells.

To determine its effect on reperfusion injury, poloxamer 188 was evaluated relative to sham and saline controls in a reperfusion model following one hour of ischemia. Treatment effects were evaluated based on histopathology, myeloperoxidase and heme-oxygenase activity and edema score, and gene expression arrays covering the spectrum of genes associated with ischemia/reperfusion injury. Study treatments were administered during reperfusion.

Compared to sham, histopathology following saline control showed marked damage to tissue cyto-architecture, as well as hemorrhage, edema, ulceration and inflammatory cell infiltration. In contrast, histopathology following treatment with poloxamer 188 appeared nearly identical to sham, with little damage to tissue architecture and none of the changes observed with saline control. Quantification of these observations using the Chui score showed the differences were statistically significant ( $2.66 \pm 0.3$  vs.  $1.16 \pm 0.16$  for saline and poloxamer 188, respectively) ( $p < 0.05$ ).

Consistent with histopathology, myeloperoxidase and heme-oxygenase activity and edema all were significantly elevated following reperfusion injury. These markers were significantly reduced following treatment with poloxamer 188, but not saline control. Gene expression arrays further validated the histopathological observations. Compared to sham, expression of important injury pathways (including acute phase reactants, adhesion receptors, coagulation enzymes, chemokines, matrix metalloproteinases, apoptosis and VEGF signaling) remained altered in saline controls. However, in almost every case, gene expression returned toward sham levels following treatment with poloxamer 188 in those instances where gene expression was altered by ischemia/reperfusion injury.

#### **Effect on re-thrombosis/re-stenosis**

Poloxamer 188 was evaluated for its effect on acute thrombosis in a model of experimental angioplasty and stent placement. Specifically, this model measured the extent of artery occlusion following placement of a coiled wire stent under excessive angioplasty pressure. Control treatment (saline plus heparin) resulted in average occlusion of about 63%. Test treatment (poloxamer 188 plus heparin) resulted in significantly less occlusion (mean of about 13%) ( $p = 0.001$ ).

Electron micrographs of the occlusive thrombi revealed that platelets adhered to areas damaged by the angioplasty with both control and test treatments. However, platelets degranulated and accumulated to form large thrombi with control treatment while, with test treatment, platelets did not de-granulate or accumulate and a smaller layer of adherent platelets was observed. These observations suggest that poloxamer 188 cannot overcome the highly specific platelet/vessel wall interactions needed to stop bleeding associated with injury. However, it is able to inhibit the extension of a platelet thrombus, when the stimulus for the growing thrombus is the thrombus itself.

#### **Effect on blood flow in experimental ischemic stroke**

The effect of poloxamer 188 on cerebral artery blood flow was measured over four hours following experimentally induced complete occlusion. Blood flow was measured using a well-established hydrogen wash-out technique. Poloxamer 188, but not placebo, increased blood flow by an average of 121% in areas of severe or moderate ischemia, but had little effect in areas with mild or no ischemia. These observations suggest poloxamer 188 improves flow in ischemic tissues without stealing flow from non-ischemic tissues. The overall difference in blood flow between



poloxamer 188 and placebo at four hours following occlusion was statistically significant ( $p = 0.001$ ).

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### ***Clinical Data***

Clinical trials directly evaluating the effect of MST-188 on clinical outcomes in ALI have not been conducted. However, its synergy with thrombolytics and its pharmacological effects on arterial and microvascular blood flow and reperfusion injury have been observed in studies of poloxamer 188 in patients with acute myocardial infarction and sickle cell crisis. We believe these previously observed effects have potential to translate into clinically meaningful benefits in ALI and other conditions where thrombolytics are indicated or useful.

The effect of poloxamer 188 on early coronary patency and reperfusion injury was evaluated in a randomized, multicenter, placebo-controlled phase 2 study in patients receiving thrombolytic therapy for acute myocardial infarction, which we refer to as the Pre-CORE Study. One hundred fourteen patients with symptoms consistent with acute myocardial infarction were randomized immediately after the initiation of thrombolytic therapy to receive poloxamer 188 (test) or placebo (control). Myocardial infarct size was assessed through SPECT imaging. Global LV ejection fraction was assessed through radionuclide angiography performed 5 to 7 days after randomization. Median infarct size was significantly smaller in the test group than in the control group ( $p=0.031$ ). Median LV ejection fraction was significantly higher in the test group than in the control group ( $p=0.020$ ). In addition, the incidence of in-hospital reinfarction was significantly lower in the test group than in the control group ( $p=0.016$ ). The study investigators concluded that poloxamer 188 may enhance early coronary patency (time to reperfusion) by accelerating thrombolysis and may reduce reperfusion injury (as evidenced by reduced myocardial infarct size and improved LV function).

The effect of poloxamer 188 on coronary artery patency also was evaluated in a randomized sub-study conducted as part of the CORE Study, an approximately 2,950-patient phase 2 study in acute myocardial infarction. In the sub-study, seventy one patients with symptoms consistent with acute myocardial infarction were randomized shortly after initiating thrombolytic therapy to receive poloxamer 188 (test) or placebo (control). Patency was assessed in the infarct-related artery with angiograms completed 70 to 100 minutes after randomization. All angiograms were analyzed in a central laboratory without knowledge of treatment assignment or clinical outcome and assigned a thrombolysis in myocardial infarction, or TIMI, grade flow score. TIMI grade flow is a scoring system from 0-3 referring to levels of coronary blood flow assessed during percutaneous coronary angioplasty. The rates of TIMI grade 2 or 3 (partial or complete perfusion) were 74% in the test group and 54% in the control group ( $p=0.11$ ). These data suggest that treatment with poloxamer 188 results in greater proportion of patients achieving clinically significant reperfusion (TIMI grades 2 or 3) compared to control. For the overall CORE Study, outcomes were equivocal in the primary endpoint a composite outcome of death, reinfarction and cardiogenic shock at 35 days post-randomization. However, the comparable dosing regimens that were evaluated and found effective in the Pre-CORE Study (described in the preceding paragraph) were discontinued within months of initiation of the CORE Study as a result of the acute renal dysfunction described above under Purified Poloxamer 188. We believe discontinuation of the two high-dose regimens and the low-dose/longer-duration regimen in the CORE Study, and that 92.5% of patients who received active drug in the CORE Study received a low-dose/shorter-duration regimen, negatively impacted the overall study results.

The effect of MST-188 on microvascular blood flow was evaluated in a randomized, double-blind, placebo-controlled sub-study conducted as part of a phase 3 study in sickle cell disease. Nine patients with sickle cell disease who were hospitalized for vaso-occlusive crisis were studied to objectively, longitudinally and quantitatively investigate the *in vivo* effects of MST-188 on real-time microcirculation in the bulbar conjunctiva during vaso-occlusive crisis. Subjects were randomly assigned to receive MST-188 (test) or placebo (control). Following treatment, compared to control, all four patients treated with MST-188 showed significant improvement in red blood cell velocity at both approximately two hours ( $p=0.001$ ) and at seven hours ( $p=0.000032$ ) after initiation of treatment. For the MST-188 subjects, the velocity values observed at seven hours after initiation of treatment were similar to historical steady-state (non-crisis) values for sickle cell patients.

### ***Planned Development***

#### **Acute Limb Ischemia**

We are planning a phase 2, clinical proof-of-concept study to evaluate the safety and efficacy of MST-188 in ALI. We plan to submit a protocol for our planned phase 2, clinical proof-of-concept study in ALI to the FDA in the third quarter of 2013 and, depending in part upon FDA input, we expect to initiate the study in late 2013 or early 2014. We anticipate that the study will enroll approximately 60 patients and compare one or more doses of MST-188 in combination with a thrombolytic against the thrombolytic alone. Efficacy will be assessed primarily on measures of improved arterial patency and tissue perfusion. We expect the study will take approximately 15 months to enroll.

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### **Acute Ischemic Cerebrovascular Infarction (Stroke)**

Although we currently are focused on ALI, there may be substantial growth opportunities for MST-188 within arterial disease. 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 ALI, an advanced form of arterial disease, 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. 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.

Treatment options for stroke are similar to those for ALI, except that surgical intervention is less viable in stroke due to proximity of the occluded artery to the brain, making intravenous and intraarterial thrombolytic therapy the dominant treatment modalities. Timely intervention is particularly critical as brain damage during acute ischemic stroke is a rapid, progressive process. In a typical large-vessel acute ischemic stroke, 1.9 million neurons may be lost each minute without management. In addition, brain cells in the ischemic penumbra that remain metabolically active may be salvageable with timely assessment and management. As described above, compared to tPA alone, poloxamer 188 accelerated time-to-reperfusion by approximately 40% when used in combination with tPA, the only FDA-approved thrombolytic treatment for acute ischemic stroke. However, tPA has not demonstrated improved outcomes if administered more than three hours after onset of stroke symptoms. If the results observed in experimental models are demonstrated in clinical studies, MST-188 may improve the effectiveness of tPA, including by lengthening the window in which tPA is effective in patients presenting with ischemic stroke.

### **Resuscitation of Shock Following Major Trauma**

#### ***Introduction***

As discussed more fully below, MST-188 has improved survival in numerous nonclinical studies in hemorrhagic shock, and we believe it has potential to improve outcomes for patients who experience shock following major trauma. However, based on our current focus on the phase 3 study in sickle cell disease and development for complications of arterial disease, it is unlikely we would initiate a clinical study in this indication without funding from the U.S. government or some other third-party collaborator.

#### ***Overview***

Trauma care is a major part of the U.S. medical economic system. Based on 2009 data, trauma-related disorders rank among the top five most costly medical conditions in the U.S., with estimated health care expenditures totaling more than \$80 billion, and we estimate that the incidence of severe hemorrhage resulting from trauma is greater than 780,000 per year. Major trauma typically involves multiple injuries, blood loss, shock, need for emergency surgical intervention and resuscitation.

Shock following massive bleeding, or hemorrhagic shock, is a physiologic response based on an imbalance between systemic oxygen delivery and oxygen consumption. Initially, as circulating blood volume falls due to hemorrhage, the body activates a variety of physiologic responses to maintain blood pressure and the flow of oxygen-rich blood to tissues. However, if circulating volume is not restored, these compensatory mechanisms begin to fail. As cells become increasingly hypoxic and their metabolic energy requirements are not met, cell membrane integrity is compromised, ions diffuse between the intracellular and extracellular environments, fluid leaks into the interstitial space and inflammatory and clotting cascades are triggered. Even following resolution of the underlying hemorrhage and restoration of circulating volume, periods of ischemia can result in tissue and organ damage and death.

The primary treatment goal in major trauma is to stop the bleeding, typically through surgery, followed by restoration of circulating blood volume and pressure, referred to as resuscitation. Resuscitation is achieved through intravenous administration of blood products (e.g., packed red blood cells, plasma) and non-blood fluids (e.g., colloids, crystalloids), as well as with the use of vasopressors to constrict blood vessels and increase blood pressure.

#### ***Significant Unmet Need***

Since World War I, the epidemiology of death from trauma has changed. Rates of early hospital death from blood loss have been reduced with the introduction of damage control surgery. The advent of regional trauma systems that enable rapid triage and intervention has improved mortality rates. However, while victims of major trauma often will survive, complications are frequent and recovery prolonged. Treatment costs are high and increase rapidly with severity. The estimated per patient cost to treat trauma-induced shock is \$51,000, rising to \$148,000 in cases of severe shock and \$312,000 if multiple organ failure presents.



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Multiple organ failure, or MOF, remains a major cause of prolonged stay in the intensive care unit, or ICU. Increased understanding of the pathogenesis of MOF suggests that shock initiates a dysfunctional inflammatory process that causes or contributes to MOF. While resuscitation is necessary for patient survival, most resuscitation fluids are not directed at modulating inflammation and, in fact, may worsen it. Reperfusion injury, where tissue and organ damage occur due to the introduction of blood and other resuscitation fluids (e.g., as a result of oxidative damage and inflammation), remains a significant concern.

Despite significant morbidity and expense, for over 20 years, there have been no major advances in therapeutics approved for resuscitation following severe hemorrhage. Based on its hemorheologic, cytoprotective and anti-inflammatory properties, MST-188 may have utility as an adjunct therapy for resuscitation following major trauma.

### ***Nonclinical Data***

The potential clinical benefits of MST-188 are suggested by the results of numerous experimental models of hemorrhagic shock. For example, an article in *Shock* (October 2009) summarized the results of MST-188 in multiple models of hemorrhagic shock. In these studies, which we refer to as the Hunter Studies, relative to control, MST-188 decreased fluid requirements required to regain and maintain hemodynamic performance goals ( $p=0.0002$ ); reduced tissue permeability/fluid extravasation in the lung and small intestine ( $p<0.01$ ); reduced myeloperoxidase, a marker of inflammation ( $p=0.02$ ), and caspases 3, 6, 8 and 9, mediators of apoptosis ( $p=0.04$ ); and improved survival ( $p<0.001$ ). The study investigators concluded that MST-188 has a significant cytoprotective effect in preventing endothelial and other cell damage during hypotension and reperfusion and inhibited both necrosis and apoptosis induced by trauma.

A study published in *Resuscitation* (June 2011) and funded by the Defense Advanced Research Projects Agency (DARPA) Surviving Blood Loss (SBL) program, which we refer to as the DARPA Study, evaluated MST-188 in a severe hemorrhage model developed specifically for evaluating low volume resuscitation products as part of the DARPA SBL program. MST-188 significantly improved median survival time after severe controlled hemorrhage, compared to control ( $p=0.0186$ ). The DARPA Study also evaluated thrombelastography, or TEG, a measure of the efficiency of blood coagulation. Results from the DARPA Study suggested that MST-188 caused TEG abnormalities consistent with an anti-coagulant effect. Thus, while the survival results were positive and consistent with prior studies, the study investigators were uncertain as to the utility of MST-188 in uncontrolled hemorrhage due to its negative effect on coagulation, as measured by TEG, and recommended additional experiments to determine the physiological significance of the TEG results.

Notably, the Hunter Studies also evaluated MST-188 in an experimental model of uncontrolled hemorrhage, and reached a contrary conclusion to that in the DARPA Study with regard to the effect of MST-188 on bleeding risk. In the uncontrolled hemorrhage model conducted as part of the Hunter Studies, mean blood loss was similar in the MST-188 and control groups, as was distribution around the mean. In fact, the MST-188 group had slightly less bleeding. These findings were consistent with prior studies demonstrating that MST-188 did not adversely affect blood coagulation, platelet aggregation or bleeding time. However, TEG data were not collected in the Hunter Studies.

### ***Planned Development and Other Activities***

#### **Nonclinical Activities**

We plan to evaluate the physiologic significance of the TEG results observed in the DARPA Study through series of nonclinical studies, which we refer to as the TEG Studies. We believe that MST-188's hydrophobic interactions decrease the number of RBCs in a forming clot, which would affect TEG. However, while MST-188 affects TEG, we believe it does not negatively affect clot integrity or hemostatic function because the tensile strength of a clot is largely dependent on fibrin polymerization and not the presence of RBCs within the clot structure. This position is supported by a direct, *in vivo* evaluation of bleeding in a model of uncontrolled hemorrhage, as reported in the *Shock* article, as well as substantial *in vitro* and *ex vivo* data from numerous nonclinical and clinical studies demonstrating that MST-188 does not adversely affect blood coagulation, platelet aggregation or bleeding time. We expect to announce the results of the TEG Studies in the second half of 2013.

#### **Phase 2 Clinical Study**

If the results of the TEG Studies support that MST-188 does not increase bleeding risk, and subject to the third-party funding described below, we plan to conduct a dose-finding, phase 2, clinical proof-of-concept study. Over the past several months, in collaboration with a leading university in the research and care of trauma patients, we have developed the protocol for a randomized, placebo-controlled, dose-escalation study in patients admitted to the ICU for shock resuscitation following major torso trauma. The study would evaluate the safety of MST-188, as well as its efficacy based on clinical and nonclinical parameters, including endothelial activation, immune system response, tissue perfusion, fluid and other intervention requirements, time to resuscitation, complication rates, ICU-free days, hospital-free days and 28-day survival.



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We would expect to enroll approximately 60 patients and that enrollment would take approximately 18 to 24 months. The study would be conducted at a single site in the U.S. A key component of the study is adherence to a resuscitation protocol that incorporates goal-directed treatment and standardizes patient care across the study, an important variable that may not have been controlled adequately in prior studies of other investigational drugs in hemorrhagic shock.

### **U.S. Government or Other Third-Party Funding**

The U.S. government previously funded the DARPA Study through the SBL program. If we demonstrate that the TEG results observed in the DARPA Study do not have physiologic significance, we believe the government will have renewed interest in developing MST-188 as a therapy in major trauma.

We have identified relevant RFPs (requests-for-proposals) issued by U.S. government agencies and have prepared applications to request funding, which we plan to submit in the third quarter of 2013. However, absent interest from the U.S. government or another third party, it is unlikely we would initiate the phase 2 study described above.

### ***Limitations of Prior Studies in Hemorrhagic Shock***

Numerous drugs for hemorrhagic shock have been evaluated in large, multi-center clinical studies, without success. However, we believe these drugs and/or studies had limitations that made it difficult to demonstrate a treatment effect. We believe MST-188 and our protocol for the phase 2, clinical proof-of-concept study address these factors.

Intervention in prior studies typically was in the pre-hospital setting, before hemorrhage had been addressed through surgery and the patient stabilized. The heterogeneity of trauma patients and variability in outcomes prior to admission to the ICU is substantial. The post-perioperative setting is a more controlled environment in which to evaluate drug effect. Patients participating in our phase 2 study would be randomized upon admission to the ICU, where patient homogeneity is greater and outcomes are more certain.

Certain drugs evaluated in hemorrhagic shock were product-line extensions not originally developed for their utility in trauma. For instance, activated recombinant human factor VII (rFVIIa, NovoSeven®) is approved for use in hemophilia with inhibitors. It was hypothesized that its pro-coagulant properties might limit bleeding and improve outcomes in trauma. Its sponsor, Novo Nordisk, initiated a 1,500-patient study to evaluate whether NovoSeven improved all-cause 30-day survival in patients with active hemorrhage caused by blunt and/or penetrating trauma who had already received between four and eight units of red blood cells. While NovoSeven reduced blood product use, the study was terminated prematurely for futility after evaluating data from 447 blunt trauma patients (11.2% probability of success). It is notable that the study was conducted in patients with active hemorrhage, despite standard hemostatic intervention, likely increasing heterogeneity of the subject population, as described above. More notable, however, is that NovoSeven targets only bleeding risk and does not address microcirculatory damage resulting from ischemia or the potential for injury during reperfusion. Patients in this study likely had experienced periods of ischemia and were at risk for reperfusion injury, for which a single pathway agent is unlikely to improve clinical outcomes. MST-188's broad activity may resolve multiple pathologies in patients undergoing resuscitation following major trauma.

A potentially significant limitation of prior studies, international studies in particular, may have been the failure to rigorously control resuscitation protocols across subjects. Studies have shown that the choice of resuscitation fluid and the timing and rate of intervention may impact outcome. Not all resuscitation fluids have the same physiologic effect and different compositions may affect clinical outcomes. Saline Albumin Fluid Evaluation, Translation of Research into Practice Study (SAFE-TRIPS), an international collaboration that assessed worldwide fluid resuscitation practices in the ICU, concluded that the choice of resuscitation fluid depended primarily on geographic location. Inconsistent resuscitation practices alone might undermine an effective drug in an otherwise well-designed study. Our planned phase 2, clinical proof-of-concept study incorporates an ICU protocol that minimizes variability and increases uniformity of care for all clinical trial subjects.

Evolving standards of care for trauma victims may have hindered prior development of drugs in hemorrhagic shock. Previously, advanced trauma support called for resuscitation with large volumes of fluid, even before hemorrhage control. However, it is now believed that such approach may lead to increased bleeding and mortality. Hypotensive resuscitation, where blood pressure of 60 mmHg is targeted, is becoming standard of care and may better maintain perfusion of vital organs without causing further bleeding. Not controlling for this unidentified, underlying variability would reduce statistical power and potentially mask the treatment benefit of an effective drug.

Finally, several companies with large studies in hemorrhagic shock were developing blood substitutes known as hemoglobin-based oxygen carriers, or HBOCs. HBOC development largely has been discontinued due to associations with significant cardiovascular dysfunction (e.g., hypertension, low cardiac output). A meta-analysis of several different HBOCs found that, as a class, patients treated with HBOCs had a 30% increased risk of mortality and a 2.7-fold increased risk for myocardial infarction. Multiple HBOC studies were terminated prematurely due to

increased mortality in the HBOC arm.



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### **Manufacturing**

We do not have, and have not made plans to establish, our own manufacturing facilities. We meet our requirements for nonclinical and clinical trial material (including manufacturing active pharmaceutical ingredient, or API, formulating and assembling final drug product, labeling, testing and release, packaging, storing API and finished drug product and similar activities) by establishing relationships with third-party manufacturers and other service providers to perform these services for us.

For MST-188 clinical trial material, we have entered into supply agreements with Pierre Fabre Médicament (PFM) and Patheon Inc. for API and finished drug product, respectively. There are a limited number of manufacturers with the technical capabilities and desire to perform the specialized, proprietary processes required to produce MST-188. We have not made plans to engage alternative suppliers for clinical trial material. Therefore, if PFM or Patheon become unable or unwilling to perform, we could experience protracted delays or interruptions in the supply of clinical trial material. Our current agreements with PFM and Patheon may not cover all of our clinical trial material needs and we may meet future clinical trial material needs through 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 and initiation of new studies. As development of MST-188 progresses, we plan to pursue agreements for commercial production of MST-188. In the event negotiations are protracted or unsuccessful, commercialization of MST-188, if it receives regulatory approval, may be delayed.

In addition, although commercially available, there are a limited number of sources of poloxamer 188, the API starting material for MST-188. We do not have a direct relationship with BASF, the current supplier of the API starting material and, although BASF has extensive, worldwide operations and poloxamer 188 is part of its standard product portfolio, we do not have any control over its production and BASF may change its manufacturing process and/or limit the availability of its poloxamer 188 product in the future. We are evaluating development of our own proprietary process for manufacturing API starting material in accordance with current good manufacturing practices applicable to API, which could enhance our control over the availability and quality of API starting material, as well as our intellectual property position with regard to MST-188.

In the future, establishing supply agreements, particularly with respect to commercial manufacturing, may require us to agree to minimum volume requirements, exclusivity arrangements, substantial investment in infrastructure and/or other restrictive terms. As discussed above, our alternatives may be limited due to the specialized nature of the technologies and methods used to manufacture MST-188. In addition, if we seek to make certain changes to the manufacturing process, including changing our sources of API starting material, API, or finished drug product, we will need FDA review and approval before the change can be implemented. Among other things, the FDA may require clinical, stability or other data for MST-188 manufactured with new materials or by new manufacturers, which data will take time and is costly to generate, and the delay associated with generating this data would increase our costs and may delay completion of development of MST-188 and/or its commercialization.

### **Intellectual Property**

Our commercial success depends in large part on our ability to prevent competitors from duplicating or developing equivalent versions of our product candidates. To protect our proprietary compounds, we have implemented and will continue to pursue a multi-faceted approach that relies on a combination of patent protection, proprietary know-how, trade secrets and marketing exclusivity. We seek to establish and protect our proprietary rights through confidentiality, licensing and other agreements, including those with our contract manufacturers, such as PFM.

For particular indications, such as rare or orphan diseases, our products may benefit from periods of post-approval marketing exclusivity. For example, the FDA has granted orphan drug designation for poloxamer 188 (purified) for the treatment of sickle cell disease, which includes the treatment and prevention of the complications of sickle cell disease. In addition, the European Commission has designated poloxamer 188 as an orphan medicinal product for the treatment of sickle cell disease. We plan to seek orphan drug designation for ALI in the U.S. (in the third quarter of 2013) and in the European Union. As described below under Government Regulation Orphan Drug Designation, if MST-188 is the first drug product in which poloxamer 188 is the active ingredient to receive FDA approval for reducing the duration of vaso-occlusive crisis in patients with sickle cell disease, the FDA may not approve any other application to market a drug product in which poloxamer 188 is the active ingredient for the same indication for a period of seven years, except in limited circumstances, such as another drug product showing clinical superiority to MST-188. With regard to the European Union, MST-188 may benefit from ten years of market exclusivity. Orphan drug designation does not necessarily convey any advantage in the regulatory review and approval process. In addition, competitors may receive approval of different drugs or biologics for the same indication for which MST-188 is approved.

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Since we acquired MST-188 in 2011, we have filed for patent protection covering our proprietary supercritical fluid extraction process, methods of using poloxamers in various clinical settings, and the use of poloxamers in combination therapy. These patents were filed in March 2013 or earlier, in each case prior to the effectiveness of the first to file rules under the America Invents Act. We continue to evaluate new patent concepts and plan to file additional patent applications. In particular, we are developing a patent position around the use and optimal dosing of MST-188 based on unpublished data from prior clinical studies, which we expect to augment with data from our on-going phase 3 study of MST-188 in sickle cell disease. In addition, pursuant to an agreement with CytRx Corporation (described below under License Agreement with CytRx Corporation), we have exclusive rights to a variety of issued patents related to poloxamers and their uses. However, we expect that many of these patents will expire prior to obtaining regulatory approval for MST-188.

In addition to patent protection related to our poloxamer purification process, we continue to expand our proprietary manufacturing know-how. For macromolecules, such as MST-188, acceptance criteria for starting materials and in-process and release specifications are critical to the quality of drug product. Without these proprietary specifications, we believe competitors will be unable to manufacture products that are equivalent to MST-188 in the manner that regulatory agencies will require. Further, we are evaluating the use of proprietary analytical standards and bioanalytical assays to further augment our control over product quality, as well as evaluating development of our own proprietary process for manufacturing API starting material, which we expect would further enhance our proprietary position around MST-188.

We are aware of a substantial number of patents issued and patent applications filed in our technical areas or fields. There is a risk that third parties may allege that they have patent rights encompassing our product candidates or methods and no assurance can be given that patents do not exist, have not been filed, or could not be filed or issued, that contain claims covering our product candidates or methods.

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. The cost of litigation to uphold the validity and prevent infringement of our patents could be substantial. Furthermore, we cannot provide assurance that others will not independently develop similar technologies or methods, duplicate our technologies or methods, or design around the patented aspects of our products, technologies or methods. We can provide no assurance that our proposed technologies will not infringe patents or rights owned by others, licenses to which might not be available to us.

In addition, the approval process for patent applications in different countries may differ significantly. The patent authorities in each country administer that country's laws and regulations relating to patents independently of the laws and regulations of any other country and the patents must be sought and obtained separately, which can add substantial cost and expense. In addition, a favorable outcome or approval in one country does not necessarily indicate that a favorable outcome or approval will be obtained in other countries.

## **Competition**

The industries in which we operate (biopharmaceutical, specialty pharmaceutical, biotechnology and pharmaceutical) are highly competitive and subject to rapid and significant change. If any of our product candidates are approved by regulatory authorities, we expect they will face significant competition. We may not be able to compete successfully against organizations with competitive products, particularly large pharmaceutical companies. Many of our potential competitors have greater clinical, regulatory, manufacturing, marketing, distribution, compliance and financial resources and experience than do we.

Over the longer term, our ability, independently or otherwise, to successfully manufacture, market, distribute and sell any approved products, expand their usage or bring additional new products to the marketplace will depend on many factors, including, but not limited to, FDA and foreign regulatory agencies' approvals of new products and indications, the efficacy and safety of our products (alone and relative to other treatment options), the degree of patent or other protection afforded to particular products, and reimbursement for use of those products.

We have focused our resources on development of MST-188, which has potential application in a wide range of serious or life-threatening diseases and conditions characterized by microcirculatory insufficiency. Many other organizations are developing drug products and other therapies intended to treat such diseases and conditions and developments by others may render potential application of MST-188 in a particular indication obsolete or noncompetitive, even prior to completion of its development for that indication.

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Further, 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, ALI, and other indications we may pursue. Legislative action may generate further interest. For instance, in July 2012, the Food and Drug Administration Safety and Innovation Act was signed into law. This Act amended the Federal Food, Drug, and Cosmetic Act in a variety of ways that encourage or facilitate the development of drugs for patients with rare diseases, including by expanding the priority review voucher system to rare pediatric diseases and encouraging the FDA to implement more effective processes for expedited development and review of new medicines intended to address unmet medical needs for serious or life-threatening diseases or conditions using a broad range of surrogate endpoints.

### ***Sickle Cell Disease***

Currently, there are few options for patients suffering complications of sickle cell disease. Patients experiencing vaso-occlusive crisis typically are treated with hydration, oxygenation and analgesia for pain, usually consisting of narcotics, such as morphine. Hydroxyurea, a form of chemotherapy used for myeloproliferative disease, is an approved product that has been shown to decrease the frequency of vaso-occlusive crisis, but it is not approved to intervene after onset of a vaso-occlusive crisis; it has not been shown to treat the crisis itself. We are not aware of any therapeutic agents that have been approved to reduce the duration or severity of an on-going vaso-occlusive crisis.

However, there is substantial interest in developing agents to treat or cure sickle cell disease and sickle cell disease-related complications. We are aware of numerous companies with product candidates in varying stages of development for the treatment of vaso-occlusive crisis, including mechanisms that target the P2Y<sub>12</sub> ADP receptor, increase oxygen binding of hemoglobin or stimulate production of fetal hemoglobin. Some of these companies 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, with clinical-stage agents for the treatment of vaso-occlusive crisis. Those deals have reported potential values of \$340 million and \$665 million to GlycoMimetics and Selexys, respectively. In addition, numerous non-profit or non-commercial foundations and interest groups also 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.

More broadly, MST-188 would compete against agents designed to treat the underlying pathology of sickle cell disease, of which vaso-occlusive crisis is a complication. Bone marrow and stem cell transplantation have been shown to be effective to treat and, in some cases, cure sickle cell disease, but current methods are not available to the majority of patients due to the risk of serious complications, including graft versus host disease and infection, the high cost of the procedures, and the unavailability of a well-matched donor. Forms of gene therapy are being pursued to correct sickle cell disease by halting production of sickled cells, but they are in preclinical or early-stage clinical development.

### ***Arterial Disease***

Current treatment options for arterial disease depend on disease severity and patient specific factors. Some forms of thrombotic arterial disease may be addressed through lifestyle changes (e.g., smoking cessation, regular physical activity, heart healthy diet) and medication to control high cholesterol, high blood pressure and blood glucose. To the extent patients are able to control symptoms and prevent disease progression with lifestyle changes and medical therapy, the potential market for MST-188 in arterial disease will be reduced. Severe expressions of PAD, such as ALI, typically require revascularization to restore blood flow, whether through administration of thrombolytics, endovascular procedures, open surgery, or various combinations of these approaches. We believe MST-188, if approved, would be compatible with the standard of care and we intend first to develop it as an adjunct to thrombolytics, but some medical professionals could perceive MST-188 as competitive with their current treatment methods and/or be adverse to a new approach.

We are aware of a number of investigational therapies for severe forms of thrombotic arterial disease, such as angiogenic growth factors, vasoactive drugs, anticoagulants, thrombolytics, anti-platelet agents, cytoprotectives, and blood substitutes. If approved, MST-188 could compete with these therapies, 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.

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***Resuscitation of Shock Following Major Trauma***

We are aware of various organizations that are developing therapies for hemorrhagic shock, including agents to improve blood flow in the microvasculature, improve oxygenation of ischemic tissues, and/or prevent reperfusion injury. Some of these organizations have received funding from the federal government to progress their research and development in this area. Efforts to improve patient outcomes after surgery for severe hemorrhage include new types and methods of fluid resuscitation (e.g., anti-platelet, hormonal, and hypertonic agents, pressors, and blood factors, additives or substitutes). To the extent other therapies demonstrate acceptable safety and efficacy and receive regulatory approval prior to MST-188, the need for MST-188 may be diminished. In addition to investigational pharmacologic approaches, new resuscitation protocols are being explored to reduce morbidity and mortality following major hemorrhage and, to the extent they are successful, they may diminish the need for MST-188, should it be approved.

**Acquisition of SynthRx, Inc.**

During 2010 and the first half of 2011, our business strategy involved a particular focus on expanding our product pipeline. We retained an investment banking firm to advise us in this regard and our board of directors formed a special committee to assist it in evaluating potential opportunities. Our management and the special committee, with assistance from the investment bank and other consultants, evaluated numerous opportunities with companies with a wide range of development programs. During this process, we identified SynthRx, Inc. as a company whose lead product candidate, which we are now developing as MST-188, was a strong fit with our pipeline expansion strategy. SynthRx was a private company formed in 2004 to acquire purified poloxamer 188 from CytRx Corporation, but after acquiring rights to purified poloxamer 188, SynthRx did not have the financial resources to pursue its development. The co-founders of SynthRx had been involved with the development of poloxamer 188 and purified poloxamer 188 as employees of CytRx.

In April 2011, we completed the acquisition of SynthRx, Inc. pursuant to an agreement and plan of merger, and SynthRx became a wholly owned subsidiary of ours. The payment terms of the merger agreement were structured such that the majority of the merger consideration would be payable only in the event of achievement of the milestones set forth in the merger agreement. All of the merger consideration was intended to be paid in shares of our common stock and, in June 2011 at our annual meeting of stockholders, our stockholders approved the issuance of shares of our common stock, in lieu of any cash payments, in accordance with the terms of the merger agreement. As of the date of this prospectus, there are outstanding an aggregate of 1,596,772 shares of our common stock that we issued to the former SynthRx stockholders. An aggregate of 2,800,851 shares were issued upon the closing of the merger, but we repurchased 1,454,079 of those shares in December 2012 for \$0.001 per share pursuant to the exercise of a repurchase right triggered as a result of the timing of and planned number of subjects in the EPIC study. We could issue up to an aggregate of 12,478,050 additional shares of our common stock to the former SynthRx stockholders if and when the development of MST-188 achieves the Second Milestone and the Third Milestone.

Under the terms of the merger agreement, we also agreed, among other things, (a) to use commercially reasonable efforts until the earlier of achievement of the Third Milestone, which is approval of an NDA covering the use of purified poloxamer 188 for the treatment of sickle cell crisis in children, or the date that is four years after February 12, 2011 to develop an intravenous injection product in which purified poloxamer 188 is an active ingredient; and (b) until the earlier of the achievement of the Third Milestone and the date that is four years following February 12, 2011, not to consummate a change of control with a third party that involves all or substantially all of SynthRx's assets, except (i) in connection with an Exempt Transaction (as described below) or (ii) with the written consent of SynthRx, which consent shall not be unreasonably withheld, conditioned or delayed. Under the merger agreement, an Exempt Transaction is a change of control that closes prior to achievement of the Third Milestone in which the acquiror agrees in writing to submit an NDA covering the use of purified poloxamer 188 for the treatment of sickle cell crisis in children, or the 188 NDA, for FDA approval (or, if there are unexpected safety or regulatory issues, to conduct activities to address or resolve such issues) until the earlier of (x) the date that, beginning on April 8, 2011 and thereafter, the aggregate expenditure related to the program involving the product candidate on which the 188 NDA is to be based is at least \$15.0 million and (y) the fourth anniversary of April 8, 2011; provided, however, such acquiror shall be relieved of such obligations under certain specified conditions.

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As discussed above under Management's Discussion and Analysis of Financial Condition and Results of Operations Acquisition of SynthRx Stockholders Agreement, in connection with our acquisition of SynthRx, we and each of the former principal stockholders of SynthRx entered into a stockholders' voting and transfer restriction agreement, pursuant to which each stockholder party agreed, with respect to every action or approval by written consent of our stockholders, to vote all shares of our common stock then beneficially owned by that stockholder that were issued pursuant to our merger agreement with SynthRx, or the Subject Shares, in such manner as we direct. In addition, each stockholder party granted an irrevocable proxy to us for the term of the agreement, which authorizes our executive officers to vote, or instruct nominees or record holders to vote, as applicable, all Subject Shares in such manner as we direct. Notwithstanding the foregoing, until the earlier of: (i) FDA approval of a new drug application covering the use of purified poloxamer 188 for the treatment of sickle cell crisis in children, which is the third milestone under our merger agreement with SynthRx, and (ii) April 8, 2015, which is the four year anniversary of the closing of our acquisition of SynthRx, each stockholder party is permitted to vote the Subject Shares in such stockholder's sole discretion solely with respect to a change of control that involves the transfer of SynthRx's assets to a third party and in which at least 80% of the consideration received by our company (or our stockholders) is non-contingent and paid in cash. The agreement terminates upon the transfer, in accordance with that agreement, of all the Subject Shares by the stockholder parties and their affiliates to non-affiliates. As of June 4, 2013, 1,320,643 outstanding shares of our common stock, which is approximately 2.8% of the aggregate outstanding shares of our common stock, were Subject Shares. While the agreement is in effect, it provides our board of directors with effective voting control over the Subject Shares.

**License Agreement with CytRx Corporation**

Through a prior license agreement between SynthRx and CytRx Corporation, we have rights to issued patents related to poloxamers and their uses. The issued patents cover, among other things, poloxamer 188, purified poloxamer 188, methods of treating sickle cell anemia using poloxamer 188 and methods of preparing purified poloxamer 188. Under this license agreement, as amended, SynthRx has an exclusive license, with the right to grant sublicenses, under specified patents to use, offer and sell covered products in all of the countries in the world and in all fields, except those fields that, at the time of the agreement, were or will be licensed pursuant to certain identified agreements. We believe that the field limitation does not prevent us from developing or commercializing MST-188 for the treatment of complications of sickle cell disease.

In partial consideration of the license grant, SynthRx agreed to pay CytRx certain non-refundable and non-creditable milestone payments based on the approval of each covered product in a major market, which includes the U.S. The amount of each milestone is in the low single-digit millions, half of which is due on the first commercial sale of the approved product and half of which is payable over time based on a percentage of quarterly net sales. In addition, SynthRx would pay a single-digit royalty on net sales of covered products. However, in the event of a sublicense under the specified patents, in lieu of the foregoing milestone and royalty payments, SynthRx, in its sole discretion, may elect to pay CytRx an amount equal to 20% of any sublicensing income received by SynthRx within 30 days of receipt thereof. Sublicense income includes, without limitation, license fees, royalties, milestone payments, license maintenance fees and strategic alliance payments, whether in cash, equity or other property, with the payment to be in the same form as the payment received by SynthRx.

**Other Product Candidates**

In prior years, we were focused on the development of ANX-514 (docetaxel for injectable emulsion) and Exelbine (vinorelbine injectable emulsion), which are novel emulsion formulations of currently marketed chemotherapy drugs. As a result of our current focus on MST-188, we elected to discontinue independent development of ANX-514 and Exelbine in 2012 and 2011, respectively, and are evaluating other opportunities for further development of these programs, such as partnering and licensing arrangements.

ANX-514 is a novel, detergent-free formulation of docetaxel, an intravenously-injected chemotherapy drug commonly used to treat solid tumors. Taxotere®, a branded formulation of docetaxel, is approved to treat breast, non-small cell lung, prostate, gastric, and head and neck cancers. ANX-514 was designed to have efficacy comparable to Taxotere without the non-active, toxic components found in Taxotere and without the corticosteroid premedication regimen required with Taxotere. In October 2011, we reached agreement with the FDA on a pivotal study for ANX-514 that would support approval of ANX-514 without a corticosteroid premedication regimen. We agreed on a 400-patient, non-inferiority study with a primary objective of comparing fluid retention following treatment with ANX-514, administered without corticosteroid premedication, and Taxotere, administered with corticosteroid premedication. However, in 2012, in accordance with our strategy to focus on MST-188, we determined not initiate any clinical studies of ANX-514 in the foreseeable future.

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Exelbine is a novel emulsion formulation of the chemotherapy drug vinorelbine. Navelbine®, a branded formulation of vinorelbine, is approved in the U.S. to treat advanced non-small cell lung cancer as a single agent or in combination with cisplatin, and approved in the European Union to treat non-small cell lung cancer and advanced or metastatic breast cancer. In August 2011, we received a complete response letter from the FDA regarding the new drug application we submitted in November 2010 seeking approval of Exelbine for the same indications as Navelbine. The FDA stated that it could not approve the Exelbine NDA in its present form and that the bioequivalence study we had sponsored would need to be repeated because the authenticity of the drug products used in the bioequivalence trial could not be verified in accordance with FDA standards. Notably, at a meeting with the FDA following our receipt of the complete response letter, FDA staff commented that no clinical deficiencies were noted with the bioequivalence study and that there were no comments regarding our conclusion that Exelbine and Navelbine are bioequivalent. However, we elected to discontinue independent development of Exelbine and are seeking a partner or outside investor for the program to complete the necessary bioequivalence study.

### **Government Regulation**

Governmental authorities in the U.S. and other countries extensively regulate the testing, manufacturing, labeling and packaging, storage, recordkeeping, advertising, promotion, marketing and distribution, among other things, of pharmaceutical products. In the U.S., the FDA, under the Federal Food, Drug and Cosmetic Act, or FDCA, and other federal statutes and regulations, subjects pharmaceutical products to rigorous review. If we do not comply with applicable requirements, we may be fined, the government may refuse to approve our marketing applications or allow us to manufacture or market our products, and we may be criminally prosecuted.

We and our third-party manufacturers, distributors and CROs may also be subject to regulations under other federal, state, and local laws, including the Occupational Safety and Health Act, the Environmental Protection Act, the Clean Air Act, the Health Insurance Portability and Accountability Act, privacy laws and import, export and customs regulations, as well as the laws and regulations of other countries.

### ***FDA Approval Process***

To obtain approval of a new drug product from the FDA, we must, among other requirements, submit data supporting its safety and efficacy, as well as detailed information on the manufacture and composition of the drug and proposed product labeling. The testing and collection of data and the preparation of necessary applications are expensive and time-consuming. The FDA may not act quickly or favorably in reviewing these applications, and we may encounter significant difficulties or costs in our efforts to obtain FDA approvals that could delay or preclude us from marketing MST-188 or any other investigational agents.

The FDA approval process relating to new drug products differs depending on the nature of the particular product candidate for which approval is sought. With respect to any product candidate with API not previously approved by the FDA (e.g., MST-188) the sponsor is required to submit an NDA that includes complete reports of pre-clinical, clinical and laboratory studies and extensive manufacturing information to demonstrate the product's safety and effectiveness for its intended use. On the other hand, if the API has been previously approved by the FDA, such as with reformulation product candidates like ANX-514 and Exelbine, the sponsor may be able to rely, in part, on the FDA's findings of safety and efficacy with respect to the previously approved product.

The process required by the FDA before a new drug may be marketed in the U.S. generally involves the following:

completion of nonclinical laboratory and animal testing performed in compliance with FDA regulations;

submission of an investigational new drug application, or IND, which must become effective before human clinical trials may begin and must be updated annually;

performance of adequate and well-controlled human clinical trials to establish the safety and efficacy of the product candidate for its intended use;

submission of an NDA after completion of pivotal clinical trials;

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a determination by the FDA within 60 days of its receipt of the NDA to file the NDA for review;

satisfactory completion of an FDA pre-approval inspection of the manufacturing facilities at which the API and finished drug product are produced and tested to assess compliance with current good manufacturing practices, or cGMP; and

FDA review and approval of the NDA prior to any commercial marketing or sale of the drug product in the U.S.

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Clinical studies are conducted under protocols detailing, among other things, the objectives of the study, the parameters to be used in monitoring safety, and the efficacy criteria to be evaluated. A protocol for each clinical study and any subsequent protocol amendments must be submitted to the FDA as part of the IND.

The clinical testing of a drug product candidate generally is conducted in three sequential phases, but the phases may overlap or be combined. The three phases are as follows:

*Phase 1.* In phase 1 clinical studies, the product is tested in a small number of patients with the target condition or disease or in healthy volunteers. These studies are designed to evaluate the safety, dosage tolerance, metabolism and pharmacologic actions of the product candidate in humans, side effects associated with increasing doses, and, in some cases, to gain early evidence on efficacy. The number of participants included in phase 1 studies is generally in the range of 20 to 80.

*Phase 2.* In phase 2 studies, in addition to safety, the sponsor evaluates the efficacy of the product candidate on targeted indications to determine dosage tolerance and optimal dosage and to identify possible adverse effects and safety risks. Phase 2 studies typically are larger than phase 1 but smaller than phase 3 studies and may involve several hundred participants.

*Phase 3.* Phase 3 studies typically involve an expanded patient population at geographically-dispersed test sites. They are performed after preliminary evidence suggesting effectiveness of the product candidate has been obtained and are designed to further evaluate clinical efficacy and safety, to establish the overall benefit-risk relationship of the product candidate and to provide an adequate basis for product approval. Phase 3 studies usually involve several hundred to several thousand participants.

A clinical study may combine the elements of more than one phase and the FDA generally requires two or more phase 3 studies to support approval of a product candidate. A company's designation of a clinical study as being of a particular phase is not necessarily indicative that the study will be sufficient to satisfy the FDA requirements of that phase because this determination cannot be made until the protocol and data have been submitted to and reviewed by the FDA. In addition, a clinical study may contain elements of more than one phase notwithstanding the designation of the study as being of a particular phase.

A pivotal study is a clinical study that is believed to satisfy FDA requirements for the evaluation of a product candidate's safety and efficacy such that it can be used, alone or with other pivotal or non-pivotal studies, to justify regulatory approval. Generally, pivotal studies are phase 3 studies, but they may be phase 2 studies if the study design provides a well-controlled and reliable assessment of clinical benefit, particularly in an area of unmet medical need.

Clinical trials must be conducted in accordance with the FDA's good clinical practices, or GCP, requirements. The FDA may order the temporary or permanent discontinuation of a clinical study at any time or impose other sanctions if it believes that the clinical study is not being conducted in accordance with FDA requirements or that the participants are being exposed to an unacceptable health risk. An institutional review board, or IRB, generally must approve the clinical trial design and patient informed consent at study sites that the IRB oversees and also may halt a study, either temporarily or permanently, for failure to comply with the IRB's requirements, or may impose other conditions. Additionally, some clinical studies are overseen by an independent group of qualified experts organized by the clinical study sponsor, known as a data safety monitoring board or committee. This group recommends whether or not a trial may move forward at designated check points based on access to certain data from the study. The clinical study sponsor may also suspend or terminate a clinical study based on evolving business objectives, competitive climate and/or lack of funds.

As a product candidate moves through the clinical testing phases, manufacturing processes are further defined, refined, controlled and validated. The level of control and validation required by the FDA increases as clinical studies progress. We and the third-party manufacturers on which we rely for the manufacture of our product candidates and their respective components (including API) are subject to requirements that drugs be manufactured, packaged and labeled in conformity with cGMP. To comply with cGMP requirements, manufacturers must continue to spend time, money and effort to meet requirements relating to personnel, facilities, equipment, production and process, labeling and packaging, quality control, recordkeeping and other requirements.



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Assuming successful completion of all required testing in accordance with all applicable regulatory requirements, detailed information on the product candidate is submitted to the FDA in the form of an NDA requesting approval to market the drug for one or more indications, together with payment of a user fee, unless waived. An NDA includes all relevant data available from pertinent nonclinical and clinical studies, including negative or ambiguous results as well as positive findings, together with detailed information on the chemistry, manufacture, controls (CMC) and proposed labeling, among other things. To support marketing approval, the data submitted must be sufficient in quality and quantity to establish the safety and efficacy of the product candidate for its intended use to the satisfaction of the FDA.

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If an NDA submission is accepted for filing, the FDA begins an in-depth review of the NDA. Under the Prescription Drug User Fee Act, or PDUFA, the FDA's goal is to complete its initial review and respond to the applicant within 12 months of submission, unless the application relates to an unmet medical need in a serious or life-threatening indication and is designated for priority review, in which case the goal may be within eight months of NDA submission. However, PDUFA goal dates are not legal mandates and FDA response often occurs several months beyond the original PDUFA goal date. Further, the review process and the target response date under PDUFA may be extended if the FDA requests, or the NDA sponsor otherwise provides, additional information or clarification regarding information already provided in the NDA. The NDA review process can, accordingly, be very lengthy. During its review of an NDA, the FDA may refer the application to an advisory committee for review, evaluation and recommendation as to whether the application should be approved. The FDA is not bound by the recommendation of an advisory committee, but it typically follows such recommendations. Data from clinical studies are not always conclusive and the FDA and/or any advisory committee it appoints may interpret data differently than the NDA sponsor.

After the FDA evaluates the NDA and inspects manufacturing facilities where the drug product and/or its API will be produced, it will either approve commercial marketing of the drug product with prescribing information for specific indications or issue a complete response letter indicating that the application is not ready for approval and stating the conditions that must be met in order to secure approval of the NDA. If the complete response letter requires additional data and the applicant subsequently submits that data, the FDA nevertheless may ultimately decide that the NDA does not satisfy its criteria for approval. The FDA could also approve the NDA with a Risk Evaluation and Mitigation Strategies, or REMS, plan to mitigate risks, which could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. The FDA also may condition approval on, among other things, changes to proposed labeling, development of adequate controls and specifications, or a commitment to conduct post-marketing testing. Such post-marketing testing may include phase 4 clinical studies and surveillance to further assess and monitor the product's safety and efficacy after approval. Regulatory approval of products for serious or life-threatening indications may require that participants in clinical studies be followed for long periods to determine the overall survival benefit of the drug.

If the FDA approves MST-188 or another of our investigational drugs, we will be required to comply with a number of post-approval regulatory requirements. We would be required to report, among other things, certain adverse reactions and production problems to the FDA, provide updated safety and efficacy information and comply with requirements concerning advertising and promotional labeling for any of our products. Also, quality control and manufacturing procedures must continue to conform to cGMP after approval, and the FDA periodically inspects manufacturing facilities to assess compliance with cGMP, which imposes extensive procedural, substantive and record keeping requirements. If we seek to make certain changes to an approved product, such as certain manufacturing changes, we will need FDA review and approval before the change can be implemented. For example, if we change the manufacturer of a product or its API, the FDA may require stability or other data from the new manufacturer, which data will take time and is costly to generate, and the delay associated with generating this data may cause interruptions in our ability to meet commercial demand, if any. While physicians may use products for indications that have not been approved by the FDA, we may not label or promote the product for an indication that has not been approved. Securing FDA approval for new indications is similar to the process for approval of the original indication and requires, among other things, submitting data from adequate and well-controlled studies that demonstrate the product's safety and efficacy in the new indication. Even if such studies are conducted, the FDA may not approve any change in a timely fashion, or at all.

We rely on third parties for the manufacture of our clinical trial material and we expect to rely on third-party manufacturers to produce commercial quantities of our drugs, should they receive regulatory approval in the future. Future FDA, state and/or foreign governmental agency inspections may identify compliance issues at these third-party facilities that may disrupt production or distribution or require substantial resources to correct. In addition, discovery of previously unknown problems with a product or the failure to comply with applicable requirements may result in restrictions on a product, manufacturer or holder of an approved NDA, including withdrawal or recall of the product from the market or other voluntary, FDA-initiated or judicial action that could delay or prohibit further marketing. Newly discovered or developed safety or efficacy data may require changes to a product's approved labeling, including the addition of new warnings and contraindications, and also may require the implementation of other risk management measures. Many of the foregoing could limit the commercial value of a product or require us to commit substantial additional resources in connection with the approval of an investigational drug. Also, new government requirements, including those resulting from new legislation, may be established, or the FDA's policies may change, which could delay or prevent regulatory approval of our products under development.

***Expedited Review Programs***

Investigational drugs intended to treat serious or life-threatening conditions with unmet medical needs may be eligible for certain programs intended to expedite or facilitate the process for FDA review, such as the fast track and priority review programs. Fast track designation and priority review do not change the standards for FDA approval but may expedite the approval process.



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Investigational drugs are eligible for fast track designation if they are intended to treat a serious or life-threatening condition and demonstrate the potential to address an unmet medical need for the condition. Fast track designation applies to the combination of the drug and the specific indication for which it is being studied. For a drug with fast track designation, the FDA may consider a rolling review of the NDA, meaning it may agree to review sections of the NDA on a rolling basis before the complete application is submitted, which could expedite the FDA's review of the NDA. Fast track designation, however, does not guarantee that the FDA will agree to a rolling review of the NDA. An investigational drug is eligible for priority review if it has the potential to provide safe and effective therapy where no satisfactory alternative therapy exists or a significant improvement in the treatment, diagnosis or prevention of a disease compared to marketed products. The FDA will attempt to direct additional resources to the evaluation of an NDA for a drug product candidate designated for priority review in an effort to facilitate the review.

### ***Orphan Drug Designation***

The Orphan Drug Act, or ODA, provides for granting special status, referred to as orphan designation, to a drug intended to treat, diagnose or prevent a rare disease or condition that affects fewer than 200,000 people in the U.S. at the time of application for orphan designation. Orphan designation qualifies the sponsor of the product for the tax credit and marketing incentives of the ODA. Orphan designation must be requested by an applicant before submitting its marketing application for that drug for an orphan disease or condition. After the FDA grants orphan designation, the generic identity of the orphan drug and its potential use are disclosed publicly by the FDA. The first sponsor to receive FDA marketing approval for a drug with an orphan designation is entitled to a seven-year exclusive marketing period in the U.S. for that product for that indication and, typically, a waiver of the prescription drug user fee for its marketing application. However, a drug that the FDA considers to be clinically superior to, or different from, another approved orphan drug, even though for the same indication, may also obtain approval in the U.S. during the seven-year exclusive marketing period. Orphan drug exclusive marketing rights may also be lost if the FDA later determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the drug. The approval of an orphan designation request does not alter the standard regulatory requirements and process for obtaining marketing approval. Safety and efficacy of the product candidate must be established through adequate and well-controlled studies.

Legislation similar to the Orphan Drug Act has been enacted in countries other than the U.S., including the European Union. The legislation in the European Union is available for therapies addressing conditions that affect five or fewer out of 10,000 persons. The marketing exclusivity period is for ten years, although that period can be reduced to six years if, at the end of the fifth year, available evidence establishes that the product is sufficiently profitable not to justify maintenance of market exclusivity.

### ***Pharmaceutical Pricing and Reimbursement***

Significant uncertainty exists as to the reimbursement status of newly approved drug products, including coding, coverage and payment. Sales of any products for which we obtain marketing approval will depend in part on reimbursement from third-party payors. Third-party payors include government health administrative authorities, managed care providers, private health insurers and other organizations. The process for determining whether a payor will reimburse a product may be separate from the process of seeking approval of the product or for setting the price of the product. Third-party payors are increasingly challenging the price and examining the medical necessity and cost-effectiveness of medical products and services, in addition to their safety and efficacy. Even if reimbursement is provided, market acceptance of our products would be adversely affected if the amount of payment for our products proves to be unprofitable for healthcare providers or less profitable than alternative treatments or if administrative burdens make our products less desirable to use.

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. We expect that federal, state and local governments in the U.S. will continue to consider legislation 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 whether and how future legislation, whether domestic or abroad, could 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.

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### ***Other Healthcare Laws and Compliance Requirements***

In addition to FDA requirements, several other types of state and federal laws apply and will apply to our operations. These laws include healthcare information and data privacy protection laws and fraud and abuse laws, such as anti-kickback and false claims statutes. The federal healthcare program anti-kickback statute prohibits, among other things, knowingly and willfully offering, paying, soliciting or receiving remuneration to induce or in return for purchasing, leasing, ordering or arranging for the purchase, lease or order of any healthcare item or service reimbursable under Medicare, Medicaid or other federally financed healthcare programs. This statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, purchasers and formulary managers on the other. Violations of the anti-kickback statute are punishable by imprisonment, criminal fines, civil monetary penalties and exclusion from participation in federal healthcare programs. Although there are a number of statutory exemptions and regulatory safe harbors protecting certain common activities from prosecution or other regulatory sanctions, the exemptions and safe harbors are drawn narrowly, and practices that involve remuneration intended to induce prescribing, purchases or recommendations may be subject to scrutiny if they do not qualify for an exemption or safe harbor. Under the new Physician Payment Sunshine Act requirements, we will be subject in the future to reporting payments made to certain investigators and physicians.

Federal false claims laws prohibit any person from knowingly presenting, or causing to be presented, a false claim for payment to the federal government, or knowingly making, or causing to be made, a false statement to have a false claim paid. Recently, several pharmaceutical and other healthcare companies have been prosecuted under these laws for allegedly promoting their products for uses for which they were not approved and causing the submission of claims for payment for such use under federal healthcare programs. The majority of states also have statutes or regulations similar to the federal anti-kickback law and false claims laws, which apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor.

### ***Government Regulation Outside the U.S.***

In addition to regulations in the U.S., we may be subject to a variety of regulations in foreign jurisdictions that govern, among other things, clinical studies and any commercial sales and distribution of our products. Whether or not we obtain FDA approval for a product candidate, we must obtain the requisite approvals from regulatory authorities in foreign jurisdictions prior to the commencement of clinical studies or marketing and sale of the product in those countries. The foreign regulatory approval process includes all of the risks associated with the FDA approval described above. Some foreign jurisdictions have a drug product approval process similar to that in the U.S., which requires the submission of a clinical trial application much like the IND prior to the commencement of clinical studies. In Europe, for example, a clinical trial application, or CTA, must be submitted to each country's national health authority and an independent ethics committee, much like the FDA and IRB, respectively. Once the CTA is approved in accordance with a country's requirements, clinical trial development may proceed.

To obtain regulatory approval of a product candidate under European Union regulatory systems, we would be required to submit a marketing authorization application, which is similar to the NDA, except that, among other things, there are country-specific document requirements. For countries outside of the European Union, such as countries in Eastern Europe, Latin America or Asia, the requirements governing the conduct of clinical studies, product approval, pricing and reimbursement vary from country to country. In addition, regulatory approval of prices is required in most countries other than the U.S. We face the risk that the resulting prices would be insufficient to generate an acceptable return to us or any future partner of ours. If we fail to comply with applicable foreign regulatory requirements, we may be subject to, among other things, fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

### **Research and Development Expenses**

Our research and development expenses were \$8.1 million in 2012 and \$5.8 million in 2011. Our research and development expenses for 2012 and 2011 consisted primarily of costs associated with external nonclinical activities, such as research-related manufacturing, regulatory affairs and quality assurance-related consulting services, and commercial-readiness manufacturing for Exelbine. See Management's Discussion and Analysis of Financial Condition and Results of Operations in this prospectus for more information regarding our research and development expenses.

### **Employees**

As of June 4, 2013, we have 15 employees, 13 of which are full-time. Our employees are not unionized and we believe that our relationship with our employees is good.



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Our headcount has increased significantly since 2009, as we built out our management team and filled key positions in clinical operations, CMC, regulatory affairs, and finance and accounting. For at least the next few years, we plan to continue to operate by relying on a relatively small employee base and outsourcing key product development activities, including aspects of research-related manufacturing, clinical operations and regulatory affairs, as well as general and administrative activities, such as human resources, facilities, internal systems support and investor relations.

### **Formation**

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., a wholly-owned subsidiary, with and into us and changed our name to ADVENTRX Pharmaceuticals, Inc. In March 2013, we merged Mast Therapeutics, Inc., a wholly-owned subsidiary, with and into us and changed our name to Mast Therapeutics, Inc.

### **Trademarks**

SynthRx® is our registered trademark. We have applied for trademark registration for Mast Therapeutics, our corporate logo, and EXELBINE in the U.S. We are developing commercial names for our other product candidates. All other trademarks, service marks or trade names appearing in this prospectus, including but not limited to Taxotere®, Navelbine®, and NovoSeven® are the property of their respective owners. Use or display by us of other parties' trademarks, service marks, trade names, trade dress or products is not intended to and does not imply a relationship with, or endorsements or sponsorship of, us by the trademark, service mark, trade name, trade dress or product owners.

### **Legal Proceedings.**

In the normal course of business, we may become subject to lawsuits and other claims and proceedings. Such matters are subject to uncertainty and outcomes are often not predictable with assurance. We are not currently a party to any material pending litigation or other material legal proceeding.

### **Properties.**

We lease approximately 9,300 square feet of office space for our headquarters in San Diego, California. That lease will expire in January 2015, unless we exercise our option to extend through October 2018. The average rent for this space is approximately \$21,614 per month through January 2014 and \$26,677 per month through January 2015. We believe that the facilities we lease are adequate to meet our current requirements and our requirements for the remaining term of the lease. We have no laboratory, research or manufacturing facilities.

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The following table sets forth certain information regarding our executive officers and directors as of June 4, 2013:

| <b>Name</b>           | <b>Age</b> | <b>Position</b>                                   |
|-----------------------|------------|---------------------------------------------------|
| Brian M. Culley       | 42         | Chief Executive Officer and Director              |
| Patrick L. Keran      | 41         | President and Chief Operating Officer             |
| Santosh J. Vetticaden | 54         | Chief Medical Officer and Senior Vice President   |
| Brandi L. Roberts     | 39         | Chief Financial Officer and Senior Vice President |
| R. Martin Emanuele    | 58         | Senior Vice President, Development                |
| Gregory D. Gorgas     | 50         | Senior Vice President, Commercial                 |
| Jack Lief             | 67         | Chair of the Board                                |
| Ted W. Love           | 54         | Director                                          |
| David A. Ramsay       | 48         | Director                                          |
| Lewis J. Shuster      | 57         | Director                                          |

**Biographical Information of Executive Officers and Directors**

Set forth below is biographical information regarding each of our executive officers and directors.

*Brian M. Culley, M.A., M.B.A.* Mr. Culley has served as our chief executive officer since February 2010 and as a member of our board of directors since December 2011. He has served as our principal executive officer since February 2009. Previously, from January 2007 to February 2010, he served as our chief business officer and senior vice president, from February 2006 to January 2007, he served as our senior vice president, business development, and, from December 2004 to February 2006, he served as our vice president, business development. From 2002 until 2004, Mr. Culley managed all strategic collaborations and licensing agreements for iTherx, Inc. (formerly, Immusol, Inc.) in San Diego, where his most recent title was director of business development and marketing. From 1999 until 2000, he was a licensing and marketing associate at the University of California, San Diego, department of technology transfer & intellectual property services and from 1996 to 1999, he was a research associate for Neurocrine Biosciences, Inc., where he performed drug discovery research. Mr. Culley has 20 years of experience in the life science industry, including deal structure and negotiation, licensing, due diligence, market and competitive research, and venture funding. He received a B.S. in biology from Boston College, a masters in biochemistry from the University of California, Santa Barbara and an M.B.A. from The Johnson School of Business at Cornell University with an emphasis on private equity and entrepreneurship. Mr. Culley's extensive experience with our company and our board of directors' belief that our chief executive officer should serve on the board of directors, as well as Mr. Culley's substantial business development experience, leadership skills and scientific background, led our board of directors to conclude that Mr. Culley should serve as a director.

*Patrick L. Keran, J.D.* Mr. Keran has served as our president and chief operating officer since February 2010. From August 2006 to February 2010, he served as our general counsel. He also has served as our secretary since September 2006 and served as our principal financial officer from July 2009 to January 2013. Previously, from April 2004 to August 2006, Mr. Keran was associate general counsel at Isis Pharmaceuticals, Inc., a publicly held drug discovery and development company. From February 2003 to April 2004, Mr. Keran practiced corporate law at the law firm of Heller Ehrman LLP, specializing in public and private financings, licensing arrangements, mergers and acquisitions and corporate governance matters. From September 1999 to February 2003, Mr. Keran practiced law at the law firm of Brobeck Phleger & Harrison LLP where he had a similar corporate practice. Mr. Keran is licensed to practice law in the State of California. Mr. Keran received a B.A. from the University of California at San Diego and a J.D. from the University of California at Berkeley, Boalt Hall School of Law.



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*Santosh J. Vetticaden, M.D., Ph.D.* Dr. Vetticaden has served as our chief medical officer and senior vice president since September 2012. Dr. Vetticaden has held several senior level positions leading drug development across phase 1 through phase 4 clinical studies at biotech and large pharmaceutical companies. Prior to joining our company, Dr. Vetticaden was at Cubist Pharmaceuticals, Inc., a publicly held biopharmaceutical company that develops and commercializes pharmaceutical products for use in acute care settings, where he served as senior vice president, chief medical and development officer from September 2010 to January 2012 and as senior vice president, clinical development and chief medical officer from December 2008 to September 2010. Dr. Vetticaden served as an independent consultant from January 2012 until joining our company and from August 2008 until joining Cubist. From February 2007 to August 2008, he was senior vice president and chief medical officer at Maxygen, Inc., a publicly held biopharmaceutical company. From April 2003 to February 2007, Dr. Vetticaden held senior management positions at Scios, Inc., a subsidiary of Johnson & Johnson, including vice president, clinical research. Previously, he held senior roles related to drug development at Aventis Pharmaceuticals, Inc. (now Sanofi) and the Whitehall-Robins Healthcare division of American Home Products Corporation (now Pfizer). Dr. Vetticaden earned his M.D. from the University of Maryland and a Ph.D. in pharmacokinetics and pharmacodynamics from Virginia Commonwealth University. He completed his residency in internal medicine at the Baylor College of Medicine.

*Brandi L. Roberts, C.P.A., M.B.A.* Ms. Roberts joined our company in March 2011 and currently serves as our chief financial officer and senior vice president. She previously served as our vice president, finance from March 2011 to January 2013 and from June 2008 to January 2009. From January 2009 to March 2011, Ms. Roberts served as vice president, accounting and corporate controller of Alphatec Spine, Inc., the wholly-owned operating subsidiary of Alphatec Holdings, Inc., a medical technology company listed on the NASDAQ Global Select Market where she was responsible for managing all accounting activities, including SEC reporting and compliance with Sarbanes-Oxley Act requirements. From June 2007 to June 2008, Ms. Roberts served as executive director, corporate controller of Artes Medical, Inc., a publicly traded medical technology company, and from September 2005 to June 2007, she served as director, finance of Stratagene Corporation, a publicly traded life science company acquired by Agilent Technologies, Inc. in June 2007. Ms. Roberts' experience also includes seven years at Pfizer's laboratories in La Jolla, California (formerly Agouron), most recently as director, finance, and three years with the public accounting firm of PricewaterhouseCoopers LLP. She is a certified public accountant with the State of California. Ms. Roberts received a B.S. in Business Administration from the University of Arizona and an M.B.A. from the University of San Diego.

*R. Martin Emanuele, Ph.D., M.B.A.* Dr. Emanuele has served as our senior vice president, development since he joined our company in April 2011 following our acquisition of SynthRx, Inc., which he co-founded. Previously, from April 2010 to April 2011, Dr. Emanuele was vice president, pharmaceutical strategy at DaVita, Inc., a FORTUNE 500® company and leading provider of kidney care in the United States. Dr. Emanuele's responsibilities while at DaVita focused on evaluating business opportunities related to emerging renal therapeutics, biomarkers and diagnostics. Prior to DaVita, from June 2008 to April 2010, Dr. Emanuele provided consulting services to a range of life science companies regarding corporate partnering and business development. From November 2006 to May 2008, Dr. Emanuele was senior vice president, business development at Kemia, Inc., a venture-backed privately-held company focused on discovering and developing small molecule therapeutics. From 2002 to 2006, Dr. Emanuele held various senior-level positions with Avanir Pharmaceuticals, Inc., most recently as vice president, business development and portfolio management, and from 1988 to 2002, Dr. Emanuele held positions of increasing responsibility at CytRx Corporation, most recently as vice president, research and business development. He earned a Ph.D. in pharmacology and experimental therapeutics from Loyola University of Chicago, Stritch School of Medicine and a B.S. in biology from Colorado State University. He also holds an M.B.A. with an emphasis in healthcare and pharmaceutical management from the University of Colorado.

*Gregory D. Gorgas, M.B.A.* Mr. Gorgas joined our company in July 2011 as our senior vice president, commercial. Prior to joining our company, from November 2009 to July 2011, Mr. Gorgas was managing director at Theragen, Inc., a privately-held company he co-founded, that applies proprietary computational intelligence to analyze clinical data. From November 2008 to July 2011, Mr. Gorgas also served as an independent consultant, providing commercial and business development consulting services to pharmaceutical, biotechnology and medical device companies. From 1997 to October 2008, Mr. Gorgas held positions of increasing responsibility with Biogen Idec Inc., a publicly held biotechnology company that develops therapies for the treatment of neurodegenerative diseases, hemophilia and autoimmune disorders. Most recently, from March 2006 to October 2008, Mr. Gorgas served as senior director, global and U.S. marketing at Biogen Idec, where he was responsible for the strategic vision and operational commercialization of the company's worldwide cancer business, and, prior to such time, he had responsibilities in sales, commercial operations and project team and alliance management. Prior to Biogen Idec, he held sales and manager positions with Chiron Corporation, Cetus Corporation and The Upjohn Company. Mr. Gorgas holds an M.B.A. from the University of Phoenix and a B.A. in economics from California State University, Northridge.

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*Jack Lief.* Mr. Lief has served as a director since September 2006 and as chair of our board of directors since May 2007. Mr. Lief is a co-founder and, since April 1997, has served as president, chief executive officer and a director of Arena Pharmaceuticals, Inc., a publicly held biopharmaceutical company focused on discovering, developing and commercializing novel drugs for weight management, cardiovascular disease, inflammation and other disorders. He also has served as chairman of Arena's board of directors since October 2007. From 1995 to April 1997, Mr. Lief served as an advisor and consultant to numerous biopharmaceutical organizations. From 1989 to 1994, Mr. Lief served as senior vice president, corporate development and secretary of Cephalon, Inc., a biopharmaceutical company. From 1983 to 1989, Mr. Lief served as director of business development and strategic planning for Alpha Therapeutic Corporation, a manufacturer of biological products. Mr. Lief joined Abbott Laboratories, a pharmaceutical company, in 1972, where he served until 1983, most recently as the head of international marketing research. Mr. Lief is an executive board member of BIOCOM, a life science industry association representing more than 550 member companies in Southern California, and he was the chairman of the board of directors of BIOCOM from March 2005 to March 2006. Mr. Lief holds a B.A. from Rutgers University and an M.S. in psychology (experimental and neurobiology) from Lehigh University. Mr. Lief's extensive and current executive leadership and management experience in biopharmaceutical companies brings to our board of directors the perspective of a leader managing similar drug development, regulatory, commercialization and financing issues as our company. In addition, his over 40 years of experience in the life science industry provides unique insight to our board. Mr. Lief also serves on our Audit, Compensation (chair) and Nominating & Corporate Governance Committees.

*Ted W. Love, M.D.* Dr. Love has served as a director since September 2012. He was recommended to our nominating and governance committee by one of our non-employee directors and our nominating and governance committee recommended his appointment to our board of directors. From February 2010 until his retirement in August 2012, Dr. Love served as executive vice president of Onyx Pharmaceuticals, Inc., a publicly held biopharmaceutical company developing and commercializing therapies for cancer, most recently as executive vice president and head of research & development and technical operations. Prior to Onyx, from 2001 to January 2009, Dr. Love served as president, chief executive officer and a member of the board of directors of Nuvelo, Inc., a publicly held biopharmaceutical company, and as chairman of the board from 2005 through 2009, prior to Nuvelo's merger with ARCA biopharma, Inc. From 1998 to 2001, Dr. Love served as senior vice president of development of Theravance, Inc., a biopharmaceutical company. Prior to Theravance, he spent six years at Genentech, Inc., most recently as vice president, product development. Dr. Love currently serves on the boards of directors of Affymax, Inc., Amicus Therapeutics, Inc., Bio-Rad Laboratories, Inc., KaloBios Pharmaceuticals, Inc. and Santarus, Inc. He holds a B.A. in molecular biology from Haverford College and a M.D. from Yale Medical School. He completed his residency and fellowship training in internal medicine and cardiology at Harvard Medical School and Massachusetts General Hospital, where he later served on the faculty. In selecting Dr. Love to serve as a director, our board of directors considered, among other things, his valuable medical, drug development and business expertise, including his prior service with Nuvelo, Onyx Pharmaceuticals, Theravance, and Genentech. Our board of directors also determined that it benefits from Dr. Love's experience as a director of other publicly held life science companies on which he currently serves.

*David A. Ramsay.* Mr. Ramsay has served as a director since June 2011. Mr. Ramsay is currently chief financial officer of Halozyme Therapeutics, Inc., a publicly held biopharmaceutical company developing and commercializing products targeting the extracellular matrix, a position he has held since May 2013. He previously served as Halozyme's vice president, corporate development from May 2009 to May 2013. From 2003 to May 2009, he served as Halozyme's vice president, chief financial officer. From 2000 to 2003, Mr. Ramsay was vice president, chief financial officer of Lathian Systems, Inc., a provider of technology-based sales solutions for the life science industry. From 1998 to 2000, he was with Valeant Pharmaceuticals International, Inc. (formerly ICN Pharmaceuticals, Inc.), a multinational specialty pharmaceutical company, where he served as vice president, treasurer and director, corporate finance. Mr. Ramsay began his career at Deloitte & Touche, where he obtained his CPA license. Mr. Ramsay holds a B.S. in business administration from the University of California, Berkeley and a M.B.A. with a dual major in finance and strategic management from The Wharton School at the University of Pennsylvania. Mr. Ramsay's significant experience as chief financial officer of life science companies, particularly his experiences at Halozyme during its successful development and its commercialization of its first products, and at a large audit and financial advisory firm, provide our board of directors with valuable financial and accounting perspectives and skills. Mr. Ramsay also serves on our Audit (chair), Compensation and Nominating & Corporate Governance Committees.

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*Lewis J. Shuster.* Mr. Shuster joined our board of directors in April 2011 immediately following our acquisition of SynthRx, Inc. In 2002, Mr. Shuster founded Shuster Capital, a strategic and operating advisor to and angel investor in life science companies, and has served as its chief executive officer since that time. From June 2003 to November 2007, Mr. Shuster served as chief executive officer of Kemia, Inc., a drug discovery and development company. From February 2000 to December 2001, Mr. Shuster held various operating executive positions at Invitrogen Corporation, a biotechnology company that merged with Applied Biosystems Inc. and became Life Technologies Corporation. Between 1994 and 1999, Mr. Shuster served as chief financial officer and executive vice president corporate development of Pharmacoepia, Inc., a drug discovery product and service company, and also as president and chief operating officer of Pharmacoepia Labs, a division of Pharmacoepia, Inc. Mr. Shuster joined Human Genome Sciences, Inc. as its first employee in September 1992 and served as its executive vice president, operations and finance until 1994. Mr. Shuster currently serves as a member of the board of directors of Response Biomedical Corporation, a medical device company engaged in the research, development, commercialization, and distribution of diagnostic technologies for the medical point of care and on-site environmental testing markets. From April 2010 to March 2013, he served as a director of Complete Genomics, Inc., a life science company, and, from September 2009 to February 2010, as a director of Sorrento Therapeutics, Inc., a biopharmaceutical company. Mr. Shuster received a B.A. in economics from Swarthmore College and an M.B.A. from Stanford University. Mr. Shuster's extensive executive background in strategic planning and managing rapid operations growth for multiple public and private life science companies provide our board of directors with expertise in evaluating and managing the operational and financial challenges and opportunities we may face as we grow our company. Mr. Shuster also serves on our Audit, Compensation and Nominating & Corporate Governance (chair) Committees.

**Director Independence**

Our board of directors has determined that each of Mr. Lief, Dr. Love, Mr. Ramsay and Mr. Shuster, is an independent director as such term is defined in Section 803(A)(2) of the NYSE MKT LLC Company Guide.

**Director Compensation**

The following table shows compensation information for the individuals who served as our non-employee directors during the year ended December 31, 2012. Mr. Culley, our only director who is also one of our employees, does not receive any additional compensation for his service as a director.

**Director Compensation for Fiscal Year 2012**

| Name             | Fees Earned<br>or Paid in<br>Cash | Stock<br>Awards | Option<br>Awards<br>(1)(2) | Non-Equity<br>Incentive<br>Plan<br>Compensation | Nonqualified<br>Deferred<br>Compensation<br>Earnings | All Other<br>Compensation | Total     |
|------------------|-----------------------------------|-----------------|----------------------------|-------------------------------------------------|------------------------------------------------------|---------------------------|-----------|
| Jack Lief        | \$ 62,500                         |                 | \$ 16,042                  |                                                 |                                                      |                           | \$ 78,542 |
| Ted W. Love(3)   | \$ 8,374                          |                 | \$ 20,357                  |                                                 |                                                      |                           | \$ 28,731 |
| David A. Ramsay  | \$ 47,500                         |                 | \$ 16,042                  |                                                 |                                                      |                           | \$ 63,542 |
| Lewis J. Shuster | \$ 43,500                         |                 | \$ 16,042                  |                                                 |                                                      |                           | \$ 59,542 |

- (1) The amounts in this column represent the aggregate grant date fair value of option awards granted to the directors in 2012, calculated in accordance with the provisions of FASB ASC Topic 718, *Stock Compensation*, except that any estimate of forfeitures was disregarded. For a description of the assumptions used to calculate these amounts, see Note 9 to our audited consolidated financial statements included at the end of this prospectus. The actual value of any option award to a director, if any, will depend on the excess of our stock price over the exercise price on the date the option award is exercised. The actual value realized by the director upon exercise of the option awards may be higher or lower than the value shown in this column.
- (2) As of December 31, 2012, our non-employee directors had option awards outstanding to purchase the following number of shares of our common stock:

| Name | Shares<br>Underlying<br>Outstanding<br>Options |
|------|------------------------------------------------|
|------|------------------------------------------------|

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|                  |        |
|------------------|--------|
| Jack Lief        | 60,449 |
| Ted W. Love      | 33,066 |
| David A. Ramsay  | 48,270 |
| Lewis J. Shuster | 50,016 |

- (3) Dr. Love was appointed to our board of directors on September 5, 2012.

**Table of Contents****Overview of Non-Employee Director Compensation**

Compensation of the non-employee members of our board of directors for their service on the board and its committees is set forth in a written policy adopted by our board of directors. With the assistance of its compensation committee, our board of directors periodically reviews and evaluates the director compensation policy and adopts changes to ensure our director compensation enables us to recruit and retain individuals with the requisite experience, skills and characteristics for membership on our board of directors. During 2012, our non-employee director compensation was governed by the non-employee director compensation policy adopted by our board of directors on March 16, 2011, which provides for a combination of cash compensation in the form of a fixed retainer, which varies based on the director's role on our board and its committees, meeting attendance fees, and equity compensation in the form of stock option awards. We also reimburse our directors for travel and other reasonable out-of-pocket expenses related to attendance at meetings of our board of directors and its committees. In March 2013, our board of directors modified the non-employee director compensation policy such that the annual cash retainer paid to the chairperson of each of the compensation committee and nominating and governance committee will be the same amount as the annual cash retainer paid to the chairperson of the audit committee, retroactive to January 1, 2013.

***Retainer***

The following table reflects the amount of the cash retainer payable to each non-employee director under the director compensation policy in effect during 2012 based on the director's role on our board and its committees.

**2012 Cash Retainer(1)**

|                                        | <b>Chairperson</b> | <b>Member</b> |
|----------------------------------------|--------------------|---------------|
| Board of Directors                     | \$ 40,000          | \$ 20,000     |
| Audit Committee                        | \$ 7,500           | \$            |
| Compensation Committee(2)              | \$ 3,500           | \$            |
| Nominating and Governance Committee(2) | \$ 3,500           | \$            |

(1) The amounts listed in this table are the annual amounts payable, which we pay in four equal installments on a quarterly basis. A non-employee director whose service begins or ends during a quarter receives a pro-rated portion of the applicable payment.

(2) For 2013, the retainer payable to the chairperson of this committee is \$7,500.

***Meeting Fees***

Pursuant to our director compensation policy, we pay our non-employee directors \$1,000 for attendance at each meeting of our board of directors and each meeting of a board committee of which such director is a member (whether such attendance is in person or by telephone, video conference or other comparable communication device).

***Equity Compensation***

Pursuant to our director compensation policy, non-employee directors are eligible, in connection with each annual meeting of our stockholders, to receive an annual option to purchase up to such number of shares of our common stock that is equal to the sum of (a) an amount, which we refer to as the allocated amount, equal to the product of 0.0396% multiplied by the number of shares of our common stock outstanding as of the date of the applicable annual meeting of stockholders and (b) an amount, which we refer to as the adjustment amount, equal to the difference between (i) the allocated amount for the current year's annual meeting of stockholders, minus (ii) the allocated amount that was applicable to the prior year's annual meeting of stockholders (unless a director was not a non-employee director at the time of the prior year's annual meeting of stockholders, in which case the adjustment amount for that director will be based on the number of shares of our common stock outstanding as of the date of that director's appointment or election to our board of directors). However, the adjustment amount will be included in the annual option for a director only if (x) the adjustment amount for that director exceeds 20% of the allocated amount for the current year's annual meeting of stockholders, (y) our company's market capitalization (shares outstanding multiplied by stock price) has not exceeded \$100 million for a sustained period, as determined unambiguously by our board of directors, and (z) our board of directors unanimously determines to include the adjustment amount in such annual option. Each annual option will vest and become exercisable in 12 substantially equal monthly installments of 1/12<sup>th</sup> of the shares subject to the option at the end of each successive month following the date of the applicable annual meeting of stockholders, subject to the director's continuing service (as defined in the Amended and Restated 2008 Plan).



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In addition, any non-employee director initially appointed or elected to our board of directors after January 1, 2011, is eligible to receive an inducement option and a pro-rated annual option. An inducement option entitles the director to purchase up to such number of shares of our common stock that is equal to the amount, which we refer to as the new director allocated amount, that is the product of 0.0396% multiplied by the number of shares of our common stock outstanding as of the date of the director's initial appointment or election to our board of directors. A pro-rated annual option entitles the director to purchase up to such number of shares of our common stock that is equal to the product of (A) the quotient of the new director allocated amount, divided by 12, and (B) the number of full 30-day periods between the new director's date of appointment or election and the date of our next annual meeting of stockholders (or, if, on the new director's date of appointment or election, the date of our next annual meeting of stockholders has not been set, the one-year anniversary of the new director's date of appointment or election). Each inducement option will vest and become exercisable in 36 substantially equal monthly installments of 1/36<sup>th</sup> of the shares subject to the option at the end of each successive month following the date of the director's initial appointment or election to our board of directors, subject to the director's continuing service (as defined in the Amended and Restated 2008 Plan). Each pro-rated annual option will vest and become exercisable in such number of substantially equal monthly installments as is equal to the number of full 30-day periods between the director's initial appointment or election to our board of directors and the date of the next annual meeting of our stockholders.

Each stock option award granted pursuant to our director compensation policy will be granted under the Amended and Restated 2008 Plan, or any amendment or restatement thereof, will have an exercise price per share equal to the fair market value (as defined in the Amended and Restated 2008 Plan) of a share of our common stock on the date the option award is granted, and will have a term equal to the shorter of (i) ten years from the date the option award is granted and (ii) three years from the date such non-employee director ceases to provide services (as defined in the Amended and Restated 2008 Plan) to us for any reason other than such director's death or disability. In addition, in the event of a change of control of our company, each option award will vest and become exercisable on the day prior to the date of the change in control if the director is then providing services (as defined in the Amended and Restated 2008 Plan), and each option award will terminate on the date of the change in control to the extent not exercised.

## **EXECUTIVE COMPENSATION**

### **Overview**

Our executive compensation program is intended to enable us to attract and retain qualified executive officers and to align the interests of our executive officers with those of our stockholders by incentivizing and rewarding achievement of business objectives that we believe will enhance the value of our company and by promoting commitment to long-term success. The primary components of our executive compensation program are base salary, annual performance-based cash incentives, and stock option awards. Executive compensation is determined by our compensation committee, which consists entirely of independent directors.

As a development-stage biopharmaceutical company, we are focused on advancing MST-188, our lead product candidate, through clinical studies and other development activities and seeking approval from the FDA to commercialize it and we expect to continue to incur substantial operating losses for the next several years. As such, the compensation committee evaluates corporate performance principally based on progress with product development and not on financial metrics. However, our annual performance objectives also typically include the maintenance of a specified level of capital. In 2012, our primary focus was advancing MST-188 toward a pivotal phase 3 clinical study in sickle cell disease, which we initiated in January 2013. The majority of the performance objectives under our annual incentive plan were related to that goal.

Our compensation committee evaluates, on an annual basis, executive compensation, including whether it encourages excessive risk-taking and the attributes of our executive compensation policies and practices that mitigate such risks. The risk-mitigating factors considered by the compensation committee include:

a compensation committee consisting entirely of independent directors;

the regular (at least annual) review of the amount, form and terms of executive compensation by the compensation committee;

a mix of different types of compensation, which provides balance between fixed and performance-based compensation and as to the timing of pay realization, incentivizing executive officers to consider both near- and long-term value creation;

a fixed component (base salary) that constitutes a significant percentage of the executive officers' total cash compensation, which reduces incentive to take excessive risks in pursuit of annual bonuses;

corporate performance objectives under the annual cash incentive plan that reflect a variety of elements of company performance, which diversifies the risk of focusing executive officers on any single performance metric;



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corporate performance objectives under the annual cash incentive plan that have year-to-year inter-relatedness, typically in relation to product development, which discourages achievement of short-term goals that would compromise longer-term success and, consequently, future compensation;

the compensation committee's discretion under the annual cash incentive plan to modify, replace or eliminate performance objectives during the year in response to changing circumstances, which discourages risk-taking to achieve goals that the committee may determine are undesirable or irrelevant; and

multi-year, time vesting on stock option awards, which requires long-term value creation in order for an executive officer to realize a substantial part of an award's value.

Below is an overview of the 2012 compensation of our chief executive officer, Brian Culley, our president and chief operating officer, Patrick Keran, and our chief medical officer and senior vice president, Santosh Vetticaden, whom we refer to as our named executive officers or NEOs. The employment of our NEOs is at-will and we do not have employment agreements with any of them. The initial terms of Dr. Vetticaden's employment with us are set forth in his offer letter, the material terms of which are described below.

Dr. Vetticaden joined our company in September 2012, relocating from Massachusetts, and his compensation for 2012 included a \$100,000 signing bonus, which was also intended to help defray his relocation expenses. Dr. Vetticaden's compensation also included a stock option award for up to 600,000 shares of our common stock. Both the signing bonus and stock option award were specifically negotiated prior to his acceptance of our offer of employment.

***Base Salary***

The purpose of the base salary component of our NEOs' compensation is to provide a level of income that allows us to attract and retain executive talent and mitigates pressure to focus on stock price performance to the detriment of other important aspects of our business. The compensation committee did not increase Messrs. Culley's or Keran's base salary for 2012. Their base salaries were set in July 2011 at \$375,000 and \$370,000, respectively. In evaluating their base salaries for 2012, the compensation committee considered and agreed with Messrs. Culley's and Keran's recommendation that an adjustment was unnecessary for 2012.

Dr. Vetticaden's 2012 base salary was set at \$350,000 in his offer letter following an arm's length negotiation prior to his employment. Prior to Dr. Vetticaden, we had not had a chief medical officer since 2008. In determining Dr. Vetticaden's base salary, the independent members of our board of directors took into consideration his base salary at his prior position as senior vice president, chief medical and development officer of Cubist Pharmaceuticals, Inc., a publicly-traded biopharmaceutical company, as disclosed in Cubist's proxy statement for its 2011 annual meeting of stockholders, which was \$398,120 for 2010. They also reviewed salary data for chief medical officers published in the 2011 San Diego Biotechnology Employee Development Coalition (BEDC) Compensation Survey of 79 public and private biotechnology companies in San Diego, California. Although our management and board of directors used this survey data as a tool in negotiating and setting Dr. Vetticaden's base salary, they did not benchmark against any group of companies or apply any formula to the survey data.

In December 2012, our compensation committee determined to increase the base salaries of our executive officers for 2013 by approximately 5.0% relative to their 2012 base salaries, except that it determined Dr. Vetticaden's 2013 base salary would remain the same as the base salary set in his offer letter. Therefore, effective January 1, 2013, the base salaries for Messrs. Culley and Keran and Dr. Vetticaden are \$393,750, \$388,750 and \$350,000, respectively.

**Table of Contents*****Annual Performance-Based Cash Incentives***

In early 2012, our compensation committee approved the 2012 Executive Incentive Plan, pursuant to which executive officers were eligible for incentive awards, generally payable in cash, based on achievement of corporate and, potentially, individual performance objectives. At that time, taking into consideration recommendations by Messrs. Culley and Keran, the compensation committee also approved the corporate performance objectives applicable to the plan. Under the 2012 Executive Incentive Plan, each participant was assigned an incentive target that was expressed either as a specific dollar amount or as a percentage of annual base salary, and the participant's actual incentive award would be based on the level of achievement of the corporate objectives approved by the compensation committee and, if applicable, individual objectives approved by the chair of the compensation committee. The corporate objectives set by the compensation committee were applicable to all participants in order to align the interests of our executive officers with one another and with our stockholders. No individual objectives were approved under the plan, so the actual incentive awards were based 100% on achievement of corporate objectives. As part of the terms of Dr. Vetticaden's employment, as set forth in his offer letter, our board of directors made him a participant under the 2012 Executive Incentive Plan, but on a prorated basis based on salary earned in 2012. The following table lists the NEOs and their incentive targets under the 2012 Executive Incentive Plan:

| Named Executive Officer | Incentive Target |
|-------------------------|------------------|
| Brian Culley            | \$187,500 (50%)  |
| Patrick Keran           | \$187,500 (~50%) |
| Santosh Vetticaden      | 35%              |

Under the 2012 Executive Incentive Plan, the compensation committee had discretion to grant an incentive award that was less than the incentive target if it determined performance partially met objectives or was less than acceptable, and to grant an incentive award that exceeded the incentive target if it determined performance exceeded objectives or was excellent in view of prevailing conditions. Pursuant to the plan, in evaluating performance, the compensation committee was to consider the achievement of objectives, the degree to which performance exceeded the objective or an objective was partially achieved, the quality of achievement, the difficulty in achieving the objective, conditions that affected the ability to achieve objectives and such other factors as it determined appropriate.

As discussed above, because we are a development-stage biopharmaceutical company, our compensation committee typically focuses on progress with product development in setting corporate objectives and determining actual award amounts under our annual incentive plans. The corporate objectives for the 2012 Executive Plan approved by the compensation committee in early 2012 involved progress and plans relating to research and development of MST-188 and ANX-514 and achieving a specified level of capital at year-end. By mid-year, however, we had determined not to make any further significant investment in manufacturing development activities for ANX-514 and to limit its development activities to nonclinical studies, which decisions were in contrast to certain of the 2012 performance objectives related to ANX-514. At the regular second quarter meeting of our board of directors, our independent directors and management came to a consensus that, in light of the shift in corporate strategy previously approved by the board, some of the corporate objectives for the 2012 Executive Plan were no longer appropriate to pursue.

The corporate objectives under the 2012 Executive Incentive Plan and the compensation committee's assessment of achievement of such objectives are described below:

| Corporate Objective                                                                 | Achievement            |
|-------------------------------------------------------------------------------------|------------------------|
| <u>Product Development – MST-188</u>                                                |                        |
| Favorable outcome of FDA review of phase 3 study design by mid-year                 | Met objective          |
| Finalize development plan in sickle cell disease by Q3                              | Met objective          |
| Establish phase 3 trial site by Q4                                                  | Met objective          |
| Release clinical trial material by Q4                                               | Did not meet objective |
| <u>Product Development – ANX-514</u>                                                |                        |
| Finalize new development plan by Q3                                                 | Met objective          |
| Release clinical trial material by Q4                                               | Did not meet objective |
| <u>Finance</u>                                                                      |                        |
| Year-end cash, cash equivalents and short-term investments consistent with forecast | Met objective          |



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In determining the amounts of awards under the 2012 Executive Incentive Plan, the compensation committee took into consideration that the board of directors previously had agreed that aspects of the ANX-514 development objectives were not desirable to pursue. The corporate objectives had not been assigned specific weightings, but, particularly in light of the changes in corporate strategy, the compensation committee considered the objectives that related to advancing the development of MST-188 as predominant. The compensation committee considered that almost all of the corporate objectives had been achieved, but that a key objective for advancing MST-188 into a phase 3 clinical study, release of clinical trial material, was not achieved. In light of substantial achievement of the corporate goals under the 2012 Executive Incentive Plan, the compensation committee determined to award approximately 83.3% of their incentive target, or \$156,188, to each of Messrs. Culley and Keran. The compensation committee determined to award 100% of Dr. Veticaden's incentive target, or \$39,603. In making its determination with regard to Dr. Veticaden, the compensation committee took into account its general assessment of his performance since joining our company and that it did not anticipate increasing his base salary or granting him a stock option award in 2013.

### ***Stock Option Awards***

We typically grant stock option awards each year to our employees, including our executive officers, with multi-year, time-based vesting. Option awards have been granted under stockholder-approved plans and, since June 2011, under our Amended and Restated 2008 Omnibus Incentive Plan (the "Amended and Restated 2008 Plan"). The Amended and Restated 2008 Plan does not permit repricing or option exercise prices below 100% of the fair market value of our common stock on the date of grant (i.e., the closing sale price of our common stock on the NYSE MKT on the date of grant). Stock options granted to employees generally vest monthly over four years after the date of grant and have a 10-year term. Because stock options are valuable only if our stock price is greater when the option is exercised than it was at the time the option was granted, we believe these equity awards promote a long-term perspective on corporate success and directly incentivize our NEOs to build long-term value. The multi-year vesting feature and 10-year term also foster employee retention.

Since 2010, we generally have used what we refer to as a "carried interest" framework to determine the size of stock option awards for all of our employees, including our NEOs. The target carried interest for each employee, expressed as a percentage that we refer to as the carried interest percentage ("CIP"), refers to the targeted ownership stake in our company that the employee is expected to achieve over time, typically over four years. The CIP is then translated into a share number by multiplying it by the number of outstanding shares of our common stock, on an adjusted fully-diluted basis (which, for 2012, added only shares underlying outstanding warrants with exercise prices of \$2.75 or less per share). The resulting share number is then allocated over the designated period (e.g., four years), with the size of an employee's initial award typically about three times the size of the subsequent awards. For example, if the share number was 100, an employee's initial option award would be for 50 shares and in each of years 2, 3 and 4, that employee's option award would be for approximately 16 shares, assuming that the total number of our outstanding shares, on an adjusted fully-diluted basis, did not change between year 1 and year 4. We believe this framework is well-suited for our company because it provides for a coherent approach to achieving targeted ownership levels for our NEOs following changes to our capitalization, which helps ensure that these equity awards continue to achieve their intended retention and motivational purposes. To determine the CIP for each NEO, the compensation committee considers the NEO's role, responsibilities and past performance, BEDC survey data regarding ownership stakes of executives in similar positions, and the CIPs for other of our executive officers. The aggregate target CIP for our NEOs currently is approximately 6.3% and, as of the record date for the Annual Meeting, their aggregate deemed ownership stake, for purposes of applying the carried interest framework, is approximately 4.3% on an adjusted fully-diluted basis (which, for 2013, adds only shares underlying outstanding warrants with exercise prices of \$3.75 or less per share). The ownership stake utilized for the carried interest framework does not reflect the NEOs' current beneficial ownership (calculated in accordance with SEC rules) because it takes into account all shares underlying outstanding stock options, including those that are not vested or exercisable and will not be vested or exercisable within 60 days, but does not include option shares with exercise prices per share of \$57.50 or greater. Because the NEOs' options vest and become exercisable over a minimum of four years from the grant date, the NEOs' deemed ownership stake for purposes of the carried interest framework is significantly larger than the NEOs' beneficial ownership calculated in accordance with SEC rules. Notwithstanding the compensation committee's general practice of applying the carried interest framework to determine stock option awards, the compensation committee has complete discretion with regard to size and terms of stock option awards. The compensation committee may determine to adjust the CIP or, for any particular year, may determine to grant an option award that is greater or less than what would be granted by calculating the CIP share amount. The compensation committee may exercise this discretion for a variety of reasons, including the number of shares available under our stockholder-approved equity plan, an officer's ownership in our company apart from company-granted stock options, anticipated changes to an officer's role or responsibilities, and anticipated changes to our company's capitalization.

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Although the compensation committee or our board of directors typically grants employee stock option awards each year, in 2012, no option awards were granted to employees other than those employees who commenced employment with our company during 2012. From July 2005 through July 2012, under the terms of the Rights Agreement, dated July 27, 2005, among us and certain investors, including Icahn Partners LP (the Rights Agreement), we were prohibited from granting certain securities, including stock options, without complying with the provisions of the Rights Agreement. In December 2011, the compensation committee granted stock option awards to all of our employees, including Messrs. Culley and Keran, in lieu of granting such awards in the first quarter of 2012 primarily because we previously had secured waivers under the Rights Agreement that permitted us to grant the option awards, but those waivers expired on December 31, 2011 and our ability to obtain future waivers under the Rights Agreement on a timely basis, or at all, was uncertain. The option awards granted in December 2011, including those granted to Messrs. Culley and Keran, did not begin vesting until 2012 and, subject to their continued service to us, vest monthly over a four-year period.

Dr. Veticaden was granted a stock option award to purchase up to 600,000 shares of our common stock on September 5, 2013, which was his start date with our company. The option has a 10-year term and an exercise price of \$0.69 per share, which was the closing price of our common stock on the NYSE MKT on the grant date. Subject to Dr. Veticaden's continued service to us, the option vests and becomes exercisable as to 25% of the shares subject to the option, or 150,000 shares, on the first anniversary of the grant date and as to the remaining shares in 36 substantially equal monthly installments thereafter.

In December 2012, the compensation committee considered the timing of the grant of annual employee option awards generally and determined that the option awards would better serve their intended retention and motivational purposes by changing the practice of granting option awards once a year at the beginning of the year to a twice-yearly schedule, with one grant generally occurring around the beginning of the year and the other generally occurring around the time of our annual meeting of stockholders, with the size of each semi-annual award generally equal to one-half of the amount that otherwise would have been granted. The compensation committee determined to implement this new practice for 2013, and the first semi-annual employee option awards were granted in January 2013. Messrs. Culley and Keran each received an option to purchase 138,650 shares of our common stock. The options have a 10-year term, an exercise price of \$0.59 per share, which was the closing price of our common stock on the NYSE MKT on the grant date, and vest and become exercisable, subject to the officer's continued service to us, in 48 substantially equal monthly installments. In light of the size and timing of his initial option award in September 2012, the compensation committee determined not to grant Dr. Veticaden an option award in January 2013.

***Other Benefits and Post-Termination Compensation***

Our NEOs, as well as our other regular, full-time employees are eligible for a variety of health and welfare and paid time-off benefits. We believe that these benefits enable us to offer more competitive compensation packages and support employee focus and productivity. In addition, as described below, our NEOs may be entitled to receive additional benefits upon termination of their employment. These arrangements are intended to keep our NEOs focused on corporate interests while employed, including in the face of potential change in control transactions, and, at the time they were implemented, were deemed necessary to attract or retain the employment of the NEOs. Additional advantages to us include our receipt of a release of claims as a precondition to paying any cash severance.

*401(k) Plan and Company Match.* We have a defined contribution savings plan pursuant to Section 401(k) of the Internal Revenue Code of 1986. The plan is for the benefit of all employees and permits voluntary contributions by qualifying employees of up to 100% of eligible compensation, subject to Internal Revenue Service-imposed maximum limits. Under the terms of the plan, we are required to make matching contributions equal to 100% of employee contributions up to 6% of eligible compensation, limited by the IRS-imposed maximum, for all employees. With respect to the NEOs, we incurred total expenses of approximately \$37,665 and \$29,400 in matching contributions in 2012 and 2011, respectively.

*Life Insurance Policies.* We provide all regular, full-time employees, including the NEOs, with a life insurance policy equal to two times the employee's annual base salary, up to a maximum coverage of \$750,000.

*Paid Time-off.* Messrs. Culley and Keran and Dr. Veticaden accrue 28, 26 and 20 vacation days per year, respectively, subject to adjustment based on the number of years of the officer's employment with us. Under our policy, the maximum amount of vacation days that an employee, including our NEOs, can accrue is two times the employee's annual accrual limit. If the NEOs' employment with us had terminated as of December 31, 2012, our aggregate payment obligation for this benefit would have been approximately \$81,000, \$74,000 and \$6,000 for Messrs. Culley and Keran and Dr. Veticaden, respectively.

*Perquisites.* We did not provide any of our NEOs with perquisites in 2012 that exceeded \$10,000 in the aggregate for any person.



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*Accelerated Vesting of Stock Options.* As described in more detail below under Acceleration of Vesting of Option Awards, the vesting and exercisability of stock options held by our NEOs may accelerate to various degrees under circumstances involving a change in control and/or involuntary termination, depending on the particular terms of the agreement governing the stock option.

*Employment Retention and Severance Arrangements.* The employment of each of our NEOs is at-will and they or we may terminate their employment with us at any time with or without prior notice. In July 2009, the compensation committee adopted a retention and severance plan (the Retention Plan ) applicable to each of Messrs. Culley and Keran. The compensation committee determined that this plan was necessary to incentivize and retain Messrs. Culley and Keran, who at the time were our only employees, and reinforce their dedication to us during a period when they would have been likely seek alternative employment otherwise. We agreed to provide Dr. Vetticaden with similar arrangements, which are set forth in his offer letter.

Under the Retention Plan, in the cases of Messrs. Culley and Keran, and pursuant to the terms of Dr. Vetticaden s offer letter, if the employment of Mr. Culley, Mr. Keran or Dr. Vetticaden, as applicable, terminates at any time as a result of an involuntary termination, and Mr. Culley, Mr. Keran or Dr. Vetticaden, as the case may be, delivers and does not revoke a general release of claims, which confirms any post-termination obligations and/or restrictions applicable to him, he will be entitled to (i) an amount equal to 12 months (for Messrs. Culley and Keran) or nine months (for Dr. Vetticaden) of his then-current base salary, less applicable withholdings, and (ii) an amount equal to the estimated cost of continuing his healthcare coverage and the coverage of his dependents who are covered at the time of the involuntary termination under the Consolidated Omnibus Budget Reconciliation Act of 1985, as amended, for a period equal to 12 months (for Messrs. Culley and Keran) or nine months (for Dr. Vetticaden). These severance benefits will be paid in a lump-sum on the date the general release of claims becomes effective. If the NEOs employment with us had been involuntarily terminated as of December 31, 2012, our aggregate payment obligations to them under the Retention Plan and under Dr. Vetticaden s offer letter, as applicable, would have been approximately \$402,000 for Mr. Culley, \$397,000 for Mr. Keran and \$292,000 for Dr. Vetticaden.

For purposes of the Retention Plan, an involuntary termination means (i) without the officer s express written consent, an action by our board of directors or external events causing or immediately portending a material reduction or alteration of the officer s duties, position or responsibilities relative to the officer s duties, position or responsibilities in effect immediately prior to such reduction or alteration, or the removal of the officer from such position, duties or responsibilities; provided, however, that an involuntary termination will not be deemed to occur with respect to Mr. Culley, if Mr. Culley remains the head of and most senior individual within our company s (or our successor s) business development function, and with respect to Mr. Keran, if Mr. Keran remains the head of and most senior individual within our company s (or our successor s) legal function; (ii) without the officer s express written consent, a material reduction by us of the officer s base salary as in effect immediately prior to such reduction; (iii) without the officer s express written consent, the relocation of the officer s principal place of employment with us by more than 50 miles; (iv) any termination of the officer s employment by us without cause (as defined below), or (v) a material breach of the plan, including, but not limited to our failure to obtain the assumption of the plan by any successors, as contemplated in the plan. For purposes of the Retention Plan, cause means (A) any act of personal dishonesty taken by the officer in connection with his responsibilities as an employee which is intended to result in substantial personal enrichment of the officer; (B) the officer s conviction of a felony that our board of directors reasonably believes has had or will have a material detrimental effect on our reputation or business; (C) a willful act by the officer that constitutes misconduct and is materially injurious to us, or (D) continued willful violations by the officer of the officer obligations to us after there has been delivered to the officer a written demand for performance from us that describes the basis for our belief that the officer has not substantially performed his duties.

Dr. Vetticaden s offer letter contains the same definitions of involuntary termination and cause, except that, with respect to involuntary termination, in lieu of clause (v) above, the offer letter includes: (v) our failure to obtain the assumption of the offer letter by any successors as contemplated in the offer letter. With regard to cause, the offer letter includes any act of personal dishonesty by Dr. Vetticaden in connection with his hiring process that our board of directors believes has had or will have a material detrimental effect on our reputation or business.

**Summary Compensation Table**

The following table sets forth information concerning compensation earned for services rendered to us during the years ended December 31, 2012 and December 31, 2011 by our principal executive officer and our two most highly compensated executive officers other than our principal executive officer as of December 31, 2012. We refer to the executive officers named in the following table as the named executive officers or NEOs.

**Table of Contents****Summary Compensation Table**

| Name and Principal Position                                                 | Year | Salary     | Bonus         | Stock Awards | Option Awards(1) | Non-Equity                | Nonqualified          | All Other Compensation(3) | Total |
|-----------------------------------------------------------------------------|------|------------|---------------|--------------|------------------|---------------------------|-----------------------|---------------------------|-------|
|                                                                             |      |            |               |              |                  | Incentive Compensation(2) | Deferred Compensation |                           |       |
| Brian M. Culley(4)<br>Chief Executive Officer                               | 2012 | \$ 375,000 |               |              |                  | \$ 156,188                | \$ 16,680             | \$ 547,868                |       |
|                                                                             | 2011 | \$ 360,750 |               |              | \$ 1,164,247     | \$ 131,250                | \$ 17,648             | \$ 1,673,895              |       |
| Patrick L. Keran<br>President and Chief Operating Officer                   | 2012 | \$ 370,000 |               |              |                  | \$ 156,188                | \$ 15,828             | \$ 542,016                |       |
|                                                                             | 2011 | \$ 343,950 |               |              | \$ 1,164,247     | \$ 131,250                | \$ 17,662             | \$ 1,657,109              |       |
| Santosh J. Vetticaden(5)<br>Chief Medical Officer and Senior Vice President | 2012 | \$ 113,750 | \$ 100,000(6) |              | \$ 370,860       | \$ 39,603                 | \$ 7,274              | \$ 631,487                |       |

- (1) The amounts in this column represent the aggregate grant date fair value of option awards granted to the named executive officers in 2012 and 2011, respectively, calculated in accordance with the provisions of Financial Accounting Standards Board, or FASB, Accounting Standards Codification, or ASC, Topic 718, Stock Compensation, except that any estimate of forfeitures was disregarded. For a description of the assumptions used to calculate these amounts, see Note 9 to our audited consolidated financial statements included at the end of this prospectus. These option awards were granted under our 2008 Omnibus Incentive Plan (the 2008 Plan) and the Amended and Restated 2008 Plan and, pursuant to the terms of those plans, the exercise price per share of the option awards cannot be lowered without prior approval of our stockholders, except in the event of a merger, reorganization, consolidation, recapitalization, dividend or distribution (whether in cash, shares or other property, other than a regular cash dividend), stock split, reverse stock split, spin-off or similar transaction or other change in corporate structure affecting our common stock or the value thereof, in each case as our compensation committee may deem equitable or appropriate. The actual value of any option award to an officer, if any, will depend on the excess of our stock price over the exercise price on the date the option is exercised. The actual value realized by the officer upon exercise of the option awards may be higher or lower than the value shown in this column.
- (2) We paid the amounts set forth in this column pursuant to the terms of our 2012 Executive Incentive Plan and 2011 Mid-Year Incentive Plan, respectively. See Overview Annual Performance-Based Cash Incentives above for information regarding the 2012 Executive Incentive Plan.
- (3) The amounts in this column consist of (a) matching contributions made pursuant to our tax-qualified 401(k) plan and (b) premiums paid for life insurance policies for the benefit of our executives.
- (4) Mr. Culley also serves as a member of our board of directors, but he does not receive any additional compensation for such service.
- (5) Dr. Vetticaden joined our company in September 2012. He was not a named executive officer in 2011. Accordingly, this table does not include 2011 compensation information for Dr. Vetticaden.
- (6) This amount was paid to Dr. Vetticaden as a signing bonus, which was also intended to help defray his relocation expenses from Massachusetts. If Dr. Vetticaden voluntarily resigns before September 1, 2014, other than in connection with an involuntary termination for which he is entitled to severance benefits under the terms of his offer letter, he must reimburse us the full amount of the signing bonus within 30 days of such resignation.



**Table of Contents****Outstanding Equity Awards at Fiscal Year-End 2012**

The following table sets forth information regarding outstanding equity awards held by our named executive officers at the end of fiscal 2012. All share and per share information included in this table for option awards granted before April 23, 2010 reflects retrospective application of the 1-for-25 reverse split of our outstanding common stock effected on April 23, 2010.

| Name                  | Option Awards<br>Equity Incentive Plan<br>Awards: Number of<br>Securities |                                                                  | Underlying<br>Unexercised<br>Options<br>(#) | Price<br>(\$) | Option Expiration<br>Date |
|-----------------------|---------------------------------------------------------------------------|------------------------------------------------------------------|---------------------------------------------|---------------|---------------------------|
|                       | Number of Securities<br>Underlying Unexercised<br>Options<br>(#)          | Number of Securities<br>Underlying Unexercised<br>Options<br>(#) |                                             |               |                           |
| Brian M. Culley       | 4,000                                                                     |                                                                  |                                             | \$ 57.50      | 07/13/2015                |
|                       | 3,200                                                                     |                                                                  |                                             | \$ 118.75     | 01/30/2016                |
|                       | 5,999                                                                     |                                                                  |                                             | \$ 68.75      | 01/11/2017                |
|                       | 6,400(2)                                                                  | 1,600(2)                                                         |                                             | \$ 13.50      | 03/30/2018                |
|                       | 51,000(3)                                                                 | 16,999(3)                                                        |                                             | \$ 3.25       | 07/20/2019                |
|                       | 32,002(4)                                                                 | 31,997(4)                                                        |                                             | \$ 8.00       | 02/02/2020                |
|                       | 25,000(5)                                                                 | 75,000(5)                                                        |                                             | \$ 2.29       | 02/01/2021                |
|                       | 88,541(6)                                                                 | 161,459(6)                                                       |                                             | \$ 3.26       | 07/05/2021                |
| Patrick L. Keran      | 97,395(7)                                                                 | 327,605(7)                                                       |                                             | \$ 0.60       | 12/07/2021                |
|                       | 4,000                                                                     |                                                                  |                                             | \$ 74.75      | 08/17/2016                |
|                       | 1,999                                                                     |                                                                  |                                             | \$ 68.75      | 01/11/2017                |
|                       | 6,400(2)                                                                  | 1,600(2)                                                         |                                             | \$ 13.50      | 03/30/2018                |
|                       | 51,000(3)                                                                 | 16,999(3)                                                        |                                             | \$ 3.25       | 07/20/2019                |
|                       | 32,002(4)                                                                 | 31,997(4)                                                        |                                             | \$ 8.00       | 02/02/2020                |
|                       | 25,000(5)                                                                 | 75,000(5)                                                        |                                             | \$ 2.29       | 02/01/2021                |
|                       | 88,541(6)                                                                 | 161,459(6)                                                       |                                             | \$ 3.26       | 07/05/2021                |
| Santosh J. Vetticaden | 97,395(7)                                                                 | 327,605(7)                                                       |                                             | \$ 0.60       | 12/07/2021                |
|                       |                                                                           | 600,000(8)                                                       |                                             | \$ 0.69       | 09/04/2022                |

- (1) The agreements covering these option awards contain vesting acceleration provisions triggered by certain change in control and/or involuntary termination circumstances as described below under Acceleration of Vesting of Option Awards. Consequently, the vesting schedules described for each option in this table are subject to acceleration in connection with a change in control or involuntary termination, as described below. Otherwise, vesting is subject to the NEO's continued service to our company.
- (2) This option was granted under our 2005 Equity Incentive Plan in March 2008. It vests and becomes exercisable in five equal annual installments. One-fifth of the total underlying shares vested and became exercisable on January 1 of each of 2009, 2010, 2011 and 2012, and the final installment will vest and become exercisable on January 1, 2013.
- (3) This option was granted under the 2008 Plan in July 2009. It vests and becomes exercisable in four substantially equal annual installments. Approximately 1/4 of the total underlying shares vested and became exercisable on January 1 of each of 2010, 2011 and 2012, and the final installment will vest and become exercisable on January 1, 2013.
- (4) This option was granted under the 2008 Plan in February 2010. It vests and becomes exercisable in four substantially equal annual installments. Approximately 1/4 of the total underlying shares vested and became exercisable on January 1 of each of 2011 and 2012 and will vest and become exercisable on January 1 of each of 2013 and 2014.
- (5) This option was granted under the 2008 Plan in February 2011. It vests and becomes exercisable in four equal annual installments. One-fourth of the total underlying shares vested and became exercisable on January 1, 2012 and will vest and become exercisable on January 1 of each of 2013, 2014 and 2015.
- (6) This option was granted under the Amended and Restated 2008 Plan in July 2011. It vests and becomes exercisable in substantially equal monthly installments over four years. Approximately 1/48 of the total underlying shares vested and became exercisable on August 1, 2011 and will vest and become exercisable on the first day of each month thereafter.
- (7) This option was granted under the Amended and Restated 2008 Plan in December 2011. It vests and becomes exercisable in substantially equal monthly installments over four years. Approximately 1/48 of the total underlying shares vested and became exercisable on February 1, 2012 and will vest and become exercisable on the first day of each month thereafter.

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- (8) This option was granted under the Amended and Restated 2008 Plan in September 2012. It vests and becomes exercisable in substantially equal monthly installments over three years after a one-year cliff vesting. Approximately 1/4 of the total underlying shares will vest and become exercisable on September 5, 2013 and approximately 1/48 of the total underlying shares will vest and become exercisable on the fifth day of each of the 36 months thereafter.

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**Table of Contents****Acceleration of Vesting of Option Awards**

Stock option awards granted to Messrs. Culley and Keran and Dr. Veticaden contain vesting acceleration provisions triggered by certain change in control and/or involuntary termination circumstances. With regard to option awards granted to Messrs. Culley and Keran in 2010 and 2011, in the event Mr. Culley or Mr. Keran ceases to provide services to us as an employee by reason of an involuntary termination, his option award will, immediately prior to such involuntary termination, vest and become exercisable with respect to 25% of the total number of shares subject to the option award, and the exercisability of the then-vested portion of the option award (after taking into account the foregoing acceleration) will be extended such that the option award will be exercisable for a period of 12 months following the date of such involuntary termination but not later than the 10-year term expiration, subject to limited exceptions. In addition, the vesting and/or exercisability of each option award will accelerate or be extended under certain circumstances, including, (a) in the event of a change in control (as defined in the 2008 Plan or the Amended and Restated 2008 Plan, depending on whether the option award was granted under the 2008 Plan or the Amended and Restated 2008 Plan), acceleration of vesting with respect to 50% of the then unvested shares on the day prior to the date of the change in control and, subject to the respective officer's continuous service, with respect to the remaining 50% of the then unvested shares on the one year anniversary of the date of the change in control, (b) subject to the preceding clause (a), in the event of a change of control, to the extent the successor company (or a subsidiary or parent thereof) does not assume or substitute for the option award, acceleration in full on the day prior to the date of the change in control if the officer is then providing services or was the subject of an involuntary termination in connection with, related to or in contemplation of the change in control and exercisability for a period of 24 months following the date of such involuntary termination but not later than the 10-year term expiration, subject to limited exceptions, and (c) subject to the preceding clause (a), in the event of a change in control, to the extent the successor company (or a subsidiary or parent thereof) assumes or substitutes for the option award, and in the event of an involuntary termination of the officer within 12 months following the date of the change in control, acceleration in full of vesting and exercisability for a period of 24 months following the date of such involuntary termination but not later than the 10-year term expiration, subject to limited exceptions. Option awards granted to Messrs. Culley and Keran in 2009 contain the same change in control-related vesting acceleration provisions. Option awards granted to Messrs. Culley and Keran before 2009 were granted under our 2005 Equity Incentive Plan, and, as of January 1, 2013, all such option awards were vested and exercisable in full. For purposes of the option awards granted to Messrs. Culley and Keran in 2009, 2010 and 2011, the definitions of involuntary termination and cause are the same as described above with respect to the Retention Plan, except that for option awards granted in 2011, the definition of involuntary termination does not include exceptions in the event that Mr. Culley remains the head of and most senior individual within our company's (or our successor's) business development function or in the event that Mr. Keran remains the head of and most senior individual within our company's (or our successor's) legal function.

In the event Dr. Veticaden ceases to provide services to us as an employee by reason of an involuntary termination, his option award will, immediately prior to such involuntary termination, vest and become exercisable with respect to 18.75% of the total number of shares subject to the option award, and the exercisability of the then-vested portion of the option award (after taking into account the foregoing acceleration) will be extended such that the option award will be exercisable for a period of nine months following the date of such involuntary termination but not later than the 10-year term expiration, subject to limited exceptions. In addition, in the event of a change in control (as defined in the Amended and Restated 2008 Plan), (i) to the extent the successor company (or a subsidiary or parent thereof) does not assume or substitute for the option award, acceleration in full on the day prior to the date of the change in control if Dr. Veticaden is then providing services or was the subject of an involuntary termination in connection with, related to or in contemplation of the change in control and exercisability for a period of 18 months following the date of such involuntary termination, and (ii) to the extent the successor company (or a subsidiary or parent thereof) assumes or substitutes for the option award, and in the event of an involuntary termination of Dr. Veticaden within 24 months following the date of the change in control, acceleration in full of vesting and exercisability for a period of 18 months following the date of such involuntary termination. For purposes of this option award, the definitions of involuntary termination and cause are the same as described above in Dr. Veticaden's offer letter.

Generally, under the 2008 Plan and the Amended and Restated 2008 Plan, a change in control occurs upon (a) a merger or consolidation of our company with or into another entity, (b) the sale, transfer or other disposition of all or substantially all of our assets, (c) certain changes in the majority of our board of directors within a period of 36 consecutive months, (d) the acquisition, pursuant to a tender or exchange offer made directly to our stockholders that our board of directors does not recommend, of more than 50% of the total combined voting power in our outstanding securities, (e) approval by our stockholders of a plan of complete liquidation or dissolution, or (f) a determination by the majority of our board of directors that a change in control has occurred.

Although the terms of the option awards granted to Messrs. Culley and Keran and Dr. Veticaden provide for acceleration of vesting in the circumstances as described above, none of the accelerated option awards would have had intrinsic value on December 31, 2012 because none of the NEOs' outstanding option awards have an exercise price that is less than the closing sale price of our common stock on December 31, 2012, which was \$0.57 per share. In other words, none of the option awards were in-the-money on December 31, 2012.



**Table of Contents****CERTAIN RELATIONSHIPS AND RELATED PARTY TRANSACTIONS**

We have incorporated into our written review and approval policies certain procedures designed to ensure that any proposed transaction in which we would be a participant and in which any of our directors, executive officers, holders of more than 5% of our common stock, or any member of the immediate family of any of the foregoing, would have a direct or indirect material interest is reviewed by individuals within our company familiar with the requirements of Item 404 of Regulation S-K promulgated by the SEC. If any such proposed transaction would require disclosure pursuant to Item 404(a) of Regulation S-K, it will be presented to the audit committee for review and, if appropriate, approval.

Other than the following transactions and the transactions described under **Executive Officer Compensation** and **Director Compensation** elsewhere in this prospectus, since January 1, 2011, there has not been, nor currently are there proposed, any transactions or series of similar transactions in which we were or are to be a participant and the amount involved exceeds or will exceed the lesser of \$120,000 or 1% of the average of our total assets as of December 31, 2011 and 2012, which is approximately \$544,141, and in which any of our directors, executive officers, holders of more than 5% of our common stock or any member of the immediate family of any of the foregoing persons, had or will have a direct or indirect material interest.

**Sandivino, Inc.**

During 2011, we paid an aggregate of \$239,383 to Sandivino, Inc. for consulting services, principally for consulting services provided by Gregory D. Gorgas, our senior vice president, commercial, prior to his employment by us. Mr. Gorgas and his wife are the only shareholders and he is an officer of Sandivino.

**SynthRx Acquisition – Milestone Shares**

We acquired SynthRx, Inc. in April 2011. The merger agreement pursuant to which we acquired SynthRx provided that the former stockholders of SynthRx would receive, for no additional consideration and based on their percentage ownership in SynthRx immediately prior to the closing of the merger transaction, additional shares of our common stock upon achievement of three specified milestones related to SynthRx's lead product candidate, which we are developing as MST-188. The first of the three milestones in the merger agreement has been achieved and, as a result, we issued an aggregate of 250,000 shares of our common stock to the former stockholders of SynthRx on a pro rata basis based on each such stockholder's ownership percentage of SynthRx immediately prior to the effective time of the merger. As one of the former stockholders of SynthRx, 52,543 of the shares were issued to Dr. Emanuele, our senior vice president, development.

**Indemnification of Officers and Directors**

Our amended and restated certificate of incorporation and our bylaws provide that we will indemnify each of our directors and officers to the fullest extent permitted by the Delaware General Corporation Law. Further, we have entered into indemnification agreements with each of our directors and officers, and we have purchased directors' and officers' liability insurance that insures our directors and officers against the cost of defense, settlement or payment of a judgment under certain circumstances.

**SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT**

The following table sets forth information regarding beneficial ownership of our common stock as of June 4, 2013 (the **Evaluation Date**), or an earlier date for information based on filings with the SEC, by (a) each director, (b) each of the named executive officers and (c) all of our current directors and executive officers as a group. The information in this table is based solely on statements in filings with the SEC or other reliable information. We do not know of any person who beneficially owns more than 5% of the outstanding shares of our common stock as of the Evaluation Date. Percent of beneficial ownership is based on 46,515,286 shares of our common stock outstanding as of the Evaluation Date.

| <b>Name and Address of Beneficial Owner (1)</b> | <b>Shares Beneficially Owned (2)</b> | <b>Percent of Outstanding</b> |
|-------------------------------------------------|--------------------------------------|-------------------------------|
| <b>Directors and Named Executive Officers:</b>  |                                      |                               |
| Brian M. Culley (3)                             | 540,353                              | 1.1%                          |
| Jack Lief (4)                                   | 60,449                               | *                             |
| Ted W. Love (5)                                 | 19,419                               | *                             |

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|                                                                  |           |      |
|------------------------------------------------------------------|-----------|------|
| David A. Ramsay (6)                                              | 145,067   | *    |
| Lewis J. Shuster (7)                                             | 47,396    | *    |
| Patrick L. Keran (8)                                             | 498,652   | 1.1% |
| Santosh J. Vetticaden                                            |           | *    |
| All directors and executive officers as a group (10 persons) (9) | 1,845,183 | 3.8% |

\* Less than 1%

(1) Unless otherwise indicated, the address of each of the listed persons is c/o Mast Therapeutics, Inc., 12390 El Camino Real, Suite 150, San Diego, California 92130.

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- (2) Beneficial ownership of shares is determined in accordance with SEC rules and generally includes any shares over which a person exercises sole or shared voting or investment power, or of which a person has the right to acquire ownership within 60 days of the Evaluation Date. Except as otherwise noted, (a) each person or entity has sole voting and investment power with respect to the shares shown and (b) none of the shares shown as beneficially owned on this table are subject to pledge. In calculating the percentage ownership of each person identified in the table, shares underlying options, warrants or other rights to acquire shares of our common stock held by that person that are either currently exercisable or exercisable within 60 days of the Evaluation Date are deemed outstanding. These shares, however, are not deemed outstanding for the purposes of computing the percentage ownership of any other individual or entity. Percentage ownership for each person is based on the number of shares of our common stock outstanding as of the Evaluation Date, together with the applicable number of shares of common stock subject to options, warrants or other rights to acquire shares of our common stock currently exercisable or exercisable within 60 days of the Evaluation Date for that person or group of persons.
- (3) Consists of (a) 505,853 shares of common stock subject to options currently exercisable or exercisable within 60 days of the Evaluation Date and (b) 34,500 shares of common stock held directly by Mr. Culley.
- (4) Consists of 60,449 shares of common stock subject to options currently exercisable or exercisable within 60 days of the Evaluation Date.
- (5) Consists of 19,419 shares of common stock subject to options currently exercisable or exercisable within 60 days of the Evaluation Date.
- (6) Consists of (a) 45,067 shares of common stock subject to options currently exercisable or exercisable within 60 days of the Evaluation Date and (b) 100,000 shares of common stock held directly by Mr. Ramsay.
- (7) Consists of 47,396 shares of common stock subject to options currently exercisable or exercisable within 60 days of the Evaluation Date.
- (8) Consists of 498,652 shares of common stock subject to options currently exercisable or exercisable within 60 days of the Evaluation Date.
- (9) Consists of (a) 429,098 shares of common stock, which includes 294,598 shares beneficially owned by Dr. Emanuele that were issued to him in his capacity as a former stockholder of SynthRx, Inc. pursuant to our merger agreement with SynthRx, which we acquired in April 2011, and (b) 1,416,085 shares of common stock subject to options currently exercisable or exercisable within 60 days of the Evaluation Date. The 294,598 shares of common stock beneficially owned by Dr. Emanuele are subject to the stockholders' voting and transfer restriction agreement described under Business Acquisition of SynthRx, Inc. above and, as a result, our board of directors effectively has control over how these shares are voted, subject to limited exceptions.

**DESCRIPTION OF CAPITAL STOCK**

The following description of our common stock and preferred stock, summarizes the material terms and provisions of our common stock and the preferred stock that we may offer under this prospectus. 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. The terms of these securities may also be affected by Delaware General Corporation Law. The summary below and that contained in 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**

Our certificate of incorporation authorizes us to issue 500,000,000 shares of common stock, par value \$0.001 per share, of which 46,265,286 shares were issued and outstanding and 1,454,079 were issued and held as treasury stock as of March 31, 2013. 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.

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### ***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.

### **Preferred Stock**

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 description of preferred stock above is 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



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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.

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*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.

*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;

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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.

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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.

### **MATERIAL U.S. FEDERAL INCOME TAX CONSEQUENCES FOR NON-US HOLDERS**

#### **General**

The following is a discussion of the material U.S. federal income tax consequences of the acquisition, ownership, and disposition of our common stock by a non-U.S. holder, as defined below, that acquires our common stock pursuant to this offering. This discussion assumes that a non-U.S. holder will hold our common stock issued pursuant to this offering as a capital asset within the meaning of Section 1221 of the IRC. This discussion does not address all aspects of U.S. federal income taxation that may be relevant to a particular investor in light of the investor's individual circumstances. In addition, this discussion does not address (i) U.S. federal non-income tax laws, such as gift or estate tax laws, (ii) state, local or non-U.S. tax consequences, (iii) the special tax rules that may apply to certain investors, including, without limitation, banks, insurance companies, financial institutions, controlled foreign corporations, passive foreign investment companies, broker-dealers, grantor trusts, personal holding companies, taxpayers who have elected mark-to-market accounting, tax-exempt entities, regulated investment companies, real estate investment trusts, a partnership or other entity or arrangement classified as a partnership for United States federal income tax purposes or other pass-through entities, or an investor in such entities or arrangements, or U.S. expatriates or former long-term residents of the United States, (iv) the special tax rules that may apply to an investor that acquires, holds, or disposes of our common stock as part of a straddle, hedge, constructive sale, conversion or other integrated transaction, or (v) the impact, if any, of the alternative minimum tax.

This discussion is based on current provisions of the U.S. Internal Revenue Code of 1986, as amended, which we refer to as the IRC, existing and proposed U.S. Treasury Regulations promulgated thereunder, current administrative rulings and judicial decisions, all as in effect as of the date of this prospectus and all of which are subject to change or to differing interpretation, possibly with retroactive effect. Any change could alter the tax consequences to non-U.S. holders described in this prospectus. In addition, the Internal Revenue Service, or the IRS, could challenge one or more of the tax consequences described in this prospectus.

As used in this discussion, the term U.S. person means a person that is, for U.S. federal income tax purposes, (i) a citizen or individual resident of the United States, (ii) a corporation (or other entity taxed as a corporation) created or organized (or treated as created or organized) in the United States or under the laws of the United States or any state thereof or the District of Columbia, (iii) an estate the income of which is subject to U.S. federal income taxation regardless of its source, or (iv) a trust if (A) a court within the United States is able to exercise primary supervision over the administration of the trust and one or more U.S. persons have the authority to control all substantial decisions of the trust, or (B) it has in effect a valid election under applicable U.S. Treasury Regulations to be treated as a U.S. person. As used in this discussion, the term non-U.S. holder means a beneficial owner of our common stock (other than a partnership or other entity treated as a partnership or as a disregarded entity for U.S. federal income tax purposes) that is not a U.S. person.

The tax treatment of a partnership and each partner thereof will generally depend upon the status and activities of the partnership and such partner. A holder that is treated as a partnership for U.S. federal income tax purposes or a partner in such partnership should consult its own tax advisor regarding the U.S. federal income tax consequences applicable to it and its partners of the acquisition, ownership and disposition of our common stock.

THIS DISCUSSION IS ONLY A SUMMARY OF MATERIAL U.S. FEDERAL INCOME TAX CONSEQUENCES TO NON-U.S. HOLDERS OF THE ACQUISITION, OWNERSHIP AND DISPOSITION OF OUR COMMON STOCK. IT IS NOT TAX ADVICE. EACH PROSPECTIVE INVESTOR SHOULD CONSULT ITS OWN TAX ADVISOR WITH RESPECT TO THE PARTICULAR TAX CONSEQUENCES OF THE ACQUISITION, OWNERSHIP AND DISPOSITION OF OUR COMMON STOCK, INCLUDING THE APPLICABILITY AND EFFECT OF ANY STATE, LOCAL, AND NON-U.S. TAX LAWS, AS WELL AS U.S. FEDERAL ESTATE AND GIFT TAX LAWS, AND ANY APPLICABLE TAX TREATY.

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**Income Tax Consequences of an Investment in Common Stock*****Distributions on Common Stock***

As discussed under **Dividend Policy**, we do not anticipate paying dividends. If we pay cash or distribute property to holders of shares of common stock, such distributions generally will constitute dividends for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. Distributions in excess of current and accumulated earnings and profits will constitute a return of capital that will be applied against and reduce (but not below zero) the holder's adjusted tax basis in our common stock. Any remaining excess will be treated as gain from the sale or exchange of the common stock and will be treated as described under **Gain or Loss on Sale, Exchange or Other Taxable Disposition of Common Stock** below.

Dividends paid to a non-U.S. holder that are not effectively connected with the non-U.S. holder's conduct of a trade or business in the United States generally will be subject to withholding of U.S. federal income tax at a rate of 30% or such lower rate as may be specified by an applicable income tax treaty. A non-U.S. holder that wishes to claim the benefit of an applicable tax treaty withholding rate generally will be required to (i) complete IRS Form W-8BEN (or other applicable form) and certify under penalties of perjury that such holder is not a U.S. person and is eligible for the benefits of the applicable tax treaty or (ii) if our common stock is held through certain foreign intermediaries, satisfy the relevant certification requirements of applicable U.S. Treasury Regulations. These forms may need to be periodically updated.

A non-U.S. holder eligible for a reduced rate of withholding of U.S. federal income tax pursuant to an income tax treaty may obtain a refund of any excess amounts withheld by timely filing an appropriate claim for refund with the IRS. Non-U.S. holders should consult their own tax advisors regarding their entitlement to benefits under an applicable income tax treaty and the manner of claiming the benefits of such treaty (including, without limitation, the need to obtain a U.S. taxpayer identification number).

Dividends that are effectively connected with a non-U.S. holder's conduct of a trade or business in the United States, and, if required by an applicable income tax treaty, attributable to a permanent establishment or fixed base maintained by the non-U.S. holder in the United States, are subject to U.S. federal income tax on a net income basis at the U.S. federal income tax rates generally applicable to a U.S. holder and are not subject to withholding of U.S. federal income tax, provided that the non-U.S. holder establishes an exemption from such withholding by complying with certain certification and disclosure requirements. Any such effectively connected dividends (and, if required, dividends attributable to a U.S. permanent establishment or fixed base) received by a non-U.S. holder that is treated as a foreign corporation for U.S. federal income tax purposes may be subject to an additional branch profits tax at a 30% rate, or such lower rate as may be specified by an applicable income tax treaty.

***Gain or Loss on Sale, Exchange or Other Taxable Disposition of Common Stock***

Any gain recognized by a non-U.S. holder on a sale or other taxable disposition of our common stock generally will not be subject to U.S. federal income tax, unless:

- (i) the gain is effectively connected with a trade or business of the non-U.S. holder in the United States (and, if required by an applicable income tax treaty, is attributable to a U.S. permanent establishment or fixed base of the non-U.S. holder),
- (ii) the non-U.S. holder is an individual who is present in the United States for 183 days or more in the taxable year of that disposition, and certain other conditions are met, or
- (iii) we are or have been a United States real property holding corporation, or aUSRPHC, for U.S. federal income tax purposes at any time during the shorter of the five-year period ending on the date of disposition or the period that the non-U.S. holder held the common stock, and, in the case where the shares of our common stock are regularly traded on an established securities market, the non-U.S. holder holds or held (at any time during the shorter of the five-year period ending on the date of disposition or the non-U.S. holder's holding period) more than 5% of our common stock. A corporation generally is a USRPHC if the fair market value of its U.S. real property interests equals or exceeds 50% of the sum of the fair market value of its worldwide real property interests plus its other assets used or held for use in a trade or business. We do not believe that we have been, are, or will become, a U.S. real property holding corporation, although there can be no assurance in this regard.

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Any gain recognized by a non-U.S. holder that is described in clause (i) or (iii) of the preceding paragraph generally will be subject to tax at the U.S. federal income tax rates generally applicable to a U.S. person and be required to file a U.S. tax return. Such non-U.S. holders are urged to consult their tax advisors regarding the possible application of these rules. Any gain of a corporate non-U.S. holder that is described in clause (i) above may also be subject to an additional branch profits tax at a 30% rate, or such lower rate as may be specified by an applicable income tax treaty. An individual non-U.S. holder that is described in clause (ii) of such paragraph generally will be subject to a flat 30% tax (or a lower applicable tax treaty rate) on the U.S. source capital gain derived from the disposition, which may be offset by U.S. source capital losses during the taxable year of the disposition.

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### **Information Reporting and Backup Withholding**

We generally must report annually to the IRS and to each non-U.S. holder of our common stock the amount of dividends paid to such holder on our common stock and the tax, if any, withheld with respect to those dividends. Copies of the information returns reporting those dividends and withholding may also be made available to the tax authorities in the country in which the non-U.S. holder is a resident under the provisions of an applicable income tax treaty or agreement. Information reporting also is generally required with respect to the proceeds from sales and other dispositions of our common stock to or through the U.S. office (and in certain cases, the foreign office) of a broker.

Under some circumstances, U.S. Treasury Regulations require backup withholding of U.S. federal income tax, currently at a rate of 28%, on reportable payments with respect to our common stock. A non-U.S. holder generally may eliminate the requirement for information reporting (other than in respect to dividends, as described above) and backup withholding by providing certification of its foreign status, under penalties of perjury, on a duly executed applicable IRS Form W-8 or by otherwise establishing an exemption. Notwithstanding the foregoing, backup withholding and information reporting may apply if either we or our paying agent has actual knowledge, or reason to know, that a holder is a U.S. person.

Backup withholding is not a tax. Rather, the amount of any backup withholding will be allowed as a credit against a non-U.S. holder's U.S. federal income tax liability, if any, and may entitle such non-U.S. holder to a refund, provided that certain required information is timely furnished to the IRS. Non-U.S. holders should consult their own tax advisors regarding the application of backup withholding and the availability of and procedure for obtaining an exemption from backup withholding in their particular circumstances.

### **Additional Withholding Tax Relating to Foreign Accounts**

Withholding taxes may apply to certain types of payments made to foreign financial institutions (as specially defined in the IRC) and certain other non-United States entities.

Specifically, a 30% withholding tax may be imposed on dividends on, and gross proceeds from the sale or other disposition of, shares of our common stock paid to a foreign financial institution or to a non-financial foreign entity, unless (1) the foreign financial institution undertakes certain diligence and reporting, (2) the non-financial foreign entity either certifies it does not have any substantial United States owners or furnishes identifying information regarding each substantial United States owner, or (3) the foreign financial institution or non-financial foreign entity otherwise qualifies for an exemption from these rules. If the payee is a foreign financial institution and is subject to the diligence and reporting requirements in clause (1) above, it generally must enter into an agreement with the U.S. Treasury requiring, among other things, that it undertake to identify accounts held by certain U.S. persons or U.S.-owned foreign entities, annually report certain information about such accounts, and withhold 30% on payments to non-compliant foreign financial institutions and certain other account holders.

Final Treasury Regulations provide that the withholding provisions described above will generally apply to payments of dividends made on or after January 1, 2014 and to payments of gross proceeds from a sale or other disposition of stock on or after January 1, 2017.

Each investor should consult its own tax advisor as to particular tax consequences to it of purchasing, holding and disposing of shares of our common stock, including the applicability and effect of any state, local or foreign tax laws, and of any pending or subsequent changes in applicable laws.

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**UNDERWRITING**

Subject to the terms and conditions of the purchase agreement entered into with Piper Jaffray & Co., as representative of the several underwriters and sole book-running manager of this offering, we have agreed to sell to the underwriters, and the underwriters have severally agreed to purchase from us the number of shares indicated in the table below:

| Underwriters           | Number of Shares |
|------------------------|------------------|
| Piper Jaffray          |                  |
| Canaccord Genuity Inc. |                  |
| <b>Total</b>           |                  |

The underwriters are offering the shares of our common stock, when, as and if issued to and accepted by them, subject to approval of legal matters by their counsel, including the validity of the common stock and other conditions contained in the purchase agreement, such as the receipt by the underwriters of officers' certificates and legal opinions. The underwriters propose to offer the shares to the public at \$ \_\_\_\_\_ per share and to certain dealers at that price less a concession not in excess of \$ \_\_\_\_\_ per share. The underwriters reserve the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part.

We have granted the underwriters an option to buy up to \_\_\_\_\_ additional shares of common stock from us to cover over-allotments. The underwriters may exercise this option at any time and from time to time during the 30-day period from the date of this prospectus. If any additional shares of common stock are purchased, the underwriters will offer the additional shares on the same terms as those on which the shares are being offered.

The underwriting fee is equal to the public offering price per share of common stock less the amount paid by the underwriters to us per share of common stock. The following table shows the per share and total underwriting discounts to be paid to the underwriters in connection with this offering. These amounts are shown assuming both no exercise and full exercise of the over-allotment option:

| Per Share    | No Exercise | Full Exercise |
|--------------|-------------|---------------|
| <b>Total</b> |             |               |

We estimate that the total fees and expenses payable by us, excluding underwriting discounts and commissions will be approximately \$375,000, which includes \$150,000 that we have agreed to reimburse the underwriters for fees incurred by it in connection with this offering.

We have agreed to indemnify the underwriters against certain liabilities, including civil liabilities under the Securities Act, or to contribute to payments that the underwriters may be required to make in respect of those liabilities.

We, our directors and executive officers are subject to lock-up agreements that prohibit us and them from offering for sale, pledging, announcing the intention to sell, selling, contracting to sell, selling any option or contract to purchase, purchasing any option or contract to sell, granting any option, right or warrant to purchase, making any short sale, otherwise transferring or disposing of any shares of our common stock or any securities convertible into, exercisable or exchangeable for or that represent the right to receive our common stock, entering into any swap or other agreement that transfers any of the economic consequences of ownership of our common stock, making any demand for or exercising any right with respect to the registration of our common stock or any security convertible into or exercisable or exchangeable for our common stock or publicly disclosing the intention to do any of the foregoing for a period of at least 90 days following the date of this prospectus without the prior written consent of Piper Jaffray.



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The lock-up agreement applicable to us provides exceptions for the issuance of our securities (i) to our directors, officers, employees and consultants pursuant to employee benefit plans, equity incentive plans or other employee compensation plans existing on the date hereof and as described in this prospectus or otherwise approved by our stockholders, (ii) pursuant to the exercise or conversion of any options, warrants, rights or convertible securities outstanding on the date hereof, of which Piper Jaffray has been advised in writing, (iii) in connection with a joint venture or collaboration or other strategic or commercial relationship existing prior to, on or following the date hereof and (iv) issuable pursuant to our merger agreement with SynthRx.

The lock-up agreement applicable to our directors and executive officers provides exceptions for transfers of our securities (i) as a bona fide gift or gifts, (ii) to any trust for the direct or indirect benefit of such director or officer or his immediate family, (iii) by testate succession or intestate succession and (iv) in connection with the net or cashless exercise or settlement of restricted stock units or other equity awards acquired prior to the date hereof (including any transfer for the payment of taxes due as a result of such vesting or exercise whether by means of a net settlement or otherwise), subject to certain requirements in each case, as well as certain other exceptions.

The 90-day lock-up period in all of the lock-up agreements is subject to extension if (i) during the last 17 days of the lock-up period we issue an earnings release or material news or a material event relating to us occurs or (ii) prior to the expiration of the lock-up period, we announce that we will release earnings results during the 16-day period beginning on the last day of the lock-up period, in which case the restrictions imposed in these lock-up agreements shall continue to apply until the expiration of the 18-day period beginning on the issuance of the earnings release or the occurrence of the material news or material event, unless Piper Jaffray waives the extension in writing.

Our shares are listed on the NYSE MKT under the symbol MSTX.

To facilitate the offering, the underwriters may engage in transactions that stabilize, maintain or otherwise affect the price of our common stock during and after the offering. Specifically, the underwriters may over-allot or otherwise create a short position in the common stock for their own accounts by selling more shares of common stock than we have sold to the underwriters. Short sales involve the sale by the underwriters of a greater number of shares than the underwriters are required to purchase in the offering. The underwriters may close out any short position by either exercising their option to purchase additional shares or purchasing shares in the open market.

In addition, the underwriters may stabilize or maintain the price of the common stock by bidding for or purchasing shares of common stock in the open market and may impose penalty bids. If penalty bids are imposed, selling concessions allowed to syndicate members or other broker-dealers participating in the offering are reclaimed if shares of common stock previously distributed in the offering are repurchased, whether in connection with stabilization transactions or otherwise. The effect of these transactions may be to stabilize or maintain the market price of the common stock at a level above that which might otherwise prevail in the open market. The imposition of a penalty bid may also affect the price of the common stock to the extent that it discourages resales of the common stock. The magnitude or effect of any stabilization or other transactions is uncertain. These transactions may be effected on the NYSE MKT or otherwise and, if commenced, may be discontinued at any time. The underwriters may also engage in passive market making transactions in our common stock. Passive market making consists of displaying bids on the NYSE MKT limited by the prices of independent market makers and effecting purchases limited by those prices in response to order flow. Rule 103 of Regulation M promulgated by the Commission limits the amount of net purchases that each passive market maker may make and the displayed size of each bid. Passive market making may stabilize the market price of the common stock at a level above that which might otherwise prevail in the open market and, if commenced, may be discontinued at any time.

This prospectus may be made available on a web site maintained by one or more of the underwriters and the underwriters may distribute this prospectus electronically.

From time to time in the ordinary course of their respective businesses, the underwriters and certain of their affiliates may in the future engage in commercial banking or investment banking transactions with, or provide financial advisory services to, us and our affiliates.

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**LEGAL MATTERS**

The validity of the securities offered hereby is being passed upon for us by DLA Piper LLP (US), San Diego, California. K&L Gates LLP, Irvine, California, is acting as counsel for the underwriters in connection with this offering.

**EXPERTS**

The consolidated financial statements as of December 31, 2012 and December 31, 2011 and for each of the two years in the period ended December 31, 2012, and cumulatively, for the period January 1, 2011 to December 31, 2012 included in this prospectus have been so included 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.

The consolidated statements of operations and comprehensive income/(loss), stockholders' equity (deficit) and cash flows for the period from January 1, 2002 through December 31, 2010 are included herein in reliance upon the report of CohnReznick 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**

This prospectus is part of a registration statement on Form S-1 that we filed with the SEC. Certain information in the registration statement has been omitted from this prospectus in accordance with the rules of the SEC. We are a reporting company and file annual, quarterly and current reports, proxy statements and other information with the SEC. This prospectus does not include all of the information contained in the registration statement. You should refer to the registration statement and its exhibits for additional information. Whenever we make reference in this prospectus to any of our contracts, agreements or other documents, the references are not necessarily complete and you should refer to the exhibits attached to the registration statement for copies of the actual contract, agreement or other document. When we complete this offering, we will also be required to file annual, quarterly and special reports, proxy statements and other information with the SEC.

You may read and copy any document we file with the SEC 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. Our SEC filings are also available at the SEC's website at [www.sec.gov](http://www.sec.gov). Our SEC filings are also available at the office of the NYSE MKT. We also maintain a web site at [www.masttherapeutics.com](http://www.masttherapeutics.com), which provides additional information about our company and through which you can also access our SEC filings. Information contained in or accessible through either website is not and should not be considered a part of this prospectus and you should not rely on that information in deciding whether to invest in our common stock, unless that information is also in this prospectus.

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**Mast Therapeutics, Inc. and Subsidiaries**

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**Report of Independent Registered Public Accounting Firm**

To the Board of Directors and Stockholders of

Mast Therapeutics, Inc.

In our opinion, the accompanying consolidated balance sheets and the related consolidated statements of operations and comprehensive income/(loss), of stockholders' equity (deficit) and of cash flows present fairly, in all material respects, the financial position of Mast Therapeutics, Inc. and its subsidiaries (a development stage enterprise) at December 31, 2012, and December 31, 2011 and the results of their operations and their cash flows for the years then ended and cumulatively, for the period January 1, 2011 to December 31, 2012, in conformity with accounting principles generally accepted in the United States of America. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits. We did not audit the cumulative totals of the Company for the period from June 12, 1996 (date of inception) to December 31, 2010, which totals reflect a deficit of \$156,129,121 accumulated during the development stage. The cumulative totals for the period from January 1, 2002 to December 31, 2010, which totals reflect a deficit of \$132,085,779, were audited by other auditors whose report, dated March 10, 2011, expressed an unqualified opinion on such cumulative amounts. We conducted our audits of these statements in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. We believe that our audit provides a reasonable basis for our opinions.

/s/ PricewaterhouseCoopers LLP

San Diego, California  
March 19, 2013

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**Report of Independent Registered Public Accounting Firm**

To the Board of Directors and Stockholders of

Mast Therapeutics, Inc.

We have audited the consolidated statements of operations and comprehensive income/(loss), stockholders' equity (deficit) and cash flows of Mast Therapeutics, Inc. (formerly, ADVENTRX Pharmaceuticals, Inc.) and Subsidiaries (a development stage enterprise) for the period from January 1, 2002 through December 31, 2010. These consolidated financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these consolidated financial statements based on our audit.

We conducted our audit in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audit provides a reasonable basis for our opinion.

In our opinion, such consolidated financial statements present fairly, in all material respects, the results of operations and cash flows of Mast Therapeutics, Inc. and Subsidiaries (a development stage enterprise) for the period from January 1, 2002 through December 31, 2010, in conformity with accounting principles generally accepted in the United States of America.

/s/ CohnReznick LLP

San Diego, California  
March 10, 2011

**Table of Contents****Mast Therapeutics, Inc. and Subsidiaries**

(A Development Stage Enterprise)

**Consolidated Balance Sheets**

|                                                                                                                                                                                                                                               | December 31,  |               |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------|---------------|
|                                                                                                                                                                                                                                               | 2012          | 2011          |
| <b>Assets</b>                                                                                                                                                                                                                                 |               |               |
| Current assets:                                                                                                                                                                                                                               |               |               |
| Cash and cash equivalents                                                                                                                                                                                                                     | \$ 22,500,440 | \$ 43,569,947 |
| Short-term investments                                                                                                                                                                                                                        | 14,010,962    | 7,133,697     |
| Interest and other receivables                                                                                                                                                                                                                | 15,689        | 17,245        |
| Contingent asset                                                                                                                                                                                                                              |               | 815,011       |
| Prepaid expenses                                                                                                                                                                                                                              | 646,571       | 256,311       |
| Total current assets                                                                                                                                                                                                                          | 37,173,662    | 51,792,211    |
| Property and equipment, net                                                                                                                                                                                                                   | 198,358       | 464,465       |
| In-process research and development                                                                                                                                                                                                           | 6,549,000     | 6,549,000     |
| Goodwill                                                                                                                                                                                                                                      | 3,006,883     | 3,006,883     |
| Other assets                                                                                                                                                                                                                                  | 43,912        | 43,912        |
| Total assets                                                                                                                                                                                                                                  | \$ 46,971,815 | \$ 61,856,471 |
| <b>Liabilities and Stockholders Equity</b>                                                                                                                                                                                                    |               |               |
| Current liabilities:                                                                                                                                                                                                                          |               |               |
| Accounts payable                                                                                                                                                                                                                              | \$ 698,838    | \$ 451,705    |
| Accrued liabilities                                                                                                                                                                                                                           | 1,283,976     | 1,120,416     |
| Accrued compensation and payroll taxes                                                                                                                                                                                                        | 445,352       | 756,773       |
| Contingent liability                                                                                                                                                                                                                          | 142,500       | 140,125       |
| Total current liabilities                                                                                                                                                                                                                     | 2,570,666     | 2,469,019     |
| Deferred income tax liability                                                                                                                                                                                                                 | 2,608,755     | 2,608,755     |
| Total liabilities                                                                                                                                                                                                                             | 5,179,421     | 5,077,774     |
| Commitments (Note 10)                                                                                                                                                                                                                         |               |               |
| Stockholders equity:                                                                                                                                                                                                                          |               |               |
| Common stock, \$0.001 par value; 500,000,000 shares authorized; 47,719,365 and 47,715,709 shares issued at December 31, 2012 and 2011, respectively; 46,265,286 and 47,715,709 shares outstanding at December 31, 2012 and 2011, respectively | 47,720        | 47,716        |
| Treasury stock, at cost 1,454,079 and 0 shares at December 31, 2012 and 2011, respectively                                                                                                                                                    | (1,454)       |               |
| Additional paid-in capital                                                                                                                                                                                                                    | 226,696,863   | 226,122,331   |
| Accumulated other comprehensive loss                                                                                                                                                                                                          | (2,194)       | (2,298)       |
| Deficit accumulated during the development stage                                                                                                                                                                                              | (184,948,541) | (169,389,052) |
| Total stockholders equity                                                                                                                                                                                                                     | 41,792,394    | 56,778,697    |
| Total liabilities and stockholders equity                                                                                                                                                                                                     | \$ 46,971,815 | \$ 61,856,471 |

**Table of Contents****Mast Therapeutics, Inc. and Subsidiaries**

(A Development Stage Enterprise)

**Consolidated Statements of Operations and Comprehensive Income/(Loss)**

|                                                                 |                                  |                 | Inception<br>(June 12, 1996) |
|-----------------------------------------------------------------|----------------------------------|-----------------|------------------------------|
|                                                                 |                                  |                 | Through                      |
|                                                                 | Years Ended December 31,<br>2012 | 2011            | December 31,<br>2012         |
| Revenues:                                                       |                                  |                 |                              |
| Net sales                                                       | \$                               | \$              | \$ 174,830                   |
| Licensing revenue                                               |                                  |                 | 1,300,000                    |
| Grant revenue                                                   |                                  |                 | 618,692                      |
| Total net revenue                                               |                                  |                 | 2,093,522                    |
| Cost of goods sold                                              |                                  |                 | 51,094                       |
| Gross margin                                                    |                                  |                 | 2,042,428                    |
| Operating expenses:                                             |                                  |                 |                              |
| Research and development                                        | 8,088,152                        | 5,758,337       | 86,057,456                   |
| Selling, general and administrative                             | 7,519,405                        | 7,190,093       | 67,666,712                   |
| Transaction-related expenses                                    | (69,602)                         | 410,885         | 671,652                      |
| Depreciation and amortization                                   | 90,047                           | 37,570          | 11,025,235                   |
| Write-off of in-process research and development                |                                  |                 | 10,422,130                   |
| Goodwill impairment                                             |                                  |                 | 5,702,130                    |
| Equity in loss of investee                                      |                                  |                 | 178,936                      |
| Total operating expenses                                        | 15,628,002                       | 13,396,885      | 181,724,251                  |
| Loss from operations                                            | (15,628,002)                     | (13,396,885)    | (179,681,823)                |
| Reduction of fair value of warrants                             |                                  |                 | (12,239,688)                 |
| Interest income                                                 | 73,560                           | 65,577          | 4,832,208                    |
| Interest expense                                                |                                  |                 | (191,729)                    |
| Other income (expense), net                                     | (5,047)                          | 71,377          | 129,705                      |
| Loss before cumulative effect of change in accounting principle | (15,559,489)                     | (13,259,931)    | (187,151,327)                |
| Cumulative effect of change in accounting principle             |                                  |                 | (25,821)                     |
| Net loss                                                        | (15,559,489)                     | (13,259,931)    | (187,177,148)                |
| Preferred stock dividends                                       |                                  |                 | (621,240)                    |
| Deemed dividends on preferred stock                             |                                  |                 | (10,506,683)                 |
| Net loss applicable to common stock                             | \$ (15,559,489)                  | \$ (13,259,931) | \$ (198,305,071)             |
| Loss per common share basic and diluted                         | \$ (0.33)                        | \$ (0.47)       |                              |
| Weighted average shares outstanding basic and diluted           | 47,641,043                       | 28,175,221      |                              |

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Comprehensive Income/(Loss):

|                                                    |                 |                 |                  |
|----------------------------------------------------|-----------------|-----------------|------------------|
| Net loss                                           | \$ (15,559,489) | \$ (13,259,931) | \$ (187,177,148) |
| Unrealized gains (losses) on marketable securities | 104             | (142)           | (38)             |
| Foreign currency translation adjustments           |                 | (2,156)         | (2,156)          |
| Comprehensive net loss                             | \$ (15,559,385) | \$ (13,262,229) | \$ (187,179,342) |

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**Table of Contents****Mast Therapeutics, Inc. and Subsidiaries**

(A Development Stage Enterprise)

**Consolidated Statements of Stockholders' Equity (Deficit)**

Inception (June 12, 1996) Through December 31, 2012

|                                                                     | Cumulative convertible preferred stock, series A through C |        | Convertible preferred stock, series A (2009) |        | Cumulative convertible preferred stock, series B through F (2009 - 2010) |        | Common stock |           | Deficit                    |                                   |                                      | Total stockholders' equity (deficit) |                         |
|---------------------------------------------------------------------|------------------------------------------------------------|--------|----------------------------------------------|--------|--------------------------------------------------------------------------|--------|--------------|-----------|----------------------------|-----------------------------------|--------------------------------------|--------------------------------------|-------------------------|
|                                                                     | Shares                                                     | Amount | Shares                                       | Amount | Shares                                                                   | Amount | Shares       | Amount    | Additional paid-in capital | other comprehensive income (loss) | accumulated during development stage |                                      | Treasury stock, at cost |
| Balances at June 12, 1996 (date of incorporation)                   |                                                            | \$     |                                              | \$     |                                                                          | \$     |              | \$        |                            | \$                                |                                      | \$                                   | \$                      |
| Sale of common stock without par value                              |                                                            |        |                                              |        | 20                                                                       |        |              |           | 10                         |                                   |                                      |                                      | 10                      |
| Issuance of common stock and net liabilities assumed in acquisition |                                                            |        |                                              |        | 68,645                                                                   | 69     |              | 4,871     |                            |                                   | (18,094)                             |                                      | (13,154)                |
| Issuance of common stock                                            |                                                            |        |                                              |        | 80,405                                                                   | 80     |              | 2,386     |                            |                                   | (2,466)                              |                                      |                         |
| Net loss                                                            |                                                            |        |                                              |        |                                                                          |        |              |           |                            |                                   | (259,476)                            |                                      | (259,476)               |
| Balances at December 31, 1996*                                      |                                                            |        |                                              |        | 149,070                                                                  | 149    |              | 7,267     |                            |                                   | (280,036)                            |                                      | (272,620)               |
| Sale of common stock, net of offering costs of \$9,976              |                                                            |        |                                              |        | 40,182                                                                   | 40     |              | 1,790,939 |                            |                                   |                                      |                                      | 1,790,979               |
| Issuance of common stock in acquisition                             |                                                            |        |                                              |        | 15,036                                                                   | 15     |              | 888,235   |                            |                                   |                                      |                                      | 888,250                 |
| Minority interest deficiency at acquisition charged to the Company  |                                                            |        |                                              |        |                                                                          |        |              |           |                            |                                   | (45,003)                             |                                      | (45,003)                |
| Net loss                                                            |                                                            |        |                                              |        |                                                                          |        |              |           |                            |                                   | (1,979,400)                          |                                      | (1,979,400)             |
| Balances at December 31, 1997*                                      |                                                            |        |                                              |        | 204,288                                                                  | 204    |              | 2,686,441 |                            |                                   | (2,304,439)                          |                                      | 382,206                 |
| Rescission of acquisition                                           |                                                            |        |                                              |        | (15,036)                                                                 | (15)   |              | (888,235) |                            |                                   | 561,166                              |                                      | (327,084)               |
| Issuance of common stock at conversion of notes payable             |                                                            |        |                                              |        | 18,011                                                                   | 18     |              | 363,982   |                            |                                   |                                      |                                      | 364,000                 |

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|                                                                      |         |     |  |           |             |             |
|----------------------------------------------------------------------|---------|-----|--|-----------|-------------|-------------|
| Expense related to stock warrants issued                             |         |     |  | 260,000   |             | 260,000     |
| Net loss                                                             |         |     |  |           | (1,204,380) | (1,204,380) |
| Balances at December 31, 1998*                                       |         |     |  |           |             |             |
|                                                                      | 207,263 | 207 |  | 2,422,188 | (2,947,653) | (525,258)   |
| Sale of common stock                                                 | 27,136  | 27  |  | 134,973   |             | 135,000     |
| Expense related to stock warrants issued                             |         |     |  | 212,000   |             | 212,000     |
| Net loss                                                             |         |     |  |           | (1,055,485) | (1,055,485) |
| Balances at December 31, 1999*                                       |         |     |  |           |             |             |
|                                                                      | 234,399 | 234 |  | 2,769,161 | (4,003,138) | (1,233,743) |
| Sale of preferred stock, net of offering costs of \$76,500           | 3,200   | 32  |  | 3,123,468 |             | 3,123,500   |
| Issuance of common stock at conversion of notes and interest payable | 16,499  | 16  |  | 492,481   |             | 492,497     |
| Issuance of common stock at conversion of notes payable              | 2,814   | 3   |  | 83,997    |             | 84,000      |
| Issuance of common stock to settle obligations                       | 19,804  | 20  |  | 1,202,140 |             | 1,202,160   |
| Issuance of common stock for acquisition                             | 280,000 | 280 |  | 9,332,489 |             | 9,332,769   |
| Issuance of warrants for acquisition                                 |         |     |  | 4,767,664 |             | 4,767,664   |
| Stock issued for acquisition costs                                   | 6,000   | 6   |  | 487,494   |             | 487,500     |
| Expense related to stock warrants issued                             |         |     |  | 140,000   |             | 140,000     |
| Dividends payable on preferred stock                                 |         |     |  | (85,000)  |             | (85,000)    |
| Cashless exercise of warrants                                        | 23,963  | 24  |  | (24)      |             |             |
| Net loss                                                             |         |     |  |           | (3,701,084) | (3,701,084) |
| Balances at December 31, 2000*                                       |         |     |  |           |             |             |
|                                                                      | 3,200   | 32  |  | 583,479   | 583         | 22,313,870  |
|                                                                      |         |     |  |           | (7,704,222) | 14,610,263  |

\* Not covered by audit report included herein.

**Table of Contents****Mast Therapeutics, Inc. and Subsidiaries**

(A Development Stage Enterprise)

**Consolidated Statements of Stockholders' Equity (Deficit)**

Inception (June 12, 1996) Through December 31, 2012

|                                                       | Cumulative convertible preferred stock, series A through C |        | Convertible preferred stock, series A (2009) |        | Cumulative convertible preferred stock, series B through F (2009 - 2010) |        | Common stock            |        | Deficit         |                                   |              |                          | Total equity (deficit) |
|-------------------------------------------------------|------------------------------------------------------------|--------|----------------------------------------------|--------|--------------------------------------------------------------------------|--------|-------------------------|--------|-----------------|-----------------------------------|--------------|--------------------------|------------------------|
|                                                       | Additional paid-in capital                                 |        | other comprehensive income (loss)            |        | development stage                                                        |        | Treasury stock, at cost |        | accumulated     |                                   | stockholders |                          |                        |
|                                                       | Shares                                                     | Amount | Shares                                       | Amount | Shares                                                                   | Amount | Shares                  | Amount | paid-in capital | other comprehensive income (loss) |              | during development stage |                        |
| Dividends payable on preferred stock                  |                                                            |        |                                              |        |                                                                          |        |                         |        | (256,000)       |                                   |              |                          | (256,000)              |
| Repurchase of warrants                                |                                                            |        |                                              |        |                                                                          |        |                         |        | (55,279)        |                                   |              |                          | (55,279)               |
| Sale of warrants                                      |                                                            |        |                                              |        |                                                                          |        |                         |        | 47,741          |                                   |              |                          | 47,741                 |
| Cashless exercise of warrants                         |                                                            |        |                                              |        | 8,740                                                                    | 9      |                         |        | (9)             |                                   |              |                          |                        |
| Issuance of common stock to pay preferred dividends   |                                                            |        |                                              |        | 3,737                                                                    | 4      |                         |        | 212,996         |                                   |              |                          | 213,000                |
| Detachable warrants issued with notes payable         |                                                            |        |                                              |        |                                                                          |        |                         |        | 450,000         |                                   |              |                          | 450,000                |
| Issuance of warrants to pay operating expenses        |                                                            |        |                                              |        |                                                                          |        |                         |        | 167,138         |                                   |              |                          | 167,138                |
| Issuance of common stock to pay operating expenses    |                                                            |        |                                              |        | 4,252                                                                    | 4      |                         |        | 387,267         |                                   |              |                          | 387,271                |
| Issuance of preferred stock to pay operating expenses | 137                                                        | 1      |                                              |        |                                                                          |        |                         |        | 136,499         |                                   |              |                          | 136,500                |
| Net loss                                              |                                                            |        |                                              |        |                                                                          |        |                         |        |                 |                                   | (16,339,120) |                          | (16,339,120)           |
| Balances at December 31, 2001*                        | 3,337                                                      | 33     |                                              |        | 600,208                                                                  | 600    |                         |        | 23,404,223      |                                   | (24,043,342) |                          | (638,486)              |
| Dividends payable on preferred stock                  |                                                            |        |                                              |        |                                                                          |        |                         |        | (242,400)       |                                   |              |                          | (242,400)              |
| Repurchase of warrants                                |                                                            |        |                                              |        |                                                                          |        |                         |        |                 |                                   |              |                          |                        |
| Sale of warrants                                      |                                                            |        |                                              |        | 9,600                                                                    | 10     |                         |        | 117,843         |                                   |              |                          | 117,853                |
| Cashless exercise of warrants                         |                                                            |        |                                              |        | 4,008                                                                    | 4      |                         |        | (4)             |                                   |              |                          |                        |
|                                                       |                                                            |        |                                              |        | 13,783                                                                   | 14     |                         |        | 168,808         |                                   |              |                          | 168,822                |

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|                                                                 |          |       |         |     |            |              |             |
|-----------------------------------------------------------------|----------|-------|---------|-----|------------|--------------|-------------|
| Exercise of warrants                                            |          |       |         |     |            |              |             |
| Sale of preferred stock at \$1.50 per share                     | 200,000  | 2,000 |         |     | 298,000    |              | 300,000     |
| Sale of preferred stock at \$10.00 per share                    | 70,109   | 701   |         |     | 700,392    |              | 701,093     |
| Conversion of preferred stock into common stock                 | (3,000)  | (30)  | 72,000  | 72  | (42)       |              |             |
| Preferred stock dividends forgiven                              |          |       |         |     | 335,440    |              | 335,440     |
| Issuance of warrants to pay operating expenses                  |          |       |         |     | 163,109    |              | 163,109     |
| Issuance of common stock to pay operating expenses              |          |       | 251     |     | 12,269     |              | 12,269      |
| Issuance of preferred stock to pay operating expenses           | 136      | 1     |         |     | 6,000      |              | 6,001       |
| Share-based compensation expense employee options               |          |       |         |     | 329,296    |              | 329,296     |
| Net loss                                                        |          |       |         |     |            | (2,105,727)  | (2,105,727) |
| Balances at December 31, 2002                                   | 270,582  | 2,705 | 699,850 | 700 | 25,292,934 | (26,149,069) | (852,730)   |
| Dividends payable on preferred stock                            |          |       |         |     | (37,840)   |              | (37,840)    |
| Conversion of Series C preferred stock into common stock        | (70,109) | (701) | 560,874 | 561 | 140        |              |             |
| Issuance of common stock to pay interest on Bridge Notes        |          |       | 6,633   | 7   | 53,484     |              | 53,491      |
| Sale of common stock at \$0.40 per share, net of issuance costs |          |       | 265,630 | 266 | 2,597,066  |              | 2,597,332   |
| Sale of common stock at \$1.00 per share, net of issuance costs |          |       | 148,069 | 148 | 3,992,701  |              | 3,992,849   |
| Exchange of warrants                                            |          |       | 9,412   | 9   | 49,712     |              | 49,721      |
| Issuance of common stock to pay operating expenses              |          |       | 9,200   | 9   | 206,790    |              | 206,799     |
| Issuance of warrants to pay operating expenses                  |          |       |         |     | 156,735    |              | 156,735     |
| Share-based compensation expense employee options               |          |       |         |     | 286,033    |              | 286,033     |

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|                                     |         |       |           |       |            |              |             |
|-------------------------------------|---------|-------|-----------|-------|------------|--------------|-------------|
| Net loss                            |         |       |           |       |            | (2,332,077)  | (2,332,077) |
| Balances at<br>December 31,<br>2003 | 200,473 | 2,004 | 1,699,668 | 1,700 | 32,597,755 | (28,481,146) | 4,120,313   |

\* Not covered by audit report included herein.

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**Table of Contents****Mast Therapeutics, Inc. and Subsidiaries**

(A Development Stage Enterprise)

**Consolidated Statements of Stockholders' Equity (Deficit)**

Inception (June 12, 1996) Through December 31, 2012

|                                                                    | Cumulative convertible preferred stock, series A through C |         | Convertible preferred stock, series A (2009) |        | Cumulative convertible preferred stock, series B through F (2009 - 2010) |        | Common stock |        | Deficit                    |                                   |                               | Total stockholders' equity (deficit) |                         |
|--------------------------------------------------------------------|------------------------------------------------------------|---------|----------------------------------------------|--------|--------------------------------------------------------------------------|--------|--------------|--------|----------------------------|-----------------------------------|-------------------------------|--------------------------------------|-------------------------|
|                                                                    | Shares                                                     | Amount  | Shares                                       | Amount | Shares                                                                   | Amount | Shares       | Amount | Additional paid-in capital | other comprehensive income (loss) | accumulated development stage |                                      | Treasury stock, at cost |
| Extinguishment of dividends payable on preferred stock             |                                                            |         |                                              |        |                                                                          |        |              |        | 72,800                     |                                   |                               |                                      | 72,800                  |
| Conversion of Series A cumulative preferred stock                  | (473)                                                      | (4)     |                                              |        | 9,460                                                                    | 9      |              |        | (5)                        |                                   |                               |                                      |                         |
| Conversion of Series B preferred stock                             | (200,000)                                                  | (2,000) |                                              |        | 8,000                                                                    | 8      |              |        | 1,992                      |                                   |                               |                                      |                         |
| Cashless exercise of warrants                                      |                                                            |         |                                              |        | 18,583                                                                   | 18     |              |        | (18)                       |                                   |                               |                                      |                         |
| Exercise of warrants                                               |                                                            |         |                                              |        | 953                                                                      | 1      |              |        | 27,352                     |                                   |                               |                                      | 27,353                  |
| Issuance of warrants in settlement of a claim                      |                                                            |         |                                              |        |                                                                          |        |              |        | 86,375                     |                                   |                               |                                      | 86,375                  |
| Sale of common stock at \$1.50 per share                           |                                                            |         |                                              |        | 416,705                                                                  | 417    |              |        | 15,626,033                 |                                   |                               |                                      | 15,626,450              |
| Payment of financing and offering costs                            |                                                            |         |                                              |        |                                                                          |        |              |        | (1,366,774)                |                                   |                               |                                      | (1,366,774)             |
| Share-based compensation expense employee options                  |                                                            |         |                                              |        |                                                                          |        |              |        | 524,922                    |                                   |                               |                                      | 524,922                 |
| Acquisition of treasury stock                                      |                                                            |         |                                              |        |                                                                          |        |              |        | 34,747                     |                                   |                               | (34,747)                             |                         |
| Net loss                                                           |                                                            |         |                                              |        |                                                                          |        |              |        |                            |                                   | (6,701,048)                   |                                      | (6,701,048)             |
| Balances at December 31, 2004                                      |                                                            |         |                                              |        | 2,153,369                                                                | 2,153  |              |        | 47,605,179                 |                                   | (35,182,194)                  | (34,747)                             | 12,390,391              |
| Net loss                                                           |                                                            |         |                                              |        |                                                                          |        |              |        |                            |                                   | (24,782,646)                  |                                      | (24,782,646)            |
| Other comprehensive income/(loss)                                  |                                                            |         |                                              |        |                                                                          |        |              |        |                            | (1,722)                           |                               |                                      | (1,722)                 |
| Par value of shares issued in conjunction with mezzanine financing |                                                            |         |                                              |        | 432,432                                                                  | 433    |              |        | (433)                      |                                   |                               |                                      |                         |
| Cashless exercise of warrants                                      |                                                            |         |                                              |        | 5,985                                                                    | 6      |              |        | (6)                        |                                   |                               |                                      |                         |
| Exercise of warrants                                               |                                                            |         |                                              |        | 90,348                                                                   | 90     |              |        | 3,073,348                  |                                   |                               |                                      | 3,073,438               |
| Exercise of stock options                                          |                                                            |         |                                              |        | 7,400                                                                    | 7      |              |        | 144,993                    |                                   |                               |                                      | 145,000                 |
| Share-based compensation expense employee options                  |                                                            |         |                                              |        |                                                                          |        |              |        | 994,874                    |                                   |                               |                                      | 994,874                 |
|                                                                    |                                                            |         |                                              |        |                                                                          |        |              |        | 93,549                     |                                   |                               |                                      | 93,549                  |

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|                                                                 |           |       |             |         |              |          |              |
|-----------------------------------------------------------------|-----------|-------|-------------|---------|--------------|----------|--------------|
| Share-based compensation expense non-employee options           |           |       |             |         |              |          |              |
| Issuance of common stock to vendor                              | 5,000     | 5     | 258,495     |         |              |          | 258,500      |
| Balances at December 31, 2005, as restated                      | 2,694,534 | 2,694 | 52,169,999  | (1,722) | (59,964,840) | (34,747) | (7,828,616)  |
| Net loss                                                        |           |       |             |         | (29,331,773) |          | (29,331,773) |
| Other comprehensive income/(loss)                               |           |       |             | (368)   |              |          | (368)        |
| Cashless exercise of warrants                                   | 16,807    | 17    | (17)        |         |              |          |              |
| Exercise of warrants, net of financing costs                    | 204,150   | 204   | 7,691,386   |         |              |          | 7,691,590    |
| Acquisition of SD Pharmaceuticals, Inc.                         | 84,000    | 84    | 10,163,868  |         |              |          | 10,163,952   |
| Sale of common stock at \$2.75 per share, net of offering costs | 581,800   | 582   | 37,069,629  |         |              |          | 37,070,211   |
| Issuance of stock for severance agreement                       | 2,406     | 2     | 196,672     |         |              |          | 196,674      |
| Exercise of stock options                                       | 3,700     | 4     | 125,747     |         |              |          | 125,751      |
| Share-based compensation expense non-employee restricted stock  | 600       | 1     | 68,649      |         |              |          | 68,650       |
| Share-based compensation expense employee options               |           |       | 1,697,452   |         |              |          | 1,697,452    |
| Share-based compensation expense non-employee options           |           |       | 104,225     |         |              |          | 104,225      |
| Cancellation of treasury stock shares                           | (927)     | (1)   | (34,746)    |         |              | 34,747   |              |
| Balances at December 31, 2006, as restated                      | 3,587,070 | 3,587 | 109,252,864 | (2,090) | (89,296,613) |          | 19,957,748   |

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**Table of Contents****Mast Therapeutics, Inc. and Subsidiaries**

(A Development Stage Enterprise)

**Consolidated Statements of Stockholders' Equity (Deficit)**

Inception (June 12, 1996) Through December 31, 2012

|                                                                      | Cumulative convertible preferred stock, series A through C |        | Convertible preferred stock, series A (2009) |        | Cumulative convertible preferred stock, series B through F (2009 - 2010) |        | Common stock |             | Deficit                    |                                   |                                      | Total equity (deficit) |                          |
|----------------------------------------------------------------------|------------------------------------------------------------|--------|----------------------------------------------|--------|--------------------------------------------------------------------------|--------|--------------|-------------|----------------------------|-----------------------------------|--------------------------------------|------------------------|--------------------------|
|                                                                      | Shares                                                     | Amount | Shares                                       | Amount | Shares                                                                   | Amount | Shares       | Amount      | Additional paid-in capital | other comprehensive income (loss) | accumulated during development stage |                        | Treasurer stock, at cost |
| Cumulative effect of change in accounting principle                  |                                                            |        |                                              |        |                                                                          |        |              |             | 18,116,751                 |                                   | 12,239,688                           |                        | 30,356,439               |
| Net loss                                                             |                                                            |        |                                              |        |                                                                          |        |              |             |                            |                                   | (22,142,040)                         |                        | (22,142,040)             |
| Other comprehensive income/(loss)                                    |                                                            |        |                                              |        |                                                                          |        |              |             |                            | 4,792                             |                                      |                        | 4,792                    |
| Exercise of stock options                                            |                                                            |        |                                              |        | 23,033                                                                   | 23     |              | 441,593     |                            |                                   |                                      |                        | 441,616                  |
| Share-based compensation expense employee options                    |                                                            |        |                                              |        |                                                                          |        |              |             | 2,414,077                  |                                   |                                      |                        | 2,414,077                |
| Share-based compensation expense non-employee options                |                                                            |        |                                              |        |                                                                          |        |              |             | 1,908                      |                                   |                                      |                        | 1,908                    |
| Balances at December 31, 2007                                        |                                                            |        |                                              |        | 3,610,103                                                                | 3,610  |              | 130,227,193 | 2,702                      |                                   | (99,198,965)                         |                        | 31,034,540               |
| Net loss                                                             |                                                            |        |                                              |        |                                                                          |        |              |             |                            |                                   | (26,647,493)                         |                        | (26,647,493)             |
| Other comprehensive income/(loss)                                    |                                                            |        |                                              |        |                                                                          |        |              |             |                            | (2,702)                           |                                      |                        | (2,702)                  |
| Exercise of stock options                                            |                                                            |        |                                              |        |                                                                          |        |              |             |                            |                                   |                                      |                        |                          |
| Share-based compensation expense employee options                    |                                                            |        |                                              |        |                                                                          |        |              |             | 1,605,908                  |                                   |                                      |                        | 1,605,908                |
| Share-based compensation expense non-employee options                |                                                            |        |                                              |        |                                                                          |        |              |             | 4,982                      |                                   |                                      |                        | 4,982                    |
| Balances at December 31, 2008                                        |                                                            |        |                                              |        | 3,610,103                                                                | 3,610  |              | 131,838,083 |                            |                                   | (125,846,458)                        |                        | 5,995,235                |
| Net loss                                                             |                                                            |        |                                              |        |                                                                          |        |              |             |                            |                                   | (11,325,058)                         |                        | (11,325,058)             |
| Sale of series A preferred stock, net of offering costs of \$389,125 |                                                            |        | 1,993                                        | 2      |                                                                          |        |              |             | 1,735,627                  |                                   |                                      |                        | 1,735,629                |
| Conversion of series A preferred stock into common stock             |                                                            |        | (1,993)                                      | (2)    |                                                                          |        | 721,448      | 721         | (719)                      |                                   |                                      |                        |                          |
|                                                                      |                                                            |        |                                              |        | 1,361                                                                    | 1      |              |             | 833,030                    |                                   |                                      |                        | 833,031                  |



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|                                                                        |          |      |           |       |             |               |           |
|------------------------------------------------------------------------|----------|------|-----------|-------|-------------|---------------|-----------|
| Sale of series B preferred stock, net of offering costs of \$247,643   |          |      |           |       |             |               |           |
| Conversion of series B preferred stock into common stock               | (1,361)  | (1)  | 380,168   | 380   | (379)       |               |           |
| Sale of series C preferred stock, net of offering costs of \$143,885   | 922      | 1    |           |       | 711,198     | 711,199       |           |
| Conversion of series C preferred stock into common stock               | (922)    | (1)  | 283,692   | 284   | (283)       |               |           |
| Sale of series D preferred stock, net of offering costs of \$1,327,664 | 11,283   | 11   |           |       | 5,124,125   | 5,124,136     |           |
| Conversion of series D preferred stock into common stock               | (11,283) | (11) | 2,400,000 | 2,400 | (2,389)     |               |           |
| Deemed dividend on series A preferred stock                            |          |      |           |       | 1,207,536   | (1,207,536)   |           |
| Deemed dividend on series B preferred stock                            |          |      |           |       | 214,795     | (214,795)     |           |
| Deemed dividend on series C preferred stock                            |          |      |           |       | 186,173     | (186,173)     |           |
| Deemed dividend on series D preferred stock                            |          |      |           |       | 3,258,383   | (3,258,383)   |           |
| Share-based compensation expense employee options                      |          |      |           |       | 585,438     | 585,438       |           |
| Series A warrants exercised                                            |          |      | 240,000   | 240   | 899,760     | 900,000       |           |
| Series D warrants exercised                                            |          |      | 576,000   | 576   | 2,113,344   | 2,113,920     |           |
| Balances at December 31, 2009                                          |          |      | 8,211,411 | 8,211 | 148,703,722 | (142,038,403) | 6,673,530 |

**Table of Contents****Mast Therapeutics, Inc. and Subsidiaries**

(A Development Stage Enterprise)

**Consolidated Statements of Stockholders' Equity (Deficit)**

Inception (June 12, 1996) Through December 31, 2012

|                                                                                             | Cumulative convertible preferred stock, series A through C |        | Convertible preferred stock, series A (2009) |        | Cumulative convertible preferred stock, series B through F (2009 - 2010) |        | Common stock |            | Deficit                    |                                   |                                      | Total stockholders' equity (deficit) |                         |
|---------------------------------------------------------------------------------------------|------------------------------------------------------------|--------|----------------------------------------------|--------|--------------------------------------------------------------------------|--------|--------------|------------|----------------------------|-----------------------------------|--------------------------------------|--------------------------------------|-------------------------|
|                                                                                             | Share                                                      | Amount | Share                                        | Amount | Shares                                                                   | Amount | Shares       | Amount     | Additional paid-in capital | other comprehensive income (loss) | accumulated during development stage |                                      | Treasury stock, at cost |
|                                                                                             |                                                            |        |                                              |        |                                                                          |        |              |            |                            |                                   |                                      |                                      |                         |
| Net loss                                                                                    |                                                            |        |                                              |        |                                                                          |        |              |            |                            |                                   | (8,450,922)                          |                                      | (8,450,922)             |
| Reduction of shares and cash paid in lieu for fractional shares following the reverse split |                                                            |        |                                              |        | (31)                                                                     |        |              | (146)      |                            |                                   |                                      |                                      | (146)                   |
| Sale of series E preferred stock, net of offering costs of \$2,162,787                      |                                                            |        | 19,000                                       | 19     |                                                                          |        |              | 14,014,705 |                            |                                   |                                      |                                      | 14,014,724              |
| Conversion of series E preferred stock into common stock                                    |                                                            |        | (19,000)                                     | (19)   | 1,993,965                                                                | 1,994  |              | (1,975)    |                            |                                   |                                      |                                      |                         |
| Sale of series F preferred stock, net of offering costs of \$1,655,234                      |                                                            |        | 19,217                                       | 19     |                                                                          |        |              | 13,344,749 |                            |                                   |                                      |                                      | 13,344,768              |
| Conversion of series F preferred stock into common stock                                    |                                                            |        | (19,217)                                     | (19)   | 5,190,306                                                                | 5,190  |              | (5,171)    |                            |                                   |                                      |                                      |                         |
| Deemed dividend on series E preferred stock                                                 |                                                            |        |                                              |        |                                                                          |        |              | 2,514,920  |                            |                                   | (2,514,920)                          |                                      |                         |
| Deemed dividend on series F preferred stock                                                 |                                                            |        |                                              |        |                                                                          |        |              | 3,124,876  |                            |                                   | (3,124,876)                          |                                      |                         |
| Share-based compensation expense employee options                                           |                                                            |        |                                              |        |                                                                          |        |              | 785,943    |                            |                                   |                                      |                                      | 785,943                 |
| Series A warrants                                                                           |                                                            |        |                                              |        | 84,651                                                                   | 85     |              | 317,359    |                            |                                   |                                      |                                      | 317,444                 |

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exercised

|                                                            |               |           |                |               |                  |
|------------------------------------------------------------|---------------|-----------|----------------|---------------|------------------|
| Balances at December 31, 2010                              | 15,480,302    | 15,480    | 182,798,982    | (156,129,121) | 26,685,341       |
| Net loss                                                   |               |           |                | (13,259,931)  | (13,259,931)     |
| Sale of common stock, net of offering costs of \$1,548,123 | 8,184,556     | 8,185     | 20,951,221     |               | 20,959,406       |
| Issuance of stock in SynthRx acquisition                   | 2,800,851     | 2,801     | 5,882,522      |               | 5,885,323        |
| Sale of common stock, net of offering costs of \$1,355,196 | 21,250,000    | 21,250    | 15,623,554     |               | 15,644,804       |
| Share-based compensation expense employee options          |               |           | 866,052        |               | 866,052          |
| Other comprehensive income/(loss)                          |               |           |                | (2,298)       | (2,298)          |
| Balances at December 31, 2011                              | 47,715,709    | 47,716    | 226,122,331    | (2,298)       | 56,778,697       |
| Net loss                                                   |               |           |                | (15,559,489)  | (15,559,489)     |
| Share-based compensation expense employee options          |               |           | 1,459,330      |               | 1,459,330        |
| Exercise of stock options                                  | 3,656         | 4         | 2,190          |               | 2,194            |
| Repurchase of Subject to Vesting Shares                    | (1,454,079)   |           |                |               | (1,454)          |
| Elimination of contingent asset                            |               |           | (886,988)      |               | (886,988)        |
| Other comprehensive income/(loss)                          |               |           |                | 104           | 104              |
| Balances at December 31, 2012                              | \$ 46,265,286 | \$ 47,720 | \$ 226,696,863 | \$ (2,194)    | \$ (184,948,541) |
|                                                            |               |           |                | \$ (1,454)    | \$ 41,792,394    |

**Table of Contents****Mast Therapeutics, Inc. and Subsidiaries**

(A Development Stage Enterprise)

**Consolidated Statements of Cash Flows**

|                                                                                                | Years Ended December 31, |                 | Inception        |
|------------------------------------------------------------------------------------------------|--------------------------|-----------------|------------------|
|                                                                                                | 2012                     | 2011            | (June 12, 1996)  |
|                                                                                                |                          |                 | Through          |
|                                                                                                |                          |                 | December 31,     |
|                                                                                                |                          |                 | 2012             |
| <b>Cash flows from operating activities:</b>                                                   |                          |                 |                  |
| Net loss                                                                                       | \$ (15,559,489)          | \$ (13,259,931) | \$ (187,177,148) |
| Adjustments to reconcile net loss to net cash used in operating activities:                    |                          |                 |                  |
| Depreciation and amortization                                                                  | 90,047                   | 37,570          | 10,575,237       |
| Loss (gain) on disposals of equipment                                                          | 4,503                    | (2,973)         | 61,315           |
| Loss on fair value of warrants                                                                 |                          |                 | 12,239,688       |
| Gain on change in fair value of contingent consideration                                       | (69,602)                 | (1,459,305)     | (1,528,907)      |
| Amortization of debt discount                                                                  |                          |                 | 450,000          |
| Forgiveness of employee receivable                                                             |                          |                 | 30,036           |
| Impairment loss write-off of goodwill                                                          |                          |                 | 5,702,130        |
| Share-based compensation expense related to employee stock options and restricted stock issued | 1,459,330                | 866,052         | 11,549,324       |
| Expenses related to options issued to non-employees                                            |                          |                 | 204,664          |
| Expenses paid by issuance of common stock                                                      |                          |                 | 1,341,372        |
| Expenses paid by issuance of warrants                                                          |                          |                 | 573,357          |
| Expenses paid by issuance of preferred stock                                                   |                          |                 | 142,501          |
| Expenses related to stock warrants issued                                                      |                          |                 | 612,000          |
| Equity in loss of investee                                                                     |                          |                 | 178,936          |
| In-process research and development                                                            |                          |                 | 10,422,130       |
| Write-off of license agreement                                                                 |                          |                 | 152,866          |
| Impairment of equipment                                                                        | 402,739                  |                 | 510,739          |
| Cumulative effect of change in accounting principle                                            |                          |                 | 25,821           |
| Amortization of premium / (accretion of discount) on investments in securities                 | 21,840                   | 11,152          | (1,571,502)      |
| Changes in assets and liabilities, net of effect of acquisitions:                              |                          |                 |                  |
| (Increase) decrease in prepaid and other assets                                                | (388,704)                | 143,955         | (955,859)        |
| Increase in accounts payable and accrued liabilities                                           | 120,468                  | 196,526         | 2,295,178        |
| Net cash used in operating activities                                                          | (13,918,868)             | (13,466,954)    | (134,166,122)    |
| <b>Cash flows from investing activities:</b>                                                   |                          |                 |                  |
| Purchases of certificates of deposit                                                           | (15,822,000)             | (7,144,849)     | (23,983,179)     |
| Proceeds from maturities of certificates of deposit                                            | 8,675,000                |                 | 9,691,330        |
| Proceeds from sale of certificate of deposit                                                   | 248,000                  |                 | 248,000          |
| Purchases of other short-term investments                                                      |                          |                 | (111,183,884)    |
| Proceeds from maturities and sales of other short-term investments                             |                          |                 | 112,788,378      |
| Purchases of property and equipment                                                            | (266,175)                | (411,762)       | (1,736,804)      |
| Proceeds from sale of property and equipment                                                   |                          | 12,635          | 66,920           |

**Table of Contents****Mast Therapeutics, Inc. and Subsidiaries**

(A Development Stage Enterprise)

**Consolidated Statements of Cash Flows**

|                                                                 |                                 |               | <b>Inception</b>           |
|-----------------------------------------------------------------|---------------------------------|---------------|----------------------------|
|                                                                 |                                 |               | <b>(June 12,<br/>1996)</b> |
|                                                                 |                                 |               | <b>Through</b>             |
|                                                                 | <b>Years Ended December 31,</b> |               | <b>December 31,</b>        |
|                                                                 | <b>2012</b>                     | <b>2011</b>   | <b>2012</b>                |
| Cash paid for acquisitions, net of cash acquired                | \$                              | \$            | \$ 32,395                  |
| Payment on obligation under license agreement                   |                                 |               | (106,250)                  |
| Issuance of note receivable related party                       |                                 |               | (35,000)                   |
| Payments on note receivable                                     |                                 |               | 405,993                    |
| Advance to investee                                             |                                 |               | (90,475)                   |
| Cash transferred in rescission of acquisition                   |                                 |               | (19,475)                   |
| Cash received in rescission of acquisition                      |                                 |               | 230,000                    |
| Net cash used in investing activities                           | (7,165,175)                     | (7,543,976)   | (13,692,051)               |
| <b>Cash flows from financing activities:</b>                    |                                 |               |                            |
| Proceeds from sale of common stock                              |                                 | 39,507,529    | 123,658,871                |
| Proceeds from exercise of stock options                         | 2,194                           |               | 714,561                    |
| Proceeds from sale or exercise of warrants                      |                                 |               | 14,714,258                 |
| Proceeds from sale of preferred stock                           |                                 |               | 44,474,720                 |
| Repurchase of Subject to Vesting Shares                         | (1,454)                         |               | (1,454)                    |
| Repurchase of warrants                                          |                                 |               | (55,279)                   |
| Payments for financing and offering costs                       |                                 | (2,903,319)   | (13,897,367)               |
| Payments on notes payable and long-term debt                    |                                 |               | (605,909)                  |
| Proceeds from issuance of notes payable and detachable warrants |                                 |               | 1,344,718                  |
| Cash paid in lieu of fractional shares for reverse stock split  |                                 |               | (146)                      |
| Net cash provided by financing activities                       | 740                             | 36,604,210    | 170,346,973                |
| Effect of exchange rate changes on cash and cash equivalents    | 13,796                          | (2,156)       | 11,640                     |
| Net (decrease) increase in cash and cash equivalents            | (21,069,507)                    | 15,591,124    | 22,500,440                 |
| Cash and cash equivalents at beginning of period                | 43,569,947                      | 27,978,823    |                            |
| Cash and cash equivalents at end of period                      | \$ 22,500,440                   | \$ 43,569,947 | \$ 22,500,440              |

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**Mast Therapeutics, Inc. and Subsidiaries**

(A Development Stage Enterprise)

**Notes to Consolidated Financial Statements**

**December 31, 2012**

**1. Description of Business**

Mast Therapeutics, Inc., a Delaware corporation ( Mast Therapeutics, we or our company ), is a biopharmaceutical company focused on developing therapies for serious or life-threatening diseases. We have devoted substantially all of our resources to research and development ( R&D ), and acquisition of our product candidates. We have not yet marketed or sold any products or generated any significant revenue. Through our acquisition of SynthRx, Inc. in 2011, we acquired our Membrane Adhesion & Sealant Technology (MAST) platform, which includes proprietary poloxamer-related data and know-how developed over two decades of clinical, nonclinical and manufacturing experience, and we are leveraging the MAST platform to develop MST-188 for diseases and conditions characterized by microcirculatory insufficiency. In prior years, we were developing Exelbine and ANX-514, both of which are investigational oncology programs, but, beginning in 2012, we have focused our resources almost exclusively on development of MST-188.

In March 2013, we merged our wholly-owned subsidiary, Mast Therapeutics, Inc., with and into us and changed our name from ADVENTRX Pharmaceuticals, Inc. to Mast Therapeutics, Inc. The merger had no effect on our financial statements.

**2. Summary of Significant Accounting Policies**

***Basis of Presentation***

The consolidated financial statements include the accounts of Mast Therapeutics and its wholly-owned subsidiaries, SD Pharmaceuticals, Inc. ( SD Pharmaceuticals ) and SynthRx, Inc. ( SynthRx ). All intercompany accounts and transactions have been eliminated in consolidation.

We accounted for the acquisition of SynthRx in accordance with Accounting Standards Codification ( ASC ) Topic 805, *Business Combinations* ( ASC Topic 805 ). ASC Topic 805 establishes principles and requirements for recognizing and measuring the total consideration transferred to and the assets acquired, liabilities assumed and any non-controlling interests in the acquired target in a business combination. ASC Topic 805 also provides guidance for recognizing and measuring goodwill acquired in a business combination; requires purchased in-process research and development ( IPR&D ) to be capitalized at fair value as intangible assets at the time of acquisition; requires acquisition-related expenses and restructuring costs to be recognized separately from the business combination; expands the definition of what constitutes a business; and requires the acquirer to disclose information that users may need to evaluate and understand the financial effect of the business combination.

Certain prior year amounts have been reclassified in the consolidated financial statements to conform to the current year presentation. These reclassifications were not material and had no effect on previously reported results of operations.

***Use of Estimates***

The preparation of financial statements in conformity with United States generally accepted accounting principles ( U.S. GAAP ) requires management to make estimates and assumptions that affect the amounts reported in our consolidated financial statements and accompanying notes. On an ongoing basis, we evaluate our estimates, including estimates related to contingent consideration, R&D expenses and share-based compensation expenses. We base our estimates on historical experience and various other relevant assumptions we believe to be reasonable under the circumstances. Actual results may differ from these estimates.

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**Mast Therapeutics, Inc. and Subsidiaries**

(A Development Stage Enterprise)

**Notes to Consolidated Financial Statements**

**December 31, 2012**

***Fair Value of Financial Instruments***

Our short-term investments and our contingent asset and contingent liability are carried at fair value (see Note 5). Cash, cash equivalents, prepaid expenses and other current assets, accounts payable and accrued liabilities, are carried at cost, which we believe approximates fair value due to the short-term maturities of these instruments.

***Cash and Cash Equivalents***

Cash and cash equivalents consist of cash and highly liquid investments with original maturities of three months or less at the date of purchase. Cash equivalents are carried at cost, which we believe approximates fair value due to the short-term maturities of these instruments. At December 31, 2012 and 2011, we had \$1.0 million and \$2.9 million of cash equivalents, respectively.

***Short-Term Investments***

We consider income-yielding securities that can be readily converted to cash and have original maturities of more than three months and one year or less at the date of purchase to be short-term investments. All of our short-term investments are marketable securities under the custodianship of a major financial institution and consist primarily of FDIC-insured certificates of deposit.

We account for and report our short-term investments in accordance with ASC 320, *Accounting for Certain Investments in Debt and Equity Securities*. Our short-term investments are classified as available-for-sale securities and carried at fair value. Fair value for securities with short maturities and infrequent secondary market trades is typically determined using mathematical calculations adjusted for observable inputs when available. Net unrealized gains or losses on these securities are included in accumulated other comprehensive income (loss), which is a separate component of stockholders' equity. Realized gains and realized losses are included in other income (expense), while amortization of premiums and discounts are included in interest expense. Interest and dividends on available-for-sale securities are included in interest income. Marketable securities are evaluated periodically for impairment. If we determine that a decline in market value of any investment is other than temporary, then the investment basis would be written down to fair value and charged to earnings.

***Asset and Liability for Contingent Consideration***

Our contingent asset and contingent liability are related to our acquisition of SynthRx in April 2011 and the contingent consideration that consists solely of shares of our common stock and varies based on achievement and the circumstances of achievement of a milestone associated with the development of MST-188. We remeasure the fair values of the contingent asset and contingent liability as of the end of each fiscal quarter until the contingencies are settled. The estimated fair values of the contingent asset and contingent liability are based on our stock price at each measurement date and assumptions of management regarding the probability, timing and a design aspect of a pivotal phase 3 clinical study of MST-188 in sickle cell disease. Although we base our estimates on assumptions believed to be reasonable under the circumstances, such assumptions are highly judgmental due to the inherent unpredictability of drug-development by development-stage companies like ours and the fair values of the contingent asset and contingent liability may differ materially under different assumptions. Net changes in the fair value of this contingent consideration are recognized in earnings, as transaction-related expenses, until the contingent arrangement is settled.

***Property and Equipment***

Property and equipment are stated at cost, less accumulated depreciation. Property and equipment are depreciated using the straight-line method over the estimated useful lives of the assets (generally three to five years). Leasehold improvements are amortized over the economic life of the asset or the lease term, whichever is shorter. Repairs and maintenance are expensed as incurred.





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**Mast Therapeutics, Inc. and Subsidiaries**

(A Development Stage Enterprise)

**Notes to Consolidated Financial Statements**

**December 31, 2012**

In accordance with ASC Topic 360-10, *Property, Plant and Equipment* Overall, we test for recoverability of long-lived assets, including property and equipment, if events or changes in circumstances indicate that the carrying amount for the assets may not be recoverable. If our assessment indicates impairment, we measure the impairment loss as the amount by which the carrying amount exceeds fair value of the assets. Fair value determinations are based on an undiscounted cash flow model, or independent appraisals, as appropriate.

***Intangible Assets Goodwill and Acquired In-Process Research & Development***

In accordance with ASC Topic 350, *Intangibles Goodwill and Other* ( ASC 350 ), our goodwill and acquired IPR&D are determined to have indefinite lives and, therefore, are not amortized. Instead, they are tested for impairment annually and between annual tests if we become aware of an event or a change in circumstances that would indicate the carrying value may be impaired. We perform our annual impairment testing as of September 30 of each year. Pursuant to Accounting Standards Update, or ASU, No. 2011-08, *Intangibles Goodwill and Other (Topic 350): Testing Goodwill for Impairment*, and No. 2012-02, *Intangibles Goodwill and Other (Topic 350): Testing Indefinite-Lived Intangible Assets for Impairment*, we have the option to first assess qualitative factors to determine whether the existence of events or circumstances leads us to determine that it is more likely than not (that is, a likelihood of more than 50%) that our goodwill or our acquired IPR&D is impaired. If we choose to first assess qualitative factors and we determine that it is not more likely than not goodwill or acquired IPR&D is impaired, we are not required to take further action to test for impairment. We also have the option to bypass the qualitative assessment and perform only the quantitative impairment test, which we may choose to do in some periods but not in others. In performing the quantitative assessment for goodwill, we utilize the two-step approach prescribed under ASC 350. Step 1 requires a comparison of the carrying value of a reporting unit, including goodwill, to its estimated fair value. We test for impairment at the entity level because we operate on the basis of a single reporting unit. If our carrying value exceeds our fair value, we then perform Step 2 to measure the amount of impairment loss, if any. In Step 2, we estimate the fair value of our individual assets, including identifiable intangible assets, and liabilities to determine the implied fair value of goodwill. We then compare the carrying value of our goodwill to its implied fair value. The excess of the carrying value of goodwill over its implied fair value, if any, is recorded as an impairment charge. In performing the quantitative assessment for acquired IPR&D, we compare the carrying value of acquired IPR&D to its estimated fair value. The excess of the carrying value over its estimated fair value is recorded as an impairment charge. All impairment charges are recorded to our consolidated statements of operations and comprehensive income/(loss). Our determinations as to whether, and, if so, the extent to which, goodwill and acquired IPR&D become impaired are highly judgmental and based on significant assumptions regarding our projected future financial condition and operating results, changes in the manner of our use of the acquired assets, development of MST-188 or our overall business strategy, and regulatory, market and economic environment and trends.

For acquisitions prior to January 1, 2009, the estimated fair value of acquired IPR&D was expensed immediately for projects that, as of the acquisition date, had not reached technological feasibility, had no alternative future use and had uncertainty in receiving future economic benefits from the acquired IPR&D. In the year ended December 31, 2006, we recorded \$10.4 million of IPR&D expense related to our acquisition of SD Pharmaceuticals.

***Concentration of Credit Risk and Significant Sources of Supply***

Financial instruments that potentially subject us to concentrations of credit risk are primarily cash, cash equivalents and short-term investments. We have a board-approved investment policy that sets our investment parameters and limitations with objectives of preserving principal and liquidity. Our cash and cash equivalent balances consist primarily of money market accounts under the custodianship of major financial institutions. Short-term investments are invested in accordance with our investment policy. We do not have any financial instruments with off-balance-sheet risk of accounting loss.

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**Mast Therapeutics, Inc. and Subsidiaries**

(A Development Stage Enterprise)

**Notes to Consolidated Financial Statements**

**December 31, 2012**

We rely on single-source, third-party manufacturers and suppliers for production and supply of key components of our product candidates, and for production of the final drug products themselves. If these single-source, third-party manufacturers and suppliers are unable to continue providing a key component or the final drug products, the initiation or progress of any clinical studies of our product candidates may be severely impeded.

***Foreign Currency***

Assets and liabilities denominated in foreign currencies are translated at the rate of exchange on the balance sheet date. Revenues and expenses are translated using the average exchange rate for the period. Net gains and losses resulting from the translation of liabilities payable in foreign currencies are recorded in accumulated other comprehensive income (loss), which is a separate component of stockholders' equity. Net foreign currency gains (losses) resulting from transactions in currencies other than the functional currency are included in other income (expense) in our consolidated statement of operations and comprehensive income/(loss). For the years ended December 31, 2012 and 2011, we recorded net foreign currency gains of \$53,000 and \$11,000 respectively. As of December 31, 2012 and 2011, approximately 1% and 8% of our total liabilities, respectively, were denominated in currencies other than the U.S. dollar, which is our functional currency.

***Revenue Recognition***

We recognize revenues in accordance with authoritative guidance established by U.S. GAAP. Our revenues to date have been generated primarily through licensing agreements and federal government research grants. Licensing agreements may include upfront payments, funding of research and development, milestone payments and royalties.

We consider a variety of factors in determining the appropriate method of accounting under our licensing agreements, including whether the various elements can be separated and accounted for individually as separate units of accounting. Where there are multiple deliverables identified within a licensing agreement that are combined into a single unit of accounting, revenue is deferred and recognized over the expected period of performance. The specific methodology for the recognition of the revenue is determined on a case-by-case basis according to the facts and circumstances of the applicable agreement. Non-refundable license fees are recognized as revenue upon receipt if the licensed assets have stand-alone value, we do not have ongoing involvement or obligations, and we can determine the best estimate of the selling price for any undelivered items. When these criteria are not met, non-refundable license fees are recorded as deferred revenue upon receipt and recognized as revenue over the expected period of performance. Non-refundable license fees for R&D expenses generally are recognized as revenue over the period as the related R&D activities are performed. We evaluate milestone payments under licensing agreements on an individual basis and recognize revenue from non-refundable milestone payments when the earnings process is complete and payment is reasonably assured. Non-refundable milestone payments related to arrangements under which we have continuing performance obligations are recognized as revenue upon achievement of the associated milestone, provided that (i) the milestone event is substantive and its achievability was not reasonably assured at the inception of the agreement and (ii) the amount of the milestone payment is reasonable in relation to the effort expended or the risk associated with the milestone event. If a milestone payment does not meet these criteria, we recognize revenue using a probability-adjusted performance model over the expected period of performance.

We recognize revenue from federal government research grants during the period in which we receive the grant funds, or their collection is reasonably assured, and we incur the qualified expenditures.

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**Mast Therapeutics, Inc. and Subsidiaries**

(A Development Stage Enterprise)

**Notes to Consolidated Financial Statements**

**December 31, 2012**

***Research and Development Expense***

R&D costs are charged to expense as incurred and include, but are not limited to, employee salaries and benefits, nonclinical study costs, clinical study costs, research-related manufacturing and related costs, consulting services fees and share-based compensation cost. Clinical study costs include, but are not limited to, clinical research organization fees, investigator fees, site costs and, as applicable, comparator drug costs. Costs for certain R&D activities, such as research-related manufacturing and clinical studies, are recognized based on an evaluation of the percentage of work completed or the progress to completion of specific tasks using data such as patient enrollment, clinical site activations, duration of the study and/or information provided to us by our vendors on their actual costs incurred. Payments for these activities are based on the terms of the individual arrangements, which may differ from the pattern of costs incurred, and are reflected in the financial statements as prepaid expenses or accrued R&D costs.

Advance payments to third parties, including nonrefundable amounts, for goods and services that will be used or rendered for future R&D activities are deferred and capitalized, then expensed as the services are performed or as the underlying goods are delivered. If we do not expect the services to be rendered or goods to be delivered, any remaining capitalized amounts for nonrefundable advance payments are charged to expense immediately.

Milestone payments that we make in connection with in-licensed technology or product candidates are expensed as incurred when there is uncertainty in receiving future economic benefits from the licensed technology or product candidates. We consider the future economic benefits from the licensed technology or product candidates to be uncertain until such licensed technology is incorporated into products that, or such product candidates, are approved for marketing by the FDA or when other significant risk factors are abated. For accounting purposes, management has viewed future economic benefits for all of our licensed technology or product candidates to be uncertain.

***Share-Based Compensation***

Share-based compensation cost is measured at the grant date, based on the estimated fair value of the award using the Black-Scholes valuation model, and is recognized as expense over the vesting period on a straight-line basis. Share-based compensation expense recognized in the consolidated statements of operations for the years ended December 31, 2012 and 2011 is based on awards ultimately expected to vest and has been reduced for estimated forfeitures. This estimate will be revised in subsequent periods if actual forfeitures differ from those estimates. None of our outstanding share-based awards have market or performance conditions.

***Patent Costs***

Legal costs in connection with approved patents and patent applications are expensed as incurred, as recoverability of such expenditures is uncertain. These costs are recorded as selling, general and administrative expenses in our consolidated statement of operations and comprehensive income/(loss).

***Income Taxes***

We account for income taxes and the related accounts under the liability method. Deferred tax assets and liabilities are determined based on the differences between the financial statement carrying amounts and the income tax basis of assets and liabilities. A valuation allowance is applied against any net deferred tax asset if, based on available evidence, it is more likely than not that some or all of the deferred tax assets will not be realized.

The tax effects from an uncertain tax position can be recognized in our consolidated financial statements only if the position is more likely than not of being sustained upon an examination by tax authorities. An uncertain income tax position will not be recognized if it has less than a 50%

likelihood of being sustained.

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**Table of Contents****Mast Therapeutics, Inc. and Subsidiaries**

(A Development Stage Enterprise)

**Notes to Consolidated Financial Statements****December 31, 2012**

We account for interest and penalties related to income tax matters, if any, in income tax expense.

**Comprehensive Income/(Loss)**

Comprehensive income or loss is defined as the change in equity of a business enterprise during a period from transactions and other events and circumstances from non-owner sources, including foreign currency translation adjustments and unrealized gains and losses on marketable securities. We present comprehensive income/(loss) in our consolidated statement of operations and comprehensive income/(loss).

**Net Loss per Common Share**

Basic and diluted net loss per common share was calculated by dividing the net loss applicable to common stock for the years ended December 31, 2012 and 2011 by the weighted-average number of common shares outstanding during those periods, respectively, without consideration for outstanding common stock equivalents because their effect would have been anti-dilutive. Common stock equivalents are included in the calculation of diluted earnings per common share only if their effect is dilutive. For the periods presented, our outstanding common stock equivalents consisted of options and warrants to purchase shares of our common stock. The weighted-average number of those common stock equivalents outstanding for each of the periods presented is set forth in the table below:

|          | Years ended December 31, |            |
|----------|--------------------------|------------|
|          | 2012                     | 2011       |
| Warrants | 17,093,296               | 9,436,425  |
| Options  | 3,111,854                | 1,156,626  |
|          | 20,205,150               | 10,593,051 |

**Supplemental Cash Flow Information**

|                                                                          | Years ended December 31, |           | Inception<br>(June 12, 1996)<br>through<br>December 31, 2012 |
|--------------------------------------------------------------------------|--------------------------|-----------|--------------------------------------------------------------|
|                                                                          | 2012                     | 2011      |                                                              |
| Supplemental disclosures of cash flow information:                       |                          |           |                                                              |
| Interest paid                                                            | \$                       | \$        | \$ 180,719                                                   |
| Supplemental disclosures of non-cash investing and financing activities: |                          |           |                                                              |
| Issuance of warrants, common stock and preferred stock for:              |                          |           |                                                              |
| Conversion of notes payable and accrued interest                         |                          |           | 1,213,988                                                    |
| Prepaid services to consultants                                          |                          |           | 1,482,781                                                    |
| Conversion of preferred stock                                            |                          |           | 13,674                                                       |
| Acquisitions                                                             |                          | 5,885,323 | 30,666,878                                                   |
| Issuance of common stock to pay dividends                                |                          |           | 213,000                                                      |
| Financial advisor services in conjunction with financings                |                          | 924,017   | 3,477,571                                                    |
| Underwriter commissions in conjunction with financings                   |                          | 766,784   | 766,784                                                      |

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|                                                        |         |           |
|--------------------------------------------------------|---------|-----------|
| Acquisition of treasury stock in settlement of a claim |         | 34,737    |
| Cancellation of treasury stock                         |         | (34,737)  |
| Assumptions of liabilities in acquisitions             | 295,899 | 1,531,806 |

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**Table of Contents****Mast Therapeutics, Inc. and Subsidiaries**

(A Development Stage Enterprise)

**Notes to Consolidated Financial Statements****December 31, 2012**

|                                                                                              | Years ended December 31, |         | Inception                                       |
|----------------------------------------------------------------------------------------------|--------------------------|---------|-------------------------------------------------|
|                                                                                              | 2012                     | 2011    | (June 12, 1996)<br>through<br>December 31, 2012 |
| Fair value of contingent liabilities, net of contingent assets, recorded at acquisition date |                          | 784,419 | 784,419                                         |
| Acquisition of license agreement for long-term debt                                          |                          |         | 161,180                                         |
| Unrealized (gain)/loss on short-term investments                                             | (104)                    | 142     | 38                                              |
| Cashless exercise of warrants                                                                |                          |         | 4,312                                           |
| Dividends accrued                                                                            |                          |         | 621,040                                         |
| Trade asset converted to available-for-sale asset                                            |                          |         | 108,000                                         |
| Dividends extinguished                                                                       |                          |         | 408,240                                         |
| Trade payable converted to note payable                                                      |                          |         | 83,948                                          |
| Issuance of warrants for return of common stock                                              |                          |         | 50,852                                          |
| Detachable warrants issued with notes payable                                                |                          |         | 450,000                                         |
| Cumulative preferred stock dividends                                                         |                          |         | 13,502,403                                      |

**Recent Accounting Pronouncements**

In February 2013, the Financial Accounting Standards Board ( FASB ) issued ASU No. 2013-02, *Reporting of Amounts Reclassified Out of Accumulated Other Comprehensive Income* ( ASU 2013-02 ). This standard requires companies to provide information about the amounts reclassified out of accumulated other comprehensive income by component. In addition, companies are required to present, either on the face of the statement where net income is presented or in the accompanying notes, significant amounts reclassified out of accumulated other comprehensive income by the respective line items of net income, but only if the amount reclassified is required to be reclassified to net income in its entirety in the same reporting period. For amounts that are not required to be reclassified in their entirety to net income, companies are required to cross-reference to other disclosures that provide additional detail on those amounts. ASU 2013-02 is effective prospectively for reporting periods beginning after December 15, 2012. We do not believe that the adoption of this standard will have an impact on our consolidated financial position, results of operations or cash flows.

In July 2012, the FASB issued ASU No. 2012-02, *Intangibles – Goodwill and Other (Topic 350): Testing Indefinite-Lived Intangible Assets for Impairment* ( ASU 2012-02 ). Similar to the approach to annual goodwill impairment testing set forth in ASU 2011-08, *Intangibles – Goodwill and Other (Topic 350): Testing Goodwill for Impairment*, which FASB issued in September 2011, ASU 2012-02 is intended to reduce the cost and complexity of annual indefinite-lived intangible assets impairment testing by providing companies the option of performing a qualitative assessment to determine whether further impairment testing is necessary. Under the amendments in ASU 2012-02, an entity may first assess qualitative factors to determine whether the existence of events or circumstances leads to a determination that it is more likely than not (that is, a likelihood of more than 50%) that an indefinite-lived intangible asset is impaired (that is, that its fair value is less than its carrying value). If, after performing such qualitative assessment, an entity concludes that it is not more likely than not that an indefinite-lived intangible asset is impaired, the entity is not required to take further action to test for impairment. However, if the entity concludes otherwise, it must perform the quantitative impairment test in accordance with ASC Topic 350. An entity also has the option to bypass the qualitative assessment and perform only the quantitative impairment test. An entity that chooses to bypass the qualitative assessment in any period may choose to first perform the qualitative assessment in any subsequent period. The amendments in ASU 2012-02 are effective for annual and interim impairment tests performed for fiscal years beginning after September 15, 2012. Early adoption was permitted if an entity's financial statements for the most recent annual or interim period had not been issued. We elected to early adopt ASU No. 2012-02 and utilized this revised standard for our annual impairment testing, which was performed as of September 30, 2012.

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**Mast Therapeutics, Inc. and Subsidiaries**

(A Development Stage Enterprise)

**Notes to Consolidated Financial Statements**

**December 31, 2012**

In December 2011, FASB issued ASU 2011-11, *Balance Sheet (Topic 210): Disclosures about Offsetting Assets and Liabilities* ( ASU 2011-11 ). ASU 2011-11 requires companies to provide new disclosures about offsetting and related arrangements for financial instruments and derivatives. The provisions of ASU 2011-11 are effective for annual reporting periods beginning on or after January 1, 2013, and are required to be applied retrospectively. We do not believe that the adoption of this standard will have an impact on our consolidated financial position, results of operations or cash flows.

In June 2011, FASB issued ASU No. 2011-05, *Comprehensive Income (Topic 220): Presentation of Comprehensive Income* ( ASU 2011-05 ). The issuance of ASU 2011-05 is intended to improve the comparability, consistency and transparency of financial reporting and to increase the prominence of items reported in other comprehensive income. The guidance in ASU 2011-05 supersedes the presentation options in ASC Topic 220 and facilitates convergence of U.S. GAAP and International Financial Reporting Standards by eliminating the option to present components of other comprehensive income as part of the statement of changes in stockholders' equity and requiring that all non-owner changes in stockholders' equity be presented either in a single continuous statement of comprehensive income or in two separate but consecutive statements. In December 2011, FASB issued ASU No. 2011-12, *Comprehensive Income (Topic 820): Deferral of the Effective Date for Amendments to the Presentation of Reclassifications of Items Out of Accumulated Other Comprehensive Income in ASU No. 2011-05*, which defers the ASU 2011-05 requirement to present reclassification adjustments for each component of accumulated other comprehensive income in both net income and other comprehensive income on the face of the financial statements. ASU 2011-05 was effective for interim periods and years beginning after December 15, 2011. We adopted ASU 2011-05, as modified by ASU 2011-12, in the first quarter of 2012 by presenting a single continuous statement of operations and comprehensive income/(loss).

**3. Acquisition of SynthRx**

On February 12, 2011, we entered into an agreement and plan of merger (the *Merger Agreement* ) to acquire SynthRx, Inc., a privately-held Delaware corporation, in exchange for shares of our common stock as described below. The transaction was completed on April 8, 2011 and SynthRx became a wholly-owned subsidiary of Mast Therapeutics. As consideration for the transaction, all shares of SynthRx common stock outstanding immediately prior to the effective time of the merger were cancelled and automatically converted into the right to receive shares of our common stock, in the aggregate, as follows:

- (i) 862,078 shares of our common stock, which were issued on April 8, 2011 (the *Fully Vested Shares* ) and represent 1,000,000 shares less 137,922 shares that were deducted as a result of certain expenses of SynthRx;
- (ii) up to 1,938,773 shares of our common stock (the *Subject to Vesting Shares*, and together with the *Fully Vested Shares*, the *Closing Shares* ), which were issued on April 8, 2011 subject to various repurchase rights by us that were triggered based on the timing and circumstances of achievement of the *First Milestone* (defined below);
- (iii) up to 1,000,000 shares of our common stock (the *First Milestone Shares* ) issuable upon achievement of the *First Milestone*;
- (iv) 3,839,400 shares of our common stock (the *Second Milestone Shares* ) issuable upon achievement of the *Second Milestone* (defined below); and
- (v) 8,638,650 shares of our common stock (the *Third Milestone Shares*, and together with the *First Milestone Shares* and the *Second Milestone Shares*, the *Milestone Shares* ) issuable upon achievement of the *Third Milestone* (defined below).

The *First Milestone* was defined in the *Merger Agreement* as the dosing of the first patient in a phase 3 clinical study carried out pursuant to a protocol that is mutually agreed to by SynthRx and Mast





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Therapeutics; provided, however, that the number of evaluable patients planned to target statistical significance with a p value of 0.01 in the primary endpoint shall not exceed 250 unless otherwise mutually agreed (the First Protocol ). If the U.S. Food and Drug Administration ( FDA ) indicates that a single phase 3 clinical study will not be adequate to support approval of a new drug application covering the use of purified poloxamer 188 for the treatment of sickle cell crisis in children (the 188 NDA ), First Milestone shall mean the dosing of the first patient in a phase 3 clinical study carried out pursuant to a protocol that (a) is mutually agreed to by SynthRx and Mast Therapeutics as such and (b) describes a phase 3 clinical study that the FDA has indicated may be sufficient, with the phase 3 clinical study described in the First Protocol, to support approval of the 188 NDA. We consider the dosing of the first patient in the EPIC study, our phase 3 study of MST-188 in sickle cell disease, to be the First Milestone.

The Subject to Vesting Shares were issued subject to a repurchase option that provided us the right to repurchase up to approximately 75% of the Subject to Vesting Shares, or 1,454,079 shares, for \$0.001 per share based on the timing of achievement of the First Milestone and whether and the extent to which the number of evaluable patients planned to target statistical significance with a p value of 0.01 in the primary endpoint exceeds 250 patients, unless otherwise agreed. On December 13, 2012, based upon the timing of and planned number of patients in the EPIC study, we exercised our repurchase option in full and purchased all 1,454,079 shares from the former SynthRx stockholders for an aggregate purchase price of \$1,454.

Under the Merger Agreement, the number of shares issuable upon achievement of the First Milestone is subject to reduction by up to 75%, or 750,000 shares, based on the timing of achievement of the First Milestone and whether and the extent to which the number of evaluable patients planned to target statistical significance with a p value of 0.01 in the primary endpoint exceeds 250 patients, unless otherwise agreed. The EPIC study was not initiated on or prior to December 31, 2012.

The Second Milestone means the FDA's acceptance of the 188 NDA for review, and the Third Milestone means the approval by the FDA of the 188 NDA. Although issuance of the Second Milestone Shares and the Third Milestone Shares is contingent upon achievement of the Second Milestone and Third Milestone, respectively, the number of shares issuable upon achievement of each of those milestones is fixed.

Based on the estimated fair value of the Closing Shares and the Milestone Shares as of April 8, 2011, the acquisition date, the total purchase price was approximately \$6.7 million. The estimated fair value of the Subject to Vesting Shares was based upon estimates regarding the probability and timing of achievement of the First Milestone and number of subjects in the clinical study related to the First Milestone. The estimated fair value of the Milestone Shares was based upon estimates regarding the probability of achievement for each milestone, date of achievement for each milestone, market price per share of our common stock, and, for the First Milestone Shares only, the number of shares to be issued upon achievement.

The elements of the total purchase price of the acquisition were as follows:

| <b>Event</b>                                      | <b>Shares Issued /<br/>Issuable</b> | <b>Probability<br/>Weighted<br/>Fair Value</b> |
|---------------------------------------------------|-------------------------------------|------------------------------------------------|
| Initial consideration (Fully Vested Shares)       | 862,078                             | \$ 2,017,263                                   |
| Initial consideration (Subject to Vesting Shares) | 1,938,773                           | 2,103,375(1)                                   |
| First Milestone dosing of first patient           | 1,000,000                           | 1,084,900                                      |
| Second Milestone NDA acceptance                   | 3,839,400                           | 733,403                                        |
| Third Milestone FDA approval                      | 8,638,650                           | 730,801                                        |

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|       |            |              |
|-------|------------|--------------|
| Total | 16,278,901 | \$ 6,669,742 |
|-------|------------|--------------|

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(1) This amount is net of the probability-weighted fair value of the Subject to Vesting Shares that we estimated, as of the acquisition date, ultimately may be repurchased by us (\$300,481).

The transaction was accounted for as a business combination using the acquisition method of accounting. This method requires, among other things, that assets acquired and liabilities assumed in a business combination be recognized at their fair values as of the acquisition date and that IPR&D be recorded at fair value on the balance sheet. As of December 31, 2011, we had finalized our accounting for the transaction. The following table summarizes the estimated fair values of the net tangible and intangible assets acquired and liabilities assumed at the acquisition date, with the excess being recorded to goodwill:

|                                     |                     |
|-------------------------------------|---------------------|
| Net tangible assets acquired        | \$ 18,513           |
| Net tangible liabilities assumed    | (295,899)           |
| Acquired intangibles:               |                     |
| In-process research and development | 6,549,000           |
| Goodwill                            | 3,006,883           |
| Deferred income tax liability       | (2,608,755)         |
| <b>Total purchase price</b>         | <b>\$ 6,669,742</b> |

**Acquired In-Process Research and Development**

Our acquired IPR&D was the estimated fair value as of the acquisition date of MST-188, which was SynthRx's lead product candidate. We determined that the estimated fair value of the MST-188 program was \$6.5 million as of the acquisition date using the Multi-Period Excess Earnings Method, or MPEEM, which is a form of the income approach. Under the MPEEM, the fair value of an intangible asset is equal to the present value of the asset's incremental after-tax cash flows (excess earnings) remaining after deducting the market rates of return on the estimated value of contributory assets (contributory charge) over its remaining useful life.

To calculate fair value of the MST-188 program under the MPEEM, we used probability-weighted cash flows discounted at a rate considered appropriate given the significant inherent risks associated with drug development by development-stage companies. Cash flows were calculated based on estimated projections of revenues and expenses related to MST-188 in sickle cell disease and then reduced by a contributory charge on requisite assets employed. Contributory assets included debt-free working capital, net fixed assets and assembled workforce. Rates of return on the contributory assets were based on rates used for comparable market participants. Cash flows were assumed to extend through the market exclusivity period estimated to be provided by orphan drug designation. The resultant cash flows were then discounted to present value using a weighted-average cost of equity capital for companies with profiles substantially similar to that of SynthRx, which we believe represents the rate that market participants would use to value the assets. We compensated for the phase of development of this program by probability-adjusting our estimation of the expected future cash flows. The projected cash flows were based on significant assumptions, such as the time and resources needed to complete the development and approval of MST-188 in sickle cell disease, estimates of revenue and operating profit related to the program considering its stage of development, the life of the potential commercialized product and associated risks, including the inherent difficulties and uncertainties in drug development, such as obtaining marketing approval from the FDA and other regulatory agencies, and risks related to the viability of and potential alternative treatments in any future target markets.

We test our acquired IPR&D for impairment annually and between annual tests if we become aware of an event or a change in circumstances that would indicate the carrying value may be impaired. We perform our annual indefinite-lived intangible assets impairment testing as of September 30 of each year. As of September 30, 2012, no impairment was noted.



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***Goodwill***

A value of \$3.0 million, representing the difference between the total purchase price and the aggregate fair values of tangible and intangible assets acquired, less liabilities assumed, was recorded as goodwill. We acquired SynthRx to expand our product pipeline, enter into new therapeutic areas and address unmet market needs. These are among the factors that contributed to a purchase price for the SynthRx acquisition that resulted in the recognition of goodwill.

We test our goodwill for impairment annually and between annual tests if we become aware of an event or a change in circumstances that would indicate the carrying value may be impaired. We perform our annual goodwill impairment testing as of September 30 of each year. As of September 30, 2012, no impairment was noted.

For the quarter ended December 31, 2012, we determined that the persistently low trading price of our common stock, even after announcement of our phase 3 clinical development plans for MST-188 in sickle cell disease, may be an indicator of impairment and we performed an impairment test as of December 31, 2012. We test for goodwill impairment at the entity level because we operate on the basis of a single reporting unit. We proceeded directly to the Step 1 of the two-step quantitative test, comparing our carrying value, including goodwill and acquired IPR&D, to estimated fair value. Estimated fair value of the entity included market values for our cash, cash equivalents and short-term investments, as well as the estimated fair value of acquired IPR&D. We calculated the estimated fair value of acquired IPR&D by using the MPEEM. As described above in this Note 3, that method requires us to make long-term projections of revenues and expenses related to development and commercialization of MST-188 in sickle cell disease and assumptions regarding the rate of return on contributory assets, the weighted average cost of capital and the probability adjustment factor for estimated future after-tax cash flows. Through Step 1 of the impairment test, we concluded that, as of December 31, 2012, the fair value of the entity was substantially greater than its carrying value, and, therefore, goodwill was not considered impaired. We estimated fair value based on assumptions that we believe to be reasonable but that are highly judgmental due in part to the inherent unpredictability of drug development, particularly by a development-stage company. We will continue to monitor various potential impairment indicators and will perform another interim impairment analysis if we become aware of an event or a change in circumstances that would indicate the carrying value may be impaired.

***Deferred Income Tax Liability***

The \$2.6 million recorded for deferred income tax liability resulting from the acquisition reflects the tax impact of the difference between the book basis and tax basis of acquired IPR&D. Such deferred tax liability cannot be used to offset deferred tax assets when analyzing our end of year valuation allowance as the acquired IPR&D is considered to have an indefinite life until we complete or abandon development of MST-188.

***Contingent Asset and Contingent Liability***

The number of Subject to Vesting Shares subject to repurchase by us (1,454,079 shares) were and the Milestone Shares are contingent consideration because our repurchase rights with respect to those Subject to Vesting Shares were and our obligation to issue the Milestone Shares are contingent on future events. In order to determine the classification of the fair value of the Milestone Shares as a liability or equity, we reviewed ASC Topic 815-40, *Derivatives and Hedging - Contracts in Entity's Own Equity* (ASC 815-40). ASC 815-40 requires that contingent consideration arrangements that include potential net cash settlements or variable provisions should be classified as a liability. Classification as a liability requires fair value measurement initially and subsequently at each reporting date. Changes in the fair value of

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contingent consideration classified as a liability are recognized in earnings until the contingent consideration arrangement is settled. Classification as equity requires fair value measurement initially and there are no subsequent re-measurements. Settlement of equity-classified contingent consideration is accounted for within equity.

The probability-weighted fair values of the Second Milestone Shares and the Third Milestone Shares were recorded as equity as there is no net cash settlement provision and the number of shares that ultimately may be issued upon achievement of each of those milestones is fixed.

The probability-weighted fair value of the First Milestone Shares was recorded as a liability as there was variability with respect to the number of shares that ultimately may be issued (from 250,000 to 1,000,000 shares) based on the circumstances of achievement of the First Milestone, as described above. We remeasure this contingent liability as of the last day of each fiscal quarter until the arrangement is settled. Upon achievement of the First Milestone, the contingent liability will be remeasured, any change in its fair value as of that settlement date will be recognized in earnings as a transaction-related expense, and the contingent liability will be eliminated. The fair value of the issued First Milestone Shares will be recorded as equity. As of December 31, 2012, based on the timing of and planned number of patients in the EPIC study, the number of shares issuable is 250,000 shares.

As with the First Milestone Shares, due to the variability in to the number of Subject to Vesting Shares that could be repurchased, we recorded a contingent asset equal to the probability-weighted fair value of the Subject to Vesting Shares that we estimated may be repurchased by us and remeasured the fair value of this contingent asset as of the last day of each fiscal quarter until the arrangement was settled. This contingent asset was settled on December 13, 2012 by our exercise in full of our repurchase option and purchase of 1,454,079 shares from the former SynthRx stockholders for \$0.001 per share. We recognized the increase in fair value of the contingent asset at the settlement date relative to December 31, 2011 in earnings as a transaction-related expense and recorded the fair value of the 1,454,079 shares as of the settlement date as an adjustment to equity.

The remeasurement of the contingent asset at December 13, 2012 and the contingent liability at December 31, 2012 resulted in a net \$0.1 million reduction to transaction-related expenses for the year ended December 31, 2012.

***Pro Forma Information***

The following unaudited pro forma information presents the condensed consolidated results of operations of Mast Therapeutics and SynthRx as if the acquisition had occurred on January 1, 2010:

|                                       | <b>Year ended</b>        |
|---------------------------------------|--------------------------|
|                                       | <b>December 31, 2011</b> |
| Revenues                              | \$                       |
| Loss from operations                  | (13,795,615)             |
| Net loss applicable to common stock   | (13,658,635)             |
| Net loss per share, basic and diluted | (0.47)                   |

The pro forma condensed consolidated financial information includes the following adjustments directly attributable to the acquisition:

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|                              | <b>Year ended</b>        |
|------------------------------|--------------------------|
|                              | <b>December 31, 2011</b> |
| Transaction-related expenses | \$ 58,887                |

The pro forma information is not necessarily indicative of what the results of operations actually would have been had the acquisition been completed on the date indicated. In addition, it does not purport to project the future operating results of the combined entity. The pro forma condensed consolidated financial information is presented for illustrative purposes only.

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The operations of SynthRx were fully integrated into our operations as of the closing of the acquisition. Accordingly, we do not present SynthRx's expenses separately.

**4. Short-term Investments**

At December 31, 2012, the fair value of our short-term investments was \$14,010,962. The cost basis of such investments was \$14,011,000 and unrealized losses were \$38.

**5. Fair Value of Financial Instruments**

Our short-term investments and our asset and liability for contingent consideration are carried at fair value. The fair value of financial assets and liabilities is measured under a framework that establishes levels which are defined as follows: Level 1 fair value is determined from observable, quoted prices in active markets for identical assets or liabilities. Level 2 fair value is determined from quoted prices in active markets for similar assets or liabilities, quoted prices in markets that are not active for identical or similar items, or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the asset or liability. Level 3 fair value is determined using the entity's own assumptions about the inputs that market participants would use in pricing an asset or liability.

The fair values at December 31, 2012 and 2011 of our short-term investments and our contingent asset and liability related to the SynthRx acquisition are summarized in the following tables:

|                        | <b>December 31, 2012</b>    |                                     |                  |                  |
|------------------------|-----------------------------|-------------------------------------|------------------|------------------|
|                        | <b>Total<br/>Fair Value</b> | <b>Fair Value Determined Under:</b> |                  |                  |
|                        |                             | <b>(Level 1)</b>                    | <b>(Level 2)</b> | <b>(Level 3)</b> |
| Short-term investments | \$ 14,010,962               | \$                                  | \$ 14,010,962    | \$               |
| Contingent asset       | \$                          | \$                                  | \$               | \$               |
| Contingent liability   | \$ (142,500)                | \$                                  | \$               | \$ (142,500)     |

|                        | <b>December 31, 2011</b>    |                                     |                  |                  |
|------------------------|-----------------------------|-------------------------------------|------------------|------------------|
|                        | <b>Total Fair<br/>Value</b> | <b>Fair Value Determined Under:</b> |                  |                  |
|                        |                             | <b>(Level 1)</b>                    | <b>(Level 2)</b> | <b>(Level 3)</b> |
| Short-term investments | \$ 7,133,697                | \$                                  | \$ 7,133,697     | \$               |
| Contingent asset       | \$ 815,011                  | \$                                  | \$               | \$ 815,011       |
| Contingent liability   | \$ (140,125)                | \$                                  | \$               | \$ (140,125)     |

In 2011, our short-term investments were classified as Level 1 assets. In 2012, we reassessed their classification and determined that Level 2 classification was more appropriate. The table for December 31, 2011 above reflects this change.

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A reconciliation of the contingent asset and contingent liability that are measured and recorded at fair value on a recurring basis using significant unobservable inputs (Level 3) in the year ended December 31, 2012 is as follows:

|                                                                                                                              | Year ended December 31, 2012 |                      |
|------------------------------------------------------------------------------------------------------------------------------|------------------------------|----------------------|
|                                                                                                                              | Contingent Asset             | Contingent Liability |
| Beginning balance                                                                                                            | \$ 815,011                   | \$ (140,125)         |
| Settlements                                                                                                                  | (886,988)                    |                      |
| Total net unrealized gains (losses) included in earnings                                                                     | 71,977                       | (2,375)              |
| Total net unrealized gains (losses) included in other comprehensive income                                                   |                              |                      |
| Transfers into level 3 (gross)                                                                                               |                              |                      |
| Transfers out of level 3 (gross)                                                                                             |                              |                      |
| Ending balance                                                                                                               | \$                           | \$ (142,500)         |
| Change in unrealized gains or losses for the period included in earnings for assets or liabilities held at December 31, 2012 | \$                           | \$ (2,375)           |

As discussed in Note 2, the fair values of the contingent asset and contingent liability are based on significant estimates and assumptions of management. At each measurement date until the contingent arrangements are settled, we determine the fair values of the contingent asset and contingent liability based on the market price of our common stock on the measurement date and our estimates of the probability of achievement of the First Milestone and assumptions regarding the circumstances under which it may be achieved. As discussed in Notes 2 and 3, on December 13, 2012, the contingent asset was eliminated, or settled, by our exercise in full of our repurchase option and purchase of an aggregate of 1,454,079 of the Subject to Vesting Shares from the former SynthRx stockholders for \$0.001 per share.

The increase in fair value of the contingent asset at December 13, 2012 compared to December 31, 2011 was due to the higher market price of our common stock at December 13, 2012 (\$0.61 per share) compared to December 30, 2011 (\$0.59 per share), which was the last trading day of 2011, and updated estimates regarding the increased probability and circumstances of achievement of the First Milestone. The increase in fair value of the contingent liability at December 31, 2012 compared to December 31, 2011 was due to updated estimates regarding the probability and circumstances of achievement of the First Milestone, offset by the slight decrease in the market price of our common stock at December 31, 2012 (\$0.57 per share) relative to December 30, 2011 (\$0.59 per share).

The following inputs were used in the calculation of the contingent liability at December 31, 2012:

|                                                                                    | Contingent Liability |
|------------------------------------------------------------------------------------|----------------------|
| Number of shares to be issued                                                      | 250,000              |
| Market price of our common stock at December 31, 2012                              | \$ 0.57              |
| Probability of achievement of the First Milestone (significant unobservable input) | 100%                 |

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**Notes to Consolidated Financial Statements****December 31, 2012****6. Property and Equipment**

Property and equipment at December 31, 2012 and 2011 were as follows:

|                                                | <b>Useful Lives</b> | <b>2012</b>       | <b>2011</b>       |
|------------------------------------------------|---------------------|-------------------|-------------------|
| Office furniture, computer and lab equipment   | 3 -5 years          | \$ 421,494        | \$ 280,839        |
| Computer software                              | 3 years             | 62,509            | 63,016            |
| Leasehold improvements                         | 1 year              | 34,900            | 34,900            |
| Equipment in progress                          | n/a                 |                   | 359,897           |
|                                                |                     | 518,903           | 738,652           |
| Less accumulated depreciation and amortization |                     | (320,545)         | (274,187)         |
| <b>Property and equipment, net</b>             |                     | <b>\$ 198,358</b> | <b>\$ 464,465</b> |

Equipment in progress at December 31, 2011 relates to equipment purchased by us for use by a third party vendor in the manufacturing of ANX-514. This equipment was put into service in 2012.

Depreciation and amortization expense was \$90,047 and \$37,570 for the years ended December 31, 2012 and 2011, respectively.

In connection with our determination in 2012 to discontinue independent development of ANX-514, we assessed the classification and recoverability, at the end of each fiscal quarter, of certain equipment held and used in research and development-related manufacturing of ANX-514, which is classified in the table above as lab equipment. The original cost of the equipment was \$0.6 million. We determined, based on an independent appraisal, that the carrying amount of the equipment exceeded its estimated fair value and was not recoverable. For the year ended December 31, 2012, we recorded an impairment loss of \$0.4 million, which was the difference between the carrying amount and estimated fair value at December 31, 2012, as a research and development expense in our consolidated statement of operations and comprehensive income/(loss). The equipment was not classified separately as held for sale because the criteria for that classification, as set forth in ASC Topic 360-10, *Property, Plant and Equipment - Overall*, were not met as of December 31, 2012.

**7. Accrued Liabilities**

Accrued liabilities at December 31, 2012 and 2011 were as follows:

|                                      | <b>2012</b>         | <b>2011</b>         |
|--------------------------------------|---------------------|---------------------|
| Accrued contracts and study expenses | \$ 1,203,808        | \$ 880,608          |
| Other accrued liabilities            | 80,168              | 239,808             |
| <b>Accrued liabilities</b>           | <b>\$ 1,283,976</b> | <b>\$ 1,120,416</b> |

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Accrued contracts and study expenses at December 31, 2012 include a \$0.4 million accrual related to the discontinuation of ANX-514 manufacturing activities. This accrual reflects the entire amount of the contract manufacturer's payment demand, which amount is in dispute. We are unable to predict the outcome of the dispute as of December 31, 2012. The accrual will be adjusted through research and development expense in our consolidated statement of operations and comprehensive income/(loss) in the period that the dispute is settled.

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**Notes to Consolidated Financial Statements****December 31, 2012****8. Capital Stock and Warrants*****Common Stock and Warrant Registered Direct Equity Financing***

In January 2011, we completed a registered direct equity financing involving the issuance of units consisting of 8,184,556 shares of our common stock, 5-year warrants to purchase up to an aggregate of 2,046,139 shares of our common stock and 1-year warrants to purchase up to an aggregate of 2,046,139 shares of our common stock. The gross proceeds of this financing were \$22.5 million, and we received \$21.0 million in net proceeds after deducting the fees and expenses of our placement agent and our other offering expenses. The 1-year warrants expired unexercised in January 2012. We may receive up to \$5.6 million of additional proceeds from the exercise of the 5-year warrants. The exercise price of the warrants is \$2.75 per share. Subject to certain beneficial ownership limitations, the 5-year warrants are exercisable any time on or before January 11, 2016.

***Common Stock and Warrant Underwritten Public Offering***

In November 2011, we completed an underwritten public offering of 21,250,000 shares of our common stock and warrants to purchase up to 10,625,000 additional shares of our common stock. These securities were offered and sold to the public in multiples of a fixed combination consisting of one share of our common stock and a warrant to purchase up to 0.5 of a share of our common stock. The gross proceeds from this financing were \$17.0 million, and we received \$15.6 million in net proceeds after deducting the underwriting commissions and our other offering expenses. We may receive up to \$11.7 million of additional proceeds from the exercise of the warrants issued to investors in this financing. The exercise price of the warrants is \$1.10 per share. Subject to certain beneficial ownership limitations, the warrants are exercisable at any time on or before November 16, 2016.

We also issued warrants to purchase up to 1,062,500 shares of our common stock at an exercise price of \$1.00 per share to the underwriter of the offering and its designees as additional underwriting compensation. These compensation warrants are exercisable at any time on or before April 1, 2015.

***Warrants***

During 2011, warrants were issued to investors in conjunction with the registered direct equity financing and underwritten public offering in January 2011 and November 2011, respectively. In addition, warrants were issued to the placement agent and the underwriter for these financings and its designees. See details of the equity financings above.

At December 31, 2012, outstanding warrants to purchase shares of common stock are as follows:

| <b>Warrants</b> | <b>Exercise Price</b> | <b>Expiration Date</b> |
|-----------------|-----------------------|------------------------|
| 99,696          | \$ 11.9125            | June 2014              |
| 144,000         | \$ 5.8750             | October 2014           |
| 19,007          | \$ 4.4750             | July 2014              |
| 14,183          | \$ 4.0625             | August 2014            |
| 36,071          | \$ 3.7500             | June 2014              |
| 216,000         | \$ 3.6700             | October 2014           |
| 1,816,608       | \$ 3.6500             | May 2015               |
| 409,228         | \$ 3.4400             | April 2015             |
| 2,046,139       | \$ 2.7500             | January 2016           |

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|            |    |        |               |
|------------|----|--------|---------------|
| 1,062,500  | \$ | 1.0000 | April 2015    |
| 10,625,000 | \$ | 1.1000 | November 2016 |
| 16,488,432 |    |        |               |

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**Notes to Consolidated Financial Statements****December 31, 2012****9. Equity Incentive Plans**

At December 31, 2012, our equity-based incentive plans consisted of the 2005 Equity Incentive Plan (the 2005 Plan), the 2005 Employee Stock Purchase Plan (the Purchase Plan), the 2008 Omnibus Incentive Plan (the Original 2008 Plan) and the Amended and Restated 2008 Omnibus Incentive Plan (the Amended and Restated 2008 Plan), which are described below. The share-based compensation expense from all stock options granted that has been charged to our consolidated statements of operations and comprehensive income/(loss) in the years ended December 31, 2012 and 2011 was comprised of the following:

|                                             | <b>Years Ended December 31,</b> |             |
|---------------------------------------------|---------------------------------|-------------|
|                                             | <b>2012</b>                     | <b>2011</b> |
| Selling, general and administrative expense | \$ 1,381,554                    | \$ 888,592  |
| Research and development expense            | 77,776                          | (22,540)    |
| Share-based compensation expense            | \$ 1,459,330                    | \$ 866,052  |

***2005 Equity Incentive Plan, 2008 Omnibus Incentive Plan and Amended and Restated 2008 Omnibus Incentive Plan***

Our equity-based incentive plans, which are stockholder-approved, are intended to encourage ownership of shares of common stock by our directors, officers, employees, consultants and advisors and to provide additional incentive for them to promote the success of our business through the grant of share-based awards. Each of the 2005 Plan, the Original 2008 Plan and the Amended and Restated 2008 Plan provide for the grant of incentive and non-statutory stock options as well as share appreciation rights, restricted shares, restricted share units, performance units, shares and other share-based awards. Following approval of the Original 2008 Plan by our stockholders in May 2008, no awards have been or will be granted under the 2005 Plan, and, following approval of the Amended and Restated 2008 Plan by our stockholders in June 2011, no awards have been or will be granted under the Original 2008 Plan. Share-based awards are subject to terms and conditions established by our board of directors or the compensation committee of our board of directors.

As of December 31, 2012, the maximum aggregate number of shares of our common stock available for grant under the Amended and Restated 2008 Plan were 1,220,307 shares and, as discussed above, no shares were available for grant under the 2005 Plan or the Original 2008 Plan. Shares of common stock that are subject to awards granted under the Amended and Restated 2008 Plan shall be counted against the shares available for issuance under this plan as one share for each share subject to a stock option or stock appreciation right and as 1.5 shares for each share subject to an award other than a stock option or a stock appreciation right. If any shares of common stock subject to an award under the Amended and Restated 2008 Plan, the Original 2008 Plan or the 2005 Plan are forfeited, expire or are settled for cash pursuant to the terms of an award, the shares subject to the award may be used again for awards under the Amended and Restated 2008 Plan to the extent of the forfeiture, expiration or settlement. The shares of common stock will be added back as one share for every share of common stock if the shares were subject to a stock option or stock appreciation right granted under the Amended and Restated 2008 Plan, the Original 2008 Plan or the 2005 Plan, and as 1.5 shares for every share of common stock if the shares were subject to an award other than a stock option or stock appreciation right. However, the following shares of common stock will not be added to the shares available for issuance under the Amended and Restated 2008 Plan: (i) shares tendered by a participant or withheld by us in payment of the purchase price of a stock option, (ii) shares tendered by a participant or withheld by us to satisfy any tax withholding obligation with respect to an award, (iii) shares subject to a stock appreciation right that are not issued in connection with the stock settlement of the stock appreciation right on exercise thereof, and (iv) shares reacquired by us on the open market or otherwise using cash proceeds from the exercise of stock options. Shares of common stock under awards made in substitution or exchange for awards previously granted, or the right or obligation to





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make future awards, in each case by a company acquired by us, or with which we combine, will not reduce the number of shares available for issuance under the Amended and Restated 2008 Plan. In addition, if a company acquired by us, or with which we combine, has shares available under a pre-existing plan approved by its stockholders and not adopted in contemplation of such acquisition or combination, the shares available for issuance under such plan (adjusted to reflect the exchange or valuation ratio or other adjustment used in the acquisition or combination) may be used for awards under the Amended and Restated 2008 Plan and will not reduce the number of shares of common stock available for issuance under the Amended and Restated 2008 Plan; provided, however that awards using such available shares shall not be made after the date awards or grants could have been made under the pre-existing plan, absent the acquisition or combination, and shall only be made to individuals who were not our employees or directors prior to the acquisition or combination.

Under the Amended and Restated 2008 Plan, the purchase price of shares of common stock covered by a stock option cannot be less than 100% of the fair market value of the common stock on the date the stock option is granted. Fair market value of the common stock is generally equal to the closing price for the common stock on the principal securities exchange on which the common stock is traded on the date the stock option is granted (or if there was no closing price on that date, on the last preceding date on which a closing price is reported). Stock option awards generally have ten-year contractual terms and vest over four years based on continuous service; however, each of the 2005 Plan, the Original 2008 Plan and the Amended and Restated 2008 Plan allow for other vesting periods.

We canceled options for 236,729 and 31,004 shares of common stock in the years ended December 31, 2012 and 2011, respectively, held by employees and non-employee directors whose service to our company terminated during those respective periods. The shares underlying such options were returned to the Amended and Restated 2008 Plan and became available for re-issuance pursuant to the terms described above.

During the years ended December 31, 2012 and 2011, all awards granted under the 2008 Plan and the Amended and Restated 2008 Plan were stock options. A summary of all of our option activity as of December 31, 2012 and 2011 and of changes in options outstanding under the plans during the year ended December 31, 2012 are as follows:

|                                                  | Shares    | Weighted-<br>Average<br>Exercise<br>Price | Weighted-<br>Average<br>Remaining<br>Contractual<br>Years | Aggregate<br>Intrinsic<br>Value |
|--------------------------------------------------|-----------|-------------------------------------------|-----------------------------------------------------------|---------------------------------|
| Outstanding at December 31, 2011                 | 2,892,132 | \$ 2.83                                   |                                                           |                                 |
| Granted                                          | 933,996   | \$ 0.68                                   |                                                           |                                 |
| Exercised                                        | (3,656)   | \$ 0.60                                   |                                                           |                                 |
| Cancelled/forfeited/expired                      | (236,729) | \$ 2.25                                   |                                                           |                                 |
| Outstanding at December 31, 2012                 | 3,585,743 | \$ 2.31                                   | 8.67                                                      | \$                              |
| Options exercisable at December 31, 2012         | 988,743   | \$ 4.59                                   | 7.92                                                      | \$                              |
| Vested and expected to vest at December 31, 2012 | 3,461,169 | \$ 2.35                                   | 8.66                                                      | \$                              |

The weighted-average grant-date fair value of options granted during the years ended December 31, 2012 and 2011 was \$0.61 and \$1.52, respectively. As of December 31, 2012, there was approximately \$2.6 million of unamortized compensation cost related to unvested stock option

awards, which is expected to be recognized over a weighted-average period of approximately 2.84 years.

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Our determination of fair value is affected by our stock price as well as a number of assumptions that require judgment. The fair value of each option award is estimated on the date of grant using the Black-Scholes option-valuation model. The assumptions used in the Black-Scholes option-valuation model for option grants to employees and non-employee directors during the years ended December 31, 2012 and 2011 are as follows:

|                          | Years Ended December 31, |           |          |            |
|--------------------------|--------------------------|-----------|----------|------------|
|                          | 2012                     |           | 2011     |            |
| Risk-free interest rate  | 0.6                      | 0.8%      | 1.1      | 2.4%       |
| Dividend yield           | 0.0%                     |           | 0.0%     |            |
| Expected volatility      | 131-139%                 |           | 125-131% |            |
| Expected term (in years) | 5.2                      | 6.1 years | 5        | 6.25 years |
| Forfeiture rate          | 4%                       |           | 4%       |            |

The risk-free interest rate assumption is based on the U.S. Treasury yield for a period consistent with the expected term of the option in effect at the time of the grant. We have not paid any dividends on common stock since our inception and do not anticipate paying dividends on our common stock in the foreseeable future. The expected option term is computed using the simplified method as permitted under the provisions of Staff Accounting Bulletin (SAB) 107. SAB 107's guidance was extended indefinitely by SAB 110. The expected volatility is based on the historical volatility of our common stock based on the daily closing prices. The forfeiture rate is based on the expected forfeiture rate for our unvested stock options, which is based in large part on our historical forfeiture rates, but also on assumptions believed to be reasonable under the circumstances.

In accordance with ASC 718, *Compensation - Stock Compensation*, share-based compensation expense associated with the non-employee director options is included with employee share-based compensation expense.

**Employee Stock Purchase Plan**

The Purchase Plan was approved by our stockholders in 2005; however, we have not implemented the Purchase Plan. The Purchase Plan, if implemented, allows all eligible employees to purchase shares of common stock at 85% of the lower of the fair market value on the first or the last day of each offering period. Employees may authorize us to withhold up to 15% of their compensation during any offering period, subject to certain limitations. As of December 31, 2012, a maximum of 246,945 shares of common stock would have been issuable under the Purchase Plan had it been in effect as of that date. This maximum number is subject to an annual automatic increase on January 1 of each year (whether or not we have implemented the Purchase Plan) equal to the lesser of (i) 1% of the number of outstanding shares of common stock on such day, (ii) 30,000 or (iii) such other amount as our board of directors may specify.

**10. Commitments****Operating Leases**

We are obligated under operating leases for office space and equipment. In December 2010, we entered into a lease for office space in San Diego, California to serve as our headquarters, effective January 1, 2011. The average rent for this space was approximately \$16,900 per month. In June 2011, we amended our lease to add an additional suite in the same building. This amendment extended the term of our lease through January 31, 2013 and increased our rent to approximately \$23,800 per month through January 31, 2012 and approximately \$24,500 per month from February 1, 2012 through January 31, 2013. In October 2012, we amended our lease again to extend the lease for 24 months, expiring on

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January 31, 2015. This amendment increased our average rent to \$21,614 per month for the first year and to \$26,677 per month for the second year. We have an option to extend the lease through October 31, 2018, subject to the landlord's

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right to require for its own use all or a portion of the leased premises during such period, which right must be exercised by delivering notice to us within 10 days after receipt of our notice to exercise our option to extend the lease.

From August 2011 through August 2012, we subleased a portion of our space to another company and received rental income of \$3,100 per month, which offset our rent expense.

We lease copiers under leases that expire in 2015.

Rent expense was approximately \$262,000 and \$206,000 during the years ended December 31, 2012 and 2011, respectively.

Future rental commitments under all operating leases are as follows:

| <b>Year Ending December 31,</b> |            |
|---------------------------------|------------|
| 2013                            | \$ 264,285 |
| 2014                            | 327,638    |
| 2015                            | 27,365     |
| 2016                            |            |
| 2017                            |            |
| Total                           | \$ 619,288 |

**11. Income Taxes**

Due to our historical net loss position, and as we have recorded a full valuation allowance against net deferred tax assets, there is no provision or benefit for income taxes recorded for the years ended December 31, 2012 and 2011.

The income tax benefit is different from that which would be obtained by applying the statutory Federal income tax rate of 34% to income before income tax expense. The items causing this difference for the years ended December 31, 2012 and 2011 are as follows:

|                                              | <b>December 31,</b> |                |
|----------------------------------------------|---------------------|----------------|
|                                              | <b>2012</b>         | <b>2011</b>    |
| Income tax benefit at federal statutory rate | \$ (5,289,000)      | \$ (4,508,000) |
| R & D credit                                 | 279,000             | (155,000)      |
| Stock options                                | 205,000             | 386,000        |
| Acquisition costs                            |                     | 374,000        |
| Contingent asset/liability                   |                     | (496,000)      |
| Net operating loss adjustment                | 14,433,000          |                |
| Other                                        | (20,000)            | 3,000          |
| Change in federal valuation allowance        | (9,608,000)         | 4,396,000      |

|       |    |    |
|-------|----|----|
| Total | \$ | \$ |
|-------|----|----|

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Deferred income taxes reflect the net tax effect of temporary differences between the carrying amount of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes. Significant components of deferred tax assets and liabilities at December 31, 2012 and 2011 are as follows:

|                                                                          | <b>December 31,</b>   |                       |
|--------------------------------------------------------------------------|-----------------------|-----------------------|
|                                                                          | <b>2012</b>           | <b>2011</b>           |
| <b>Deferred tax assets:</b>                                              |                       |                       |
| Accrued expenses                                                         | \$ 118,722            | \$ 96,979             |
| Stock options expense under ASC 718                                      | 1,362,557             | 1,021,202             |
| Net operating loss carry forwards                                        | 6,098,125             | 17,787,621            |
| Income tax credit carry forwards                                         | 137,123               | 445,296               |
| Property and equipment                                                   | 141,755               | 8,959                 |
| Intangibles                                                              | 2,288,961             | 2,212,680             |
| Other                                                                    | 20,110                | 10,490                |
| <b>Total deferred tax assets</b>                                         | <b>10,167,353</b>     | <b>21,583,227</b>     |
| Less: valuation allowance                                                | (10,167,353)          | (21,583,227)          |
| <b>Total deferred tax assets, net of valuation allowance</b>             | <b>\$</b>             | <b>\$</b>             |
| <b>Deferred tax liabilities:</b>                                         |                       |                       |
| Acquired intangibles                                                     | (2,608,755)           | (2,608,755)           |
| <b>Total deferred tax assets/liabilities, net of valuation allowance</b> | <b>\$ (2,608,755)</b> | <b>\$ (2,608,755)</b> |

We have established a full valuation allowance against our net deferred tax assets due to uncertainty surrounding the realization of such assets. Management has determined it is more likely than not that the deferred tax assets are not realizable due to our historical loss position.

As a result of our acquisition of SynthRx during 2011, we recorded a deferred tax liability. This deferred tax liability reflects the tax impact of the difference between the book basis and tax basis of acquired IPR&D that has not yet reached feasibility. Such deferred tax liability cannot be used to offset deferred tax assets when analyzing our end of year valuation allowance as the acquired IPR&D is considered to have an indefinite life until we complete or abandon development of MST-188. The deferred tax liability was recorded as an offset to goodwill recorded as part of the acquisition.

Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, or IRC, limit our ability to use net operating loss carry forwards and R&D tax credit carry forwards ( tax attribute carry forwards ) to offset future taxable income if we experience a cumulative change in ownership of more than 50% within a three-year testing period. During the first quarter of 2012, we completed a formal study and determined ownership changes within the meaning of IRC Section 382 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 these ownership changes, upon application of limitations prescribed by IRC Section 382, we may be ineligible to utilize any of the tax attribute carry forwards we had accumulated as of November 11, 2011 to offset future taxable income, and we adjusted our tax attribute carry forwards accordingly by \$14.4 million. Through further analysis in the future we may determine that a small amount of these tax attribute carry forwards can be utilized. As the tax attribute carry forwards accumulated as of November 11, 2011 were fully offset by a valuation allowance, a corresponding reduction in the Company's valuation allowance has also been recorded, resulting in

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no income tax impact.

As of December 31, 2012, we had federal and California net operating loss carry forwards of \$15.5 million and \$14.4 million, respectively. These tax loss carry forwards begin to expire in 2031 if unused. As of December 31, 2012, we also had federal and California R&D tax credit carry forwards of \$21,000 and \$176,000, respectively. The federal R&D tax credits will begin to expire in 2031. The California R&D tax credits do not expire. Our federal R&D tax credit carry forward as of December 31, 2012 does not include any federal R&D tax credit available for 2012 because the U.S. Congress did not renew the federal R&D tax credit until January 2, 2013 after it expired on December 31, 2011.

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In accordance with authoritative guidance, the impact of an uncertain income tax position on the income tax return must be recognized at the largest amount that is more-likely-than-not to be sustained upon audit by the relevant taxing authority. An uncertain income tax position will not be recognized if it has less than a 50% likelihood of being sustained. As of December 31, 2012, we continue to have no unrecognized tax benefits. There are no unrecognized tax benefits included on the balance sheet that would, if recognized, impact the effective tax rate. We do not anticipate there will be a significant change in unrecognized tax benefits within the next 12 months.

Our policy is to recognize interest and/or penalties related to income tax matters in income tax expense. Because we have generated net operating losses since inception, no tax liability, penalties or interest has been recognized for balance sheet or income statement purposes as of and for the years ended December 31, 2012 and 2011.

We are subject to income taxation in the U.S. and the state of California. All of our tax years are subject to examination by the tax authorities due to the carry forward of unutilized net operating losses and R&D tax credits.

**12. 401(k) Plan**

We have a defined contribution savings plan pursuant to Section 401(k) of the IRC. The plan is for the benefit of all qualifying employees and permits voluntary contributions by employees up to 100% of eligible compensation, subject to the Internal Revenue Service ( IRS ) imposed maximum limits. The terms of the plan require us to make matching contributions equal to 100% of employee contributions up to 6% of eligible compensation, limited by the IRS-imposed maximum. We incurred total expenses of \$163,171 and \$87,790 in employer matching contributions in 2012 and 2011, respectively.

**13. Segment Information**

We operate our business on the basis of a single reportable segment, which is the business of developing therapies for serious or life-threatening diseases. We evaluate our Company as a single operating segment. The majority of our operating activities and work performed by our employees are currently conducted from a single location in the U.S. We recognized no revenues in 2012 and 2011.

**14. Summary of Quarterly Financial Data (unaudited)**

The following is a summary of the unaudited quarterly results of operations for the years ended December 31, 2012 and 2011:

**Quarterly statements of operations data**

| 2012 (unaudited):                   | Quarters Ended |             |              |             |
|-------------------------------------|----------------|-------------|--------------|-------------|
|                                     | March 31       | June 30     | September 30 | December 31 |
| Revenue                             | \$             | \$          | \$           | \$          |
| Loss from operations                | (4,171,496)    | (4,221,558) | (3,218,499)  | (4,016,449) |
| Net loss                            | (4,152,517)    | (4,211,163) | (3,199,053)  | (3,996,756) |
| Net loss applicable to common stock | (4,152,517)    | (4,211,163) | (3,199,053)  | (3,996,756) |

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|                                                                                 |            |            |            |            |
|---------------------------------------------------------------------------------|------------|------------|------------|------------|
| Basic and diluted net loss per share                                            | \$ (0.09)  | \$ (0.09)  | \$ (0.07)  | \$ (0.08)  |
| Basic and diluted weighted average number of shares of common stock outstanding | 47,715,709 | 47,715,709 | 47,715,709 | 47,418,669 |

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| 2011 (unaudited):                                                               | Quarters Ended |             |              |             |
|---------------------------------------------------------------------------------|----------------|-------------|--------------|-------------|
|                                                                                 | March 31       | June 30     | September 30 | December 31 |
| Revenue                                                                         | \$             | \$          | \$           | \$          |
| Loss from operations                                                            | (2,994,415)    | (4,406,465) | (3,552,845)  | (2,443,160) |
| Net loss                                                                        | (2,956,439)    | (4,392,190) | (3,539,326)  | (2,371,976) |
| Net loss applicable to common stock                                             | (2,956,439)    | (4,392,190) | (3,539,326)  | (2,371,976) |
| Basic and diluted net loss per share                                            | \$ (0.13)      | \$ (0.17)   | \$ (0.13)    | \$ (0.06)   |
| Basic and diluted weighted average number of shares of common stock outstanding | 22,755,463     | 26,250,259  | 26,465,709   | 37,090,709  |

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**Condensed Consolidated Balance Sheets**

(Unaudited)

|                                                                                                                                                                         | March 31,<br>2013    | December 31,<br>2012 |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------|----------------------|
| <b>Assets</b>                                                                                                                                                           |                      |                      |
| Current assets:                                                                                                                                                         |                      |                      |
| Cash and cash equivalents                                                                                                                                               | \$ 21,409,923        | \$ 22,500,440        |
| Short-term investments                                                                                                                                                  | 10,597,514           | 14,010,962           |
| Interest and other receivables                                                                                                                                          | 10,831               | 15,689               |
| Prepaid expenses                                                                                                                                                        | 511,216              | 646,571              |
| <b>Total current assets</b>                                                                                                                                             | <b>32,529,484</b>    | <b>37,173,662</b>    |
| Property and equipment, net                                                                                                                                             | 198,706              | 198,358              |
| In-process research and development                                                                                                                                     | 6,549,000            | 6,549,000            |
| Goodwill                                                                                                                                                                | 3,006,883            | 3,006,883            |
| Other assets                                                                                                                                                            | 43,912               | 43,912               |
| <b>Total assets</b>                                                                                                                                                     | <b>\$ 42,327,985</b> | <b>\$ 46,971,815</b> |
| <b>Liabilities and Stockholders Equity</b>                                                                                                                              |                      |                      |
| Current liabilities:                                                                                                                                                    |                      |                      |
| Accounts payable                                                                                                                                                        | \$ 575,766           | \$ 698,838           |
| Accrued liabilities                                                                                                                                                     | 1,863,764            | 1,283,976            |
| Accrued compensation and payroll taxes                                                                                                                                  | 555,065              | 445,352              |
| Contingent liability                                                                                                                                                    | 170,000              | 142,500              |
| <b>Total current liabilities</b>                                                                                                                                        | <b>3,164,595</b>     | <b>2,570,666</b>     |
| Deferred income tax liability                                                                                                                                           | 2,608,755            | 2,608,755            |
| <b>Total liabilities</b>                                                                                                                                                | <b>5,773,350</b>     | <b>5,179,421</b>     |
| Stockholders equity:                                                                                                                                                    |                      |                      |
| Common stock, \$0.001 par value; 500,000,000 shares authorized; 47,719,365 shares issued and 46,265,286 shares outstanding at both March 31, 2013 and December 31, 2012 | 47,720               | 47,720               |
| Treasury stock, at cost 1,454,079 shares at both March 31, 2013 and December 31, 2012                                                                                   | (1,454)              | (1,454)              |
| Additional paid-in capital                                                                                                                                              | 227,048,419          | 226,696,863          |
| Accumulated other comprehensive loss                                                                                                                                    | (10,642)             | (2,194)              |
| Deficit accumulated during the development stage                                                                                                                        | (190,529,408)        | (184,948,541)        |
| <b>Total stockholders equity</b>                                                                                                                                        | <b>36,554,635</b>    | <b>41,792,394</b>    |
| <b>Total liabilities and stockholders equity</b>                                                                                                                        | <b>\$ 42,327,985</b> | <b>\$ 46,971,815</b> |

See accompanying notes to unaudited condensed consolidated financial statements.



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(A Development Stage Enterprise)

**Condensed Consolidated Statements of Operations and Comprehensive Income/(Loss)**

(Unaudited)

|                                                                 | Three months ended March 31, |                | Inception<br>(June 12, 1996)<br>through<br>March 31, 2013 |
|-----------------------------------------------------------------|------------------------------|----------------|-----------------------------------------------------------|
|                                                                 | 2013                         | 2012           |                                                           |
| Revenues:                                                       |                              |                |                                                           |
| Net sales                                                       | \$                           | \$             | \$ 174,830                                                |
| Licensing revenue                                               |                              |                | 1,300,000                                                 |
| Grant revenue                                                   |                              |                | 618,692                                                   |
| Total net revenues                                              |                              |                | 2,093,522                                                 |
| Cost of goods sold                                              |                              |                | 51,094                                                    |
| Gross margin                                                    |                              |                | 2,042,428                                                 |
| Operating expenses:                                             |                              |                |                                                           |
| Research and development                                        | 3,442,912                    | 2,210,454      | 89,500,368                                                |
| Selling, general and administrative                             | 2,112,706                    | 2,045,238      | 69,779,418                                                |
| Transaction-related expenses                                    | 27,500                       | (114,388)      | 699,152                                                   |
| Depreciation and amortization                                   | 9,795                        | 30,192         | 11,035,030                                                |
| Write-off of in-process research and development                |                              |                | 10,422,130                                                |
| Goodwill impairment                                             |                              |                | 5,702,130                                                 |
| Equity in loss of investee                                      |                              |                | 178,936                                                   |
| Total operating expenses                                        | 5,592,913                    | 4,171,496      | 187,317,164                                               |
| Loss from operations                                            | (5,592,913)                  | (4,171,496)    | (185,274,736)                                             |
| Reduction of fair value of warrants                             |                              |                | (12,239,688)                                              |
| Interest income                                                 | 14,416                       | 18,668         | 4,846,624                                                 |
| Interest expense                                                |                              |                | (191,729)                                                 |
| Other income/(expense), net                                     | (2,370)                      | 311            | 127,335                                                   |
| Loss before cumulative effect of change in accounting principle | (5,580,867)                  | (4,152,517)    | (192,732,194)                                             |
| Cumulative effect of change in accounting principle             |                              |                | (25,821)                                                  |
| Net loss                                                        | (5,580,867)                  | (4,152,517)    | (192,758,015)                                             |
| Preferred stock dividends                                       |                              |                | (621,240)                                                 |
| Deemed dividends on preferred stock                             |                              |                | (10,506,683)                                              |
| Net loss applicable to common stock                             | \$ (5,580,867)               | \$ (4,152,517) | \$ (203,885,938)                                          |
| Net loss per common share basic and diluted                     | \$ (0.12)                    | \$ (0.09)      |                                                           |
| Weighted average shares outstanding basic and diluted           | 46,265,286                   | 47,715,709     |                                                           |

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Comprehensive Income/(Loss):

|                                    |                |                |                  |
|------------------------------------|----------------|----------------|------------------|
| Net loss                           | \$ (5,580,867) | \$ (4,152,517) | \$ (192,758,015) |
| Other comprehensive gains/(losses) | (8,448)        | 139            | (10,642)         |
| Comprehensive net loss             | \$ (5,589,315) | \$ (4,152,378) | \$ (192,768,657) |

See accompanying notes to unaudited condensed consolidated financial statements.

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**Condensed Consolidated Statements of Cash Flows**

(Unaudited)

|                                                                                                | Three months ended March 31, |                | Inception<br>(June 12, 1996) |
|------------------------------------------------------------------------------------------------|------------------------------|----------------|------------------------------|
|                                                                                                | 2013                         | 2012           | through<br>March 31, 2013    |
| <b>Cash flows from operating activities:</b>                                                   |                              |                |                              |
| Net loss                                                                                       | \$ (5,580,867)               | \$ (4,152,517) | \$ (192,758,015)             |
| Adjustments to reconcile net loss to net cash used in operating activities:                    |                              |                |                              |
| Depreciation and amortization                                                                  | 9,795                        | 30,192         | 10,585,032                   |
| Loss on disposals of equipment                                                                 |                              | 4,503          | 61,315                       |
| Loss on fair value of warrants                                                                 |                              |                | 12,239,688                   |
| Loss/(gain) on change in fair value of contingent consideration                                | 27,500                       | (114,388)      | (1,501,407)                  |
| Amortization of debt discount                                                                  |                              |                | 450,000                      |
| Forgiveness of employee receivable                                                             |                              |                | 30,036                       |
| Impairment loss write-off of goodwill                                                          |                              |                | 5,702,130                    |
| Share-based compensation expense related to employee stock options and restricted stock issued | 351,556                      | 377,505        | 11,900,880                   |
| Expenses related to options issued to non-employees                                            |                              |                | 204,664                      |
| Expenses paid by issuance of common stock                                                      |                              |                | 1,341,372                    |
| Expenses paid by issuance of warrants                                                          |                              |                | 573,357                      |
| Expenses paid by issuance of preferred stock                                                   |                              |                | 142,501                      |
| Expenses related to stock warrants issued                                                      |                              |                | 612,000                      |
| Equity in loss of investee                                                                     |                              |                | 178,936                      |
| In-process research and development                                                            |                              |                | 10,422,130                   |
| Write-off of license agreement                                                                 |                              |                | 152,866                      |
| Impairment of equipment                                                                        |                              |                | 510,739                      |
| Cumulative effect of change in accounting principle                                            |                              |                | 25,821                       |
| Amortization of premium / (accretion of discount) on investments in securities                 |                              | 10,710         | (1,571,502)                  |
| Changes in assets and liabilities, net of effect of acquisitions:                              |                              |                |                              |
| Decrease/(increase) in prepaid expenses and other assets                                       | 140,213                      | (81,820)       | (815,646)                    |
| Increase/(decrease) in accounts payable and accrued liabilities                                | 563,439                      | (533,492)      | 2,858,617                    |
| Net cash used in operating activities                                                          | (4,488,364)                  | (4,459,307)    | (138,654,486)                |
| <b>Cash flows from investing activities:</b>                                                   |                              |                |                              |
| Purchases of certificates of deposit                                                           | (2,988,000)                  | (5,312,000)    | (26,971,179)                 |
| Proceeds from maturities of certificates of deposit                                            | 6,393,000                    | 1,440,000      | 16,084,330                   |
| Proceeds from sale of certificate of deposit                                                   |                              |                | 248,000                      |
| Purchases of other short-term investments                                                      |                              |                | (111,183,884)                |
| Proceeds from maturities and sales of other short-term investments                             |                              |                | 112,788,378                  |
| Purchases of property and equipment                                                            | (4,725)                      | (187,363)      | (1,741,529)                  |
| Proceeds from sale of property and equipment                                                   |                              |                | 66,920                       |
| Cash paid for acquisitions, net of cash acquired                                               |                              |                | 32,395                       |
| Payment on obligation under license agreement                                                  |                              |                | (106,250)                    |
| Issuance of note receivable related party                                                      |                              |                | (35,000)                     |
| Payments on note receivable                                                                    |                              |                | 405,993                      |
| Advance to investee                                                                            |                              |                | (90,475)                     |



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|                                                                 |               |               |               |
|-----------------------------------------------------------------|---------------|---------------|---------------|
| Cash transferred in rescission of acquisition                   |               |               | (19,475)      |
| Cash received in rescission of acquisition                      |               |               | 230,000       |
| Net cash provided by/(used in) investing activities             | 3,400,275     | (4,059,363)   | (10,291,776)  |
| <b>Cash flows from financing activities:</b>                    |               |               |               |
| Proceeds from sale of common stock                              |               |               | 123,658,871   |
| Proceeds from exercise of stock options                         |               |               | 714,561       |
| Proceeds from sale or exercise of warrants                      |               |               | 14,714,258    |
| Proceeds from sale of preferred stock                           |               |               | 44,474,720    |
| Repurchase of Subject to Vesting Shares                         |               |               | (1,454)       |
| Repurchase of warrants                                          |               |               | (55,279)      |
| Payments for financing and offering costs                       |               |               | (13,897,367)  |
| Payments on notes payable and long-term debt                    |               |               | (605,909)     |
| Proceeds from issuance of notes payable and detachable warrants |               |               | 1,344,718     |
| Cash paid in lieu of fractional shares for reverse stock split  |               |               | (146)         |
| Net cash provided by financing activities                       |               |               | 170,346,973   |
| Effect of exchange rate changes on cash                         | (2,428)       |               | 9,212         |
| Net (decrease)/increase in cash and cash equivalents            | (1,090,517)   | (8,518,670)   | 21,409,923    |
| Cash and cash equivalents at beginning of period                | 22,500,440    | 43,569,947    |               |
| Cash and cash equivalents at end of period                      | \$ 21,409,923 | \$ 35,051,277 | \$ 21,409,923 |

See accompanying notes to unaudited condensed consolidated financial statements.

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**Mast Therapeutics, Inc. and Subsidiaries**

(A Development Stage Enterprise)

**Notes to Condensed Consolidated Financial Statements (Unaudited)**

**1. Basis of Presentation**

Mast Therapeutics, Inc., a Delaware corporation ( Mast Therapeutics, we or our company ), prepared the unaudited interim condensed consolidated financial statements included in this report in accordance with United States generally accepted accounting principles ( U.S. GAAP ) for interim financial information and the rules and regulations of the Securities and Exchange Commission ( SEC ) related to quarterly reports on Form 10-Q. Accordingly, they do not include all of the information and disclosures required by U.S. GAAP for annual audited financial statements and should be read in conjunction with our audited consolidated financial statements and notes thereto included in our Annual Report on Form 10-K for the year ended December 31, 2012, filed with the SEC on March 19, 2013 ( 2012 Annual Report ). The condensed consolidated balance sheet as of December 31, 2012 included in this report has been derived from the audited consolidated financial statements included in the 2012 Annual Report. In the opinion of management, these condensed consolidated financial statements include all adjustments (consisting of normal recurring adjustments) necessary for a fair statement of the financial position, results of operations and cash flows for the periods presented. The results of operations for the interim periods shown in this report are not necessarily indicative of the results that may be expected for any future period, including the full year.

We are a biopharmaceutical company focused on developing therapies for serious or life-threatening diseases. We have devoted substantially all of our resources to research and development ( R&D ), and acquisition of our product candidates. We have not yet marketed or sold any products or generated any significant revenue. Through our acquisition of SynthRx, Inc. in 2011, we acquired our Membrane Adhesion & Sealant Technology (MAST) platform, which includes proprietary poloxamer-related data and know-how derived from over two decades of clinical, nonclinical and manufacturing experience, and we are leveraging the MAST platform to develop MST-188 for diseases and conditions characterized by microcirculatory insufficiency.

In prior years, we were developing Exelbine and ANX-514, both of which are investigational oncology programs, but, beginning in 2012, we have focused our resources almost exclusively on development of MST-188.

In March 2013, we merged our wholly-owned subsidiary, Mast Therapeutics, Inc., with and into us and changed our name from ADVENTRX Pharmaceuticals, Inc. to Mast Therapeutics, Inc. The merger had no effect on our financial statements.

Certain prior year amounts have been reclassified in the condensed consolidated financial statements to conform to the current year presentation. These reclassifications were not material and had no effect on previously reported results of operations.

**2. Use of Estimates**

The preparation of financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the amounts reported in our consolidated financial statements and accompanying notes. On an ongoing basis, we evaluate our estimates, including estimates related to contingent consideration, R&D expenses and share-based compensation expenses. We base our estimates on historical experience and various other relevant assumptions we believe to be reasonable under the circumstances. Actual results may differ from these estimates.

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**3. Acquisition of SynthRx**

On February 12, 2011, we entered into an agreement and plan of merger (the *Merger Agreement*) to acquire SynthRx, Inc. (*SynthRx*), a privately-held Delaware corporation, in exchange for shares of our common stock as described below. The transaction was completed on April 8, 2011 and SynthRx became a wholly-owned subsidiary of Mast Therapeutics. As consideration for the transaction, all shares of SynthRx common stock outstanding immediately prior to the effective time of the merger were cancelled and automatically converted into the right to receive shares of our common stock, in the aggregate, as follows:

- (i) 862,078 shares of our common stock, which were issued on April 8, 2011 (the *Fully Vested Shares*) and represent 1,000,000 shares less 137,922 shares that were deducted as a result of certain expenses of SynthRx;
- (ii) up to 1,938,773 shares of our common stock (the *Subject to Vesting Shares*, and together with the *Fully Vested Shares*, the *Closing Shares*), which were issued on April 8, 2011 subject to various repurchase rights by us that were triggered based on the timing and circumstances of achievement of the *First Milestone* (defined below);
- (iii) up to 1,000,000 shares of our common stock (the *First Milestone Shares*) issuable upon achievement of the *First Milestone*;
- (iv) 3,839,400 shares of our common stock (the *Second Milestone Shares*) issuable upon achievement of the *Second Milestone* (defined below); and
- (v) 8,638,650 shares of our common stock (the *Third Milestone Shares*, and together with the *First Milestone Shares* and the *Second Milestone Shares*, the *Milestone Shares*) issuable upon achievement of the *Third Milestone* (defined below).

The *First Milestone* was defined in the *Merger Agreement* as the dosing of the first patient in a phase 3 clinical study carried out pursuant to a protocol that is mutually agreed to by SynthRx and Mast Therapeutics; provided, however, that the number of evaluable patients planned to target statistical significance with a p value of 0.01 in the primary endpoint shall not exceed 250 unless otherwise mutually agreed (the *First Protocol*). If the U.S. Food and Drug Administration (*FDA*) indicates that a single phase 3 clinical study will not be adequate to support approval of a new drug application covering the use of purified poloxamer 188 for the treatment of sickle cell crisis in children (the *188 NDA*), *First Milestone* shall mean the dosing of the first patient in a phase 3 clinical study carried out pursuant to a protocol that (a) is mutually agreed to by SynthRx and Mast Therapeutics as such and (b) describes a phase 3 clinical study that the FDA has indicated may be sufficient, with the phase 3 clinical study described in the *First Protocol*, to support approval of the *188 NDA*. We consider the dosing of the first patient in the EPIC (Evaluation of Purified 188 In Children) study, our phase 3 study of MST-188 in sickle cell disease, to be the *First Milestone*.

The *Subject to Vesting Shares* were issued subject to a repurchase option that provided us the right to repurchase up to approximately 75% of the *Subject to Vesting Shares*, or 1,454,079 shares, for \$0.001 per share based on the timing of achievement of the *First Milestone* and whether and the extent to which the number of evaluable patients planned to target statistical significance with a p value of 0.01 in the primary endpoint exceeds 250 patients, unless otherwise agreed.

Under the *Merger Agreement*, the number of shares issuable upon achievement of the *First Milestone* is subject to reduction by up to 75%, or 750,000 shares, based on the timing of achievement of the *First Milestone* and whether and the extent to which the number of evaluable patients planned to target statistical significance with a p value of 0.01 in the primary endpoint exceeds 250 patients, unless otherwise agreed.

The *Second Milestone* means the FDA's acceptance of the *188 NDA* for review, and the *Third Milestone* means the approval by the FDA of the *188 NDA*. Although issuance of the *Second Milestone Shares* and the *Third Milestone Shares* is contingent upon achievement of the *Second Milestone* and *Third Milestone*, respectively, the number of shares issuable upon achievement of each of those milestones is fixed.

Based on the estimated fair value of the *Closing Shares* and the *Milestone Shares* as of April 8, 2011, the acquisition date, the total purchase price was approximately \$6.7 million.

***Acquired In-Process Research and Development***

Our acquired IPR&D was the estimated fair value as of the acquisition date of MST-188, which was SynthRx's lead product candidate. We determined that the estimated fair value of the MST-188 program was \$6.5 million



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as of the acquisition date using the Multi-Period Excess Earnings Method, or MPEEM, which is a form of the income approach. Under the MPEEM, the fair value of an intangible asset is equal to the present value of the asset's incremental after-tax cash flows (excess earnings) remaining after deducting the market rates of return on the estimated value of contributory assets (contributory charge) over its remaining useful life.

To calculate fair value of the MST-188 program under the MPEEM, we used probability-weighted cash flows discounted at a rate considered appropriate given the significant inherent risks associated with drug development by development-stage companies. Cash flows were calculated based on estimated projections of revenues and expenses related to MST-188 in sickle cell disease and then reduced by a contributory charge on requisite assets employed. Contributory assets included debt-free working capital, net fixed assets and assembled workforce. Rates of return on the contributory assets were based on rates used for comparable market participants. Cash flows were assumed to extend through the market exclusivity period estimated to be provided by orphan drug designation. The resultant cash flows were then discounted to present value using a weighted-average cost of equity capital for companies with profiles substantially similar to that of SynthRx, which we believe represents the rate that market participants would use to value the assets. We compensated for the phase of development of this program by applying a probability factor to our estimation of the expected future cash flows. The projected cash flows were based on significant assumptions, such as the time and resources needed to complete the development and approval of MST-188 in sickle cell disease, estimates of revenue and operating profit related to the program considering its stage of development, the life of the potential commercialized product and associated risks, including the inherent difficulties and uncertainties in drug development, such as obtaining marketing approval from the FDA and other regulatory agencies, and risks related to the viability of and potential alternative treatments in any future target markets.

We test our acquired IPR&D for impairment annually (and between annual tests if we become aware of an event or a change in circumstances that would indicate the carrying amount may be impaired) in accordance with Accounting Standards Codification (ASC) Topic 350, *Intangibles Goodwill and Other* and Accounting Standards Update (ASU) No. 2012-02, *Intangibles Goodwill and Other (Topic 350): Testing Indefinite-Lived Intangible Assets for Impairment*. We perform our annual indefinite-lived intangible assets impairment testing as of September 30 of each year. As of September 30, 2012, no impairment was noted. There were no events or changes in circumstances during the three months ended March 31, 2013 that we considered indications of impairment of our acquired IPR&D.

***Goodwill***

A value of \$3.0 million, representing the difference between the total purchase price and the aggregate fair values of tangible and intangible assets acquired, less liabilities assumed, was recorded as goodwill. We acquired SynthRx to expand our product pipeline, enter into new therapeutic areas and address unmet market needs. These are among the factors that contributed to a purchase price for the SynthRx acquisition that resulted in the recognition of goodwill.

We test our goodwill for impairment annually (and between annual tests if we become aware of an event or a change in circumstances that would indicate the carrying amount may be impaired) in accordance with ASC Topic 350, *Intangibles Goodwill and Other*, and ASU No. 2011-08, *Intangibles Goodwill and Other (Topic 350): Testing Goodwill for Impairment*. We perform our annual goodwill impairment testing as of September 30 of each year. As of September 30, 2012, no impairment was noted. For the quarter ended December 31, 2012, we determined that the persistently low trading price of our common stock, even after announcement during that quarter of our phase 3 clinical development plans for MST-188 in sickle cell disease, may be an indicator of impairment of our goodwill and we performed an impairment test as of December 31, 2012. Through Step 1 of the two-step quantitative impairment test, we concluded that, as of December 31, 2012, our goodwill was not impaired. There were no events or changes in circumstances during the three months ended March 31, 2013 that we considered indications of impairment of our goodwill.

***Deferred Income Tax Liability***

The \$2.6 million recorded for deferred income tax liability resulting from the acquisition reflects the tax impact of the difference between the book basis and tax basis of acquired IPR&D. Such deferred income tax liability cannot be used to offset deferred tax assets when analyzing our end of year valuation allowance as the acquired IPR&D is considered to have an indefinite life until we complete or abandon development of MST-188.

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**Table of Contents*****Contingent Consideration***

The Milestone Shares and 1,454,079 of the Subject to Vesting Shares were considered contingent consideration at the acquisition date because our obligation to issue the Milestone Shares and our repurchase rights with respect to 1,454,079 of the Subject to Vesting Shares were contingent on future events. To determine the classification of the fair value of this contingent consideration as a liability or equity, we reviewed ASC Topic 815-40, *Derivatives and Hedging - Contracts in Entity's Own Equity* (ASC 815-40), which requires that contingent consideration arrangements that include potential net cash settlements or variable provisions be classified as a liability (or an asset, as applicable). Such classification requires a fair value measurement initially and subsequently at each reporting date. Changes in the fair value of contingent consideration classified as a liability or an asset are recognized in earnings until the contingent consideration arrangement is settled. Classification as equity requires fair value measurement initially and there are no subsequent re-measurements. Settlement of equity-classified contingent consideration is accounted for within equity.

The probability-weighted fair values of the Second Milestone Shares and the Third Milestone Shares were recorded as equity as there is no net cash settlement provision and the number of shares that ultimately may be issued upon achievement of each of those milestones is fixed. However, the probability-weighted fair value of the First Milestone Shares was recorded as a contingent liability and the probability-weighted fair value of 1,454,079 of the Subject to Vesting Shares was recorded as a contingent asset because there was variability with respect to the number of shares that we ultimately would be required to issue and repurchase, respectively, based on the circumstances of achievement of the First Milestone, as described above.

In accordance with ASC 815-40, we remeasure the contingent liability related to the First Milestone Shares as of the last day of each fiscal quarter until the arrangement is settled. The remeasurement of the contingent liability as of March 31, 2013 resulted in a \$27,500 increase to transaction-related expenses for the three-month period ended March 31, 2013. Upon achievement of the First Milestone, the contingent liability will be remeasured, any change in its fair value as of that settlement date will be recognized in earnings as a transaction-related expense, and the contingent liability will be eliminated. The fair value of First Milestone Shares we ultimately issue will be recorded as equity. As of March 31, 2013, based on the timing of and the planned number of patients in the EPIC study, we will issue 25%, or 250,000, of the First Milestone Shares.

The contingent asset related to the 1,454,079 Subject to Vesting Shares was eliminated, or settled, in December 2012 by our exercise in full of our repurchase option and purchase of the 1,454,079 shares from the former SynthRx stockholders for \$0.001 per share.

**4. Short-Term Investments**

We consider income-yielding securities that can be readily converted to cash and have original maturities of more than three months and one year or less at the date of purchase to be short-term investments. All of our short-term investments are marketable securities under the custodianship of a major financial institution and consist primarily of FDIC-insured certificates of deposit.

We account for and report our short-term investments in accordance with ASC Topic 320, *Accounting for Certain Investments in Debt and Equity Securities*. Our short-term investments are classified as available-for-sale securities and carried at fair value. Fair value for securities with short maturities and infrequent secondary market trades is typically determined by using a curve-based evaluation model that utilizes quoted prices for similar securities. The evaluation model takes into consideration the days to maturity, coupon rate and settlement date convention. Net unrealized gains or losses on these securities are included in accumulated other comprehensive loss, which is a separate component of stockholders' equity. Realized gains and realized losses are included in other income/(expense), while amortization of premiums and accretion of discounts are included in interest income. Interest and dividends on available-for-sale securities are included in interest income. Marketable securities are evaluated periodically for impairment. If we determine that a decline in market value of any investment is other than temporary, then the investment basis would be written down to fair value and the decline in value would be charged to earnings.

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At March 31, 2013, the fair value of our short-term investments was \$10,597,514. The cost basis of such investments was \$10,606,000 and our unrealized losses were \$8,486.

**5. Fair Value of Financial Instruments**

Our short-term investments and our contingent liability are carried at fair value. The fair value of financial assets and liabilities is measured under a framework that establishes levels which are defined as follows: (i) Level 1 fair value is determined from observable, quoted prices in active markets for identical assets or liabilities; (ii) Level 2 fair value is determined from quoted prices for similar items in active markets or quoted prices for identical or similar items in markets that are not active; and (iii) Level 3 fair value is determined using the entity's own assumptions about the inputs that market participants would use in pricing an asset or liability.

The fair values at March 31, 2013 of our short-term investments and our contingent liability are summarized in the following table:

|                        | Total Fair<br>Value | March 31, 2013<br>Fair Value Determined Under: |               |              |
|------------------------|---------------------|------------------------------------------------|---------------|--------------|
|                        |                     | (Level 1)                                      | (Level 2)     | (Level 3)    |
| Short-term investments | \$ 10,597,514       | \$                                             | \$ 10,597,514 | \$           |
| Contingent liability   | \$ (170,000)        | \$                                             | \$            | \$ (170,000) |

A reconciliation of the contingent liability for the three months ended March 31, 2013 is as follows:

|                                                                                                                 | Three months<br>ended March 31,<br>2013 |
|-----------------------------------------------------------------------------------------------------------------|-----------------------------------------|
| Balance at December 31, 2012                                                                                    | \$ (142,500)                            |
| Settlements                                                                                                     |                                         |
| Total net unrealized gains (losses) included in earnings                                                        | (27,500)                                |
| Total net unrealized gains (losses) included in other comprehensive income                                      |                                         |
| Transfers into level 3 (gross)                                                                                  |                                         |
| Transfers out of level 3 (gross)                                                                                |                                         |
| Balance at March 31, 2013                                                                                       | \$ (170,000)                            |
| Change in unrealized gains or losses for the period included in earnings for liabilities held at March 31, 2013 | \$ (27,500)                             |

As discussed above, the fair value of the contingent liability is measured and recorded on a recurring basis using significant unobservable inputs (Level 3). At each remeasurement date until the contingent arrangement is settled, we determine the fair value of the contingent liability based on the market price of our common stock on the measurement date and our estimate of the number of First Milestone Shares we will issue, which is based on our estimates of the probability of achievement of the First Milestone and assumptions regarding the circumstances under which it is achieved. The increase in the fair value of the contingent liability at March 31, 2013 compared to December 31, 2012 was due to an increase in the market price of our common stock at March 28, 2013 (\$0.68 per share), which was the last trading day of the quarter, relative to December 31, 2012 (\$0.57 per share).

The following inputs were used in the calculation of the contingent liability at March 31, 2013:

|                               | Contingent Liability |
|-------------------------------|----------------------|
| Number of shares to be issued | 250,000              |

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|                                                    |    |      |
|----------------------------------------------------|----|------|
| Market price of our common stock at March 28, 2013 | \$ | 0.68 |
| Probability of achievement of the First Milestone  |    | 100% |

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**Table of Contents****6. Property and Equipment**

Property and equipment are stated at cost, less accumulated depreciation. Property and equipment are depreciated using the straight-line method over the estimated useful lives of the assets, which is generally three to five years. Leasehold improvements are amortized over the economic life of the asset or the lease term, whichever is shorter.

In connection with our determination in 2012 to discontinue independent development of ANX-514, we assessed the classification and recoverability, at the end of each fiscal quarter, of certain equipment held and used in research and development-related manufacturing of ANX-514 (the ANX-514 equipment) by our contract manufacturer. The original cost of the ANX-514 equipment was \$0.6 million. We determined, based on an independent appraisal, that the carrying amount of the ANX-514 equipment exceeded its estimated fair value and was not recoverable. For the year ended December 31, 2012, we recorded an impairment loss of \$0.4 million, which was the difference between the carrying amount and estimated fair value at December 31, 2012, as a research and development expense in our consolidated statement of operations and comprehensive income/(loss). The ANX-514 equipment was not classified separately as held for sale as of December 31, 2012 because the criteria for that classification, as set forth in ASC Topic 360-10, *Property, Plant and Equipment - Overall*, were not met.

In April 2013, in connection with reaching an agreement with our contract manufacturer regarding final payment for ANX-514 research-related manufacturing activities, we agreed to assign ownership of the ANX-514 equipment to the contract manufacturer. Accordingly, we disposed of the ANX-514 equipment in April 2013.

**7. Accrued Liabilities**

Accrued liabilities at March 31, 2013 and December 31, 2012 were as follows:

|                                      | March 31,<br>2013   | December 31,<br>2012 |
|--------------------------------------|---------------------|----------------------|
| Accrued contracts and study expenses | \$ 1,651,214        | \$ 1,203,808         |
| Other accrued liabilities            | 212,550             | 80,168               |
| <b>Total accrued liabilities</b>     | <b>\$ 1,863,764</b> | <b>\$ 1,283,976</b>  |

Our accrued liabilities as of December 31, 2012 included a \$0.4 million accrual that reflected the entire amount of our ANX-514 contract manufacturer's payment demand for ANX-514 manufacturing activities, which amount was in dispute. As discussed above in Note 6, in April 2013, we reached an agreement with the contract manufacturer regarding the amount in dispute. As a result of our agreement, we reduced our accrued liabilities as of March 31, 2013 by \$0.2 million.

**8. Share-Based Compensation Expense**

Estimated share-based compensation expense related to equity awards granted to our employees and non-employee directors for the three months ended March 31, 2013 and 2012 was as follows:

|                                             | Three months ended March 31, |                   |
|---------------------------------------------|------------------------------|-------------------|
|                                             | 2013                         | 2012              |
| Selling, general and administrative expense | \$ 314,428                   | \$ 351,804        |
| Research and development expense            | 37,128                       | 25,701            |
| <b>Share-based compensation expense</b>     | <b>\$ 351,556</b>            | <b>\$ 377,505</b> |

There were no employee or non-employee director stock options exercised during the three months ended March 31, 2013 or 2012. During the three months ended March 31, 2013, we granted stock options to acquire an aggregate of 484,300 shares of our common stock to our employees, with an estimated weighted-average grant date fair value of \$0.53 per share. During the three months ended March 31, 2012, we granted no

stock

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options to our employees or non-employee directors. At March 31, 2013, total unrecognized estimated compensation cost related to non-vested employee and non-employee director share-based awards granted prior to that date was \$2.6 million, which is expected to be recognized over a weighted-average period of 2.8 years.

**9. Net Loss Per Common Share**

Basic and diluted net loss per common share was calculated by dividing the net loss applicable to common stock for the three months ended March 31, 2013 and 2012 by the weighted-average number of common shares outstanding during those periods, respectively, without consideration for outstanding common stock equivalents because their effect would have been anti-dilutive. Common stock equivalents are included in the calculation of diluted earnings per common share only if their effect is dilutive. For the periods presented, our outstanding common stock equivalents consisted of options and warrants to purchase shares of our common stock. The weighted-average number of those common stock equivalents outstanding for each of the periods presented is set forth in the table below:

|          | <b>Three months ended March 31,</b> |             |
|----------|-------------------------------------|-------------|
|          | <b>2013</b>                         | <b>2012</b> |
| Options  | 4,058,751                           | 2,892,132   |
| Warrants | 16,488,432                          | 17,824,080  |

**10. Recent Accounting Pronouncements**

In February 2013, the Financial Accounting Standards Board ( FASB ) issued ASU No. 2013-02, *Reporting of Amounts Reclassified Out of Accumulated Other Comprehensive Income* ( ASU 2013-02 ). This standard requires companies to provide information about the amounts reclassified out of accumulated other comprehensive income by component. In addition, companies are required to present, either on the face of the statement where net income is presented or in the accompanying notes, significant amounts reclassified out of accumulated other comprehensive income by the respective line items of net income, but only if the amount reclassified is required to be reclassified to net income in its entirety in the same reporting period. For amounts that are not required to be reclassified in their entirety to net income, companies are required to cross-reference to other disclosures that provide additional detail on those amounts. ASU 2013-02 is effective prospectively for reporting periods beginning after December 15, 2012. We adopted this guidance effective January 1, 2013. Our adoption of this standard did not have a significant impact on our consolidated financial position, results of operations and other comprehensive income/loss or cash flows. There were no realized gains or losses on marketable securities in the three months ended March 31, 2013.

In December 2011, FASB issued ASU 2011-11, *Balance Sheet (Topic 210): Disclosures about Offsetting Assets and Liabilities* ( ASU 2011-11 ). ASU 2011-11 requires companies to provide new disclosures about offsetting and related arrangements for financial instruments and derivatives. The provisions of ASU 2011-11 are effective for annual reporting periods beginning on or after January 1, 2013, and must be applied retrospectively. We adopted this guidance effective January 1, 2013. The adoption of this standard did not have a significant impact on our consolidated financial position, results of operations and other comprehensive income/loss or cash flows.

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Non-cash investing and financing transactions presented separately from the condensed consolidated statements of cash flows for the three months ended March 31, 2013 and 2012 and for the period from inception (June 12, 1996) through March 31, 2013 are as follows:

|                                                                                              | Three months ended March 31, |      | Inception<br>(June 12, 1996)<br>through<br>March 31, 2013 |
|----------------------------------------------------------------------------------------------|------------------------------|------|-----------------------------------------------------------|
|                                                                                              | 2013                         | 2012 |                                                           |
| Supplemental disclosures of cash flow information:                                           |                              |      |                                                           |
| Interest paid                                                                                | \$                           | \$   | \$ 180,719                                                |
| Supplemental disclosures of non-cash investing and financing activities:                     |                              |      |                                                           |
| Issuance of warrants, common stock and preferred stock for:                                  |                              |      |                                                           |
| Conversion of notes payable and accrued interest                                             |                              |      | 1,213,988                                                 |
| Prepaid services to consultants                                                              |                              |      | 1,482,781                                                 |
| Conversion of preferred stock                                                                |                              |      | 13,674                                                    |
| Acquisitions                                                                                 |                              |      | 30,666,878                                                |
| Issuance of common stock to pay dividends                                                    |                              |      | 213,000                                                   |
| Financial advisor services in conjunction with financings                                    |                              |      | 3,477,571                                                 |
| Underwriter commissions in conjunction with financings                                       |                              |      | 766,784                                                   |
| Acquisition of treasury stock in settlement of a claim                                       |                              |      | 34,737                                                    |
| Cancellation of treasury stock                                                               |                              |      | (34,737)                                                  |
| Assumptions of liabilities in acquisitions                                                   |                              |      | 1,531,806                                                 |
| Fair value of contingent liabilities, net of contingent assets, recorded at acquisition date |                              |      | 784,419                                                   |
| Acquisition of license agreement for long-term debt                                          |                              |      | 161,180                                                   |
| Unrealized (loss)/gain on short-term investments                                             | (8,448)                      | 139  | (8,486)                                                   |
| Cashless exercise of warrants                                                                |                              |      | 4,312                                                     |
| Dividends accrued                                                                            |                              |      | 621,040                                                   |
| Trade asset converted to available-for-sale asset                                            |                              |      | 108,000                                                   |
| Dividends extinguished                                                                       |                              |      | 408,240                                                   |
| Trade payable converted to note payable                                                      |                              |      | 83,948                                                    |
| Issuance of warrants for return of common stock                                              |                              |      | 50,852                                                    |
| Detachable warrants issued with notes payable                                                |                              |      | 450,000                                                   |
| Cumulative preferred stock dividends                                                         |                              |      | 13,502,403                                                |

**12. Warrants**

At March 31, 2013, outstanding warrants to purchase shares of common stock are as follows:

| Warrants   | Exercise Price | Expiration Date |
|------------|----------------|-----------------|
| 99,696     | \$ 11.9125     | June 2014       |
| 144,000    | \$ 5.8750      | October 2014    |
| 19,007     | \$ 4.4750      | July 2014       |
| 14,183     | \$ 4.0625      | August 2014     |
| 36,071     | \$ 3.7500      | June 2014       |
| 216,000    | \$ 3.6700      | October 2014    |
| 1,816,608  | \$ 3.6500      | May 2015        |
| 409,228    | \$ 3.4400      | April 2015      |
| 2,046,139  | \$ 2.7500      | January 2016    |
| 1,062,500  | \$ 1.0000      | April 2015      |
| 10,625,000 | \$ 1.1000      | November 2016   |



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**Shares**  
**Mast Therapeutics, Inc.**  
**Common Stock**

**PROSPECTUS**

*Sole Book-Running Manager*

**Piper Jaffray**

*Lead Manager*

**Canaccord Genuity**

**Table of Contents****PART II - INFORMATION NOT REQUIRED IN PROSPECTUS****Item 13. Other Expenses of Issuance and Distribution.**

The following table sets forth the various expenses incurred or to be incurred in connection with the registration of the securities being registered hereby, all of which will be borne by the Company. All amounts shown are estimates except for the SEC registration fee and FINRA filing fee.

|                                   |                   |
|-----------------------------------|-------------------|
| SEC registration fee              | \$ 4,706          |
| Legal fees and expenses           | \$ 100,000        |
| Accounting fees and expenses      | \$ 55,000         |
| FINRA filing fee                  | \$ 5,000          |
| NYSE MKT Listing Application Fees | \$ 45,000         |
| Miscellaneous fees and expenses   | \$ 15,294         |
| <b>Total</b>                      | <b>\$ 225,000</b> |

**Item 14. Indemnification of Directors and Officers.**

Section 145 of the Delaware General Corporation Law authorizes a corporation to indemnify its directors and officers against liabilities arising out of actions, suits and proceedings to which they are made or threatened to be made a party by reason of the fact of their prior or current service to the corporation as a director or officer, in accordance with the provisions of Section 145, which are sufficiently broad to permit indemnification under certain circumstances for liabilities arising under the Securities Act of 1933, as amended (the Securities Act). The indemnity may cover expenses (including attorneys' fees) judgments, fines and amounts paid in settlement actually and reasonably incurred by the director or officer in connection with any such action, suit or proceeding. Section 145 permits corporations to pay expenses (including attorneys' fees) incurred by directors and officers in advance of the final disposition of such action, suit or proceeding. In addition, Section 145 provides that a corporation has the power to purchase and maintain insurance on behalf of its directors and officers against any liability asserted against them and incurred by them in their capacity as a director or officer, or arising out of their status as such, whether or not the corporation would have the power to indemnify the director or officer against such liability under Section 145.

Our amended and restated certificate of incorporation, as amended (our Certificate of Incorporation) provides that, to the fullest extent permitted by the Delaware General Corporation Law, (1) a director shall not be personally liable to us or our stockholders for monetary damages for breach of fiduciary duty as a director, and (2) we shall indemnify any director or officer made a party to an action or proceeding, whether criminal, civil, administrative or investigative, by reason of the fact of such person's current or prior service as a director or officer of the Company, any predecessor of the Company or any other enterprise per the Company's or any predecessor to the Company's request.

Our amended and restated bylaws (our Bylaws), provide that (a) we shall indemnify our directors and officers to the maximum extent and in the manner permitted by the Delaware General Corporation Law against expenses (including attorneys' fees), judgments, fines, ERISA excise taxes, settlements and other amounts actually and reasonably incurred in connection with any proceeding, whether civil, criminal, administrative or investigative, arising by reason of the fact that such person is or was an agent of the corporation, subject to certain limited exceptions, (b) we shall advance expenses incurred by any director or officer prior to the final disposition of any proceeding to which the director or officer was or is or is threatened to be made a party promptly following a request therefore, subject to certain limited exceptions, and (c) the rights conferred in our Bylaws are not exclusive.

We have entered into indemnification agreements with each of our directors and executive officers to give such directors and officers additional contractual assurances regarding the scope of the indemnification set forth in our Certificate of Incorporation and Bylaws and to provide additional procedural protections. These agreements, among other things, provide that we will indemnify our directors and executive officers for expenses (including attorneys' fees), judgments, fines, penalties and amounts paid in settlement (including all interest, assessments and other charges paid or payable in connection therewith) actually and reasonably incurred by a director or executive officer in connection with any action or proceeding to which such person was, is or is threatened to be made a party, a witness or other participant by reason of such person's services as a director or executive officer of the Company, any of the Company's subsidiaries or any other company or enterprise to which the person provides services at the Company's request, and any federal, state, local or foreign taxes imposed on the director or executive officer as a result of the actual or deemed receipt of any payments under the indemnification agreements.





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In addition, the indemnification agreements provide that, upon the request of a director or executive officer, we shall advance expenses (including attorneys' fees) to the director or officer. We intend to enter into indemnification agreements with any new directors and executive officers in the future.

We have also obtained insurance policies covering our directors and officers with respect to certain liabilities, including liabilities arising under the Securities Act.

### **Item 15. Recent Sales of Unregistered Securities.**

As partial consideration for its services as placement agent or underwriter in connection with registered offerings of our equity securities, we issued the following common stock purchase warrants to Rodman & Renshaw, LLC and its affiliated designees on the dates indicated:

on January 7, 2010, warrants to purchase an aggregate of up to 99,696 shares of our common stock at an exercise price of \$11.9125 per share, which warrants became exercisable on July 7, 2010 and may be exercised any time on or before June 3, 2014;

on January 11, 2011, warrants to purchase an aggregate of up to 409,228 shares of our common stock at an exercise price of \$3.44 per share, which warrants were exercisable upon issuance and may be exercised any time on or before April 1, 2015; and

on November 16, 2011, warrants to purchase an aggregate of up to 1,062,500 shares of our common stock at an exercise price of \$1.00 per share, which warrants were exercisable upon issuance may be exercised any time on or before April 1, 2015.

On April 8, 2011, we acquired SynthRx, Inc. and issued an aggregate of 2,800,851 shares of our common stock to the former SynthRx stockholders and U.S. Bank National Association, as escrow agent, in exchange for all of the then-outstanding shares of SynthRx's capital stock. In April 2012, pursuant to the terms of our merger agreement with SynthRx, the 200,000 shares issued to U.S. Bank National Association, as escrow agent, in April 2011 were released from escrow and registered to the former SynthRx stockholders on a pro rata basis based on each stockholder's ownership percentage of SynthRx immediately prior to the effective time of the merger. On June 4, 2013, pursuant to the terms of our merger agreement with SynthRx as a result of the achievement of a milestone set forth in the merger agreement, we issued an aggregate of 250,000 shares of our common stock to the former SynthRx stockholders on a pro rata basis based on each stockholder's ownership percentage of SynthRx immediately prior to the effective time of the merger.

The securities described above were offered and sold by us in reliance upon exemptions from the registration requirements of the Securities Act. Such securities were issued pursuant to Section 4(2) of the Securities Act, and/or Regulation D promulgated thereunder as transactions by an issuer not involving a public offering. The recipients of the securities represented their intention to acquire the securities for investment only and not with a view to or for sale in connection with any distribution thereof and appropriate legends were affixed to share certificates issued in these transactions. All recipients had adequate access to information about our company.

### **Item 16. Exhibits and Financial Statement Schedules.**

See the Exhibit Index of this Registration Statement, which follows the signature pages hereof and is incorporated herein by reference.

### **Item 17. Undertakings.**

The undersigned registrant hereby undertakes:

- (1) For purposes of determining any liability under the Securities Act of 1933, the information omitted from the form of prospectus filed as part of this registration statement in reliance upon Rule 430A and contained in a form of prospectus filed by the registrant

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pursuant to Rule 424(b)(1) or (4) or 497(h) under the Securities Act shall be deemed to be part of this registration statement as of the time it was declared effective.

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

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

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**SIGNATURES**

Pursuant to the requirements of the Securities Act of 1933, the registrant has duly caused this registration statement to be signed on its behalf by the undersigned, thereunto duly authorized in the City of San Diego, State of California.

Date: June 5, 2013

Mast Therapeutics, Inc.

By: /s/ Brian M. Culley  
 Brian M. Culley  
 Chief Executive Officer and Director

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Brian M. Culley, Patrick L. Keran and Brandi L. Roberts, and each of them acting individually, our true and lawful attorneys-in-fact and agents, with full power of substitution and resubstitution in each of them for him and in his name, place and stead, and in any and all capacities, to sign any and all amendments (including post-effective amendments) to this registration statement (or any other registration statement for the same offering that is to be effective upon filing pursuant to Rule 462(b) under the Securities Act of 1933), and to file the same, with all exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite or necessary to be done in and about the premises, as full to all intents and purposes as he might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents or any of them, or their or his substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Act of 1933, this Registration Statement has been signed by the following persons in the capacities held on the dates indicated

| Signature                                  | Title                                                                                          | Date         |
|--------------------------------------------|------------------------------------------------------------------------------------------------|--------------|
| /s/ Brian M. Culley<br>Brian M. Culley     | Chief Executive Officer and Director (Principal Executive Officer)                             | June 5, 2013 |
| /s/ Brandi L. Roberts<br>Brandi L. Roberts | Chief Financial Officer and Senior Vice President (Principal Financial and Accounting Officer) | June 5, 2013 |
| /s/ Jack Lief<br>Jack Lief                 | Chair of the Board                                                                             | June 5, 2013 |
| *<br>Ted W. Love                           | Director                                                                                       | June 5, 2013 |
| *<br>David A. Ramsay                       | Director                                                                                       | June 5, 2013 |
| *<br>Lewis J. Shuster                      | Director                                                                                       | June 5, 2013 |

\*By /s/ Brandi L. Roberts  
 Brandi L. Roberts  
 Attorney-in-fact

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**EXHIBIT INDEX**

| Exhibit    | Description                                                                                                                                                                                                                                                                           |
|------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 1.1        | Form of Underwriting Agreement                                                                                                                                                                                                                                                        |
| 2.1 (1)    | Agreement and Plan of Merger, dated April 7, 2006, among the registrant, Speed Acquisition, Inc., SD Pharmaceuticals, Inc. and certain individuals named therein (including exhibits thereto)                                                                                         |
| 2.2 (2)    | Agreement and Plan of Merger, dated February 12, 2011, by and among the registrant, SRX Acquisition Corporation, SynthRx, Inc. and, solely with respect to Sections 2 and 8, the Stockholders Agent                                                                                   |
| 3.1 (36)   | Composite Amended and Restated Certificate of Incorporation, as amended, of the registrant                                                                                                                                                                                            |
| 3.2 (4)    | Certificate of Ownership and Merger, effective as of March 11, 2013                                                                                                                                                                                                                   |
| 3.3 (4)    | Amended and Restated Bylaws of the registrant, effective as of March 11, 2013                                                                                                                                                                                                         |
| 4.1 (34)   | Form of common stock certificate of the registrant                                                                                                                                                                                                                                    |
| 5.1        | Opinion of DLA Piper LLP (US)                                                                                                                                                                                                                                                         |
| 10.1 (5)   | Form of Common Stock Purchase Warrant issued on June 12, 2009 by the registrant to the purchasers of the registrant's 0% Series A Convertible Preferred Stock and to Rodman & Renshaw, LLC and its designees                                                                          |
| 10.2 (6)   | Form of Common Stock Purchase Warrant issued on July 6, 2009 by the registrant to Rodman & Renshaw, LLC and its designees                                                                                                                                                             |
| 10.3 (7)   | Form of Common Stock Purchase Warrant issued on August 10, 2009 by the registrant to Rodman & Renshaw, LLC and its designees                                                                                                                                                          |
| 10.4 (8)   | Form of Common Stock Purchase Warrant issued on October 9, 2009 by the registrant to the purchasers of the registrant's 4.25660% Series D Convertible Preferred Stock and to Rodman & Renshaw, LLC and its designees                                                                  |
| 10.5 (9)   | Form of Common Stock Purchase Warrant issued on January 7, 2010 by the registrant to Rodman & Renshaw, LLC and its designees                                                                                                                                                          |
| 10.6 (10)  | Form of Series A and B Common Stock Purchase Warrants issued on May 6, 2010 by the registrant to the purchasers of the registrant's 2.19446320054018% Series F Convertible Preferred Stock                                                                                            |
| 10.7 (11)  | Form of [Series A/B] Common Stock Purchase Warrant issued on January 11, 2011 by the registrant to the purchasers of the registrant's common stock and to Rodman & Renshaw, LLC                                                                                                       |
| 10.8 (12)  | Warrant Agent Agreement, dated November 11, 2011, by and between the registrant and American Stock Transfer & Trust Company, including the form of Common Stock Purchase Warrant as Exhibit A                                                                                         |
| 10.9 (12)  | Form of Common Stock Purchase Warrant issued on November 16, 2011 to Rodman & Renshaw, LLC and its designees                                                                                                                                                                          |
| 10.10 (2)  | Stockholders' Voting and Transfer Restriction Agreement, dated February 12, 2011, by and among the registrant, each of the principal stockholders of SynthRx, Inc. and, solely with respect to Section 3(c), the Stockholders' Agent                                                  |
| 10.11 (13) | License Agreement, dated December 10, 2005, among SD Pharmaceuticals, Latitude Pharmaceuticals and Andrew Chen, including a certain letter, dated November 20, 2007, clarifying the scope of rights thereunder                                                                        |
| 10.12 (14) | License Agreement, dated March 25, 2009, among the registrant, SD Pharmaceuticals, Inc. and Shin Poong Pharmaceutical Co., Ltd.                                                                                                                                                       |
| 10.13 (2)  | License Agreement, dated June 8, 2004, between SynthRx, Inc. and CytRx Corporation, as amended by that certain Letter Agreement Re: Amendment to License Agreement, dated August 3, 2006, and that certain Agreement and Amendment No. 2 to License Agreement, dated December 1, 2010 |

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| Exhibit     | Description                                                                                                                                                                                                                                                   |
|-------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 10.14# (15) | 2005 Equity Incentive Plan                                                                                                                                                                                                                                    |
| 10.15# (16) | Form of Stock Option Agreement under the 2005 Equity Incentive Plan                                                                                                                                                                                           |
| 10.16# (13) | Form of Stock Option Agreement under the 2005 Equity Incentive Plan (for director option grants beginning in 2008)                                                                                                                                            |
| 10.17# (17) | Form of Stock Option Agreement under the 2005 Equity Incentive Plan (for option grants to employees approved in March 2008)                                                                                                                                   |
| 10.18# (3)  | Form of Restricted Share Award Agreement under the 2005 Equity Incentive Plan                                                                                                                                                                                 |
| 10.19# (18) | 2008 Omnibus Incentive Plan                                                                                                                                                                                                                                   |
| 10.20# (19) | Form of Notice of Grant of Restricted Stock Units under the 2008 Omnibus Incentive Plan (for grants to employees in January 2009)                                                                                                                             |
| 10.21# (19) | Form of Restricted Stock Units Agreement under the 2008 Omnibus Incentive Plan                                                                                                                                                                                |
| 10.22# (20) | Form of Non-Statutory Stock Option Grant Agreement (for directors) under the 2008 Omnibus Incentive Plan                                                                                                                                                      |
| 10.23# (20) | Form of Non-Statutory/Incentive Stock Option Grant Agreement (for consultants/employees) under the 2008 Omnibus Incentive Plan                                                                                                                                |
| 10.24# (21) | Form of Incentive Stock Option Grant Agreement under the 2008 Omnibus Incentive Plan (for grant to Brian M. Culley in July 2009)                                                                                                                              |
| 10.25# (21) | Form of Incentive Stock Option Grant Agreement under the 2008 Omnibus Incentive Plan (for grant to Patrick L. Keran in July 2009)                                                                                                                             |
| 10.26# (22) | Form of letter, dated January 20, 2010, modifying options granted to Brian M. Culley and Patrick L. Keran in July 2009                                                                                                                                        |
| 10.27# (22) | Form of Incentive Stock Option Grant Agreement under the 2008 Omnibus Incentive Plan (for grant to Brian M. Culley in January 2010)                                                                                                                           |
| 10.28# (22) | Form of Incentive Stock Option Grant Agreement under the 2008 Omnibus Incentive Plan (for grant to Patrick L. Keran in January 2010)                                                                                                                          |
| 10.29# (23) | Incentive Stock Option Grant Agreement under the 2008 Omnibus Incentive Plan, effective as of February 1, 2011, by and between the registrant and Brian M. Culley                                                                                             |
| 10.30# (23) | Incentive Stock Option Grant Agreement under the 2008 Omnibus Incentive Plan, effective as of February 1, 2011, by and between the registrant and Patrick L. Keran                                                                                            |
| 10.31# (24) | Amended and Restated 2008 Omnibus Incentive Plan                                                                                                                                                                                                              |
| 10.32# (24) | Form of [Non-Statutory][Incentive] Stock Option Grant Agreement (for consultants/employees) under the Amended and Restated 2008 Omnibus Incentive Plan                                                                                                        |
| 10.33# (24) | Form of Non-Statutory Stock Option Grant Agreement Director under the Amended and Restated 2008 Omnibus Incentive Plan                                                                                                                                        |
| 10.34# (25) | Form of Incentive Stock Option Grant Agreement (for grants to the registrant's Chief Executive Officer and President and Chief Operating Officer made in July 2011) under the Amended and Restated 2008 Omnibus Incentive Plan                                |
| 10.35# (26) | Form of Senior Executive Incentive Stock Option Grant Agreement (for grants to the registrant's Chief Executive Officer and President and Chief Operating Officer made beginning in December 2011) under the Amended and Restated 2008 Omnibus Incentive Plan |
| 10.36# (27) | Form of Incentive Stock Option Grant Agreement for grants to the registrant's Chief Medical Officer under the Amended and Restated 2008 Omnibus Incentive Plan                                                                                                |

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| Exhibit      | Description                                                                                 |
|--------------|---------------------------------------------------------------------------------------------|
| 10.37# (28)  | Offer letter, dated November 15, 2004, to Brian M. Culley                                   |
| 10.38# (29)  | Offer letter, dated February 11, 2011, to Brandi L. Roberts                                 |
| 10.39# (23)  | Offer letter, dated March 28, 2011, to R. Martin Emanuele                                   |
| 10.40# (26)  | Offer letter, dated July 21, 2011, to Gregory D. Gorgas                                     |
| 10.41# (27)  | Offer letter, dated July 20, 2012, to Santosh Vetticaden                                    |
| 10.42# (21)  | Retention and Severance Plan (as of July 21, 2009) for Brian M. Culley and Patrick L. Keran |
| 10.43# (30)  | Change in Control Severance Plan, effective as of December 6, 2012                          |
| 10.44# (31)  | 2012 Executive Incentive Plan                                                               |
| 10.45# (32)  | 2013 Executive Incentive Plan                                                               |
| 10.46# (35)  | Director Compensation Policy, adopted March 21, 2013                                        |
| 10.47 (33)   | Form of Director and Officer Indemnification Agreement                                      |
| 21.1 (34)    | List of Subsidiaries                                                                        |
| 23.1         | Consent of PricewaterhouseCoopers LLP, Independent Registered Public Accounting Firm        |
| 23.2         | Consent of CohnReznick LLP, Independent Registered Public Accounting Firm                   |
| 23.3         | Consent of DLA Piper LLP (US) (included in Exhibit 5.1)                                     |
| 101.INS XBRL | Instance Document**                                                                         |
| 101.SCH XBRL | Taxonomy Extension Schema**                                                                 |
| 101.CAL XBRL | Taxonomy Extension Calculation Linkbase**                                                   |
| 101.DEF XBRL | Taxonomy Extension Definition Linkbase**                                                    |
| 101.LAB XBRL | Taxonomy Extension Label Linkbase**                                                         |
| 101.PRE XBRL | Taxonomy Extension Presentation Linkbase**                                                  |

Indicates that confidential treatment has been requested or granted to certain portions, which portions have been omitted and filed separately with the SEC

# Indicates management contract or compensatory plan

\*\* Pursuant to Rule 406T of Regulation S-T, these interactive data files are deemed not filed or part of a registration statement or prospectus for purposes of Section 11 or 12 of the Securities Act of 1933, as amended, are deemed not filed for the purposes of Section 18 of the Securities and Exchange Act of 1934, as amended, and otherwise are not subject to liability under those sections.

- (1) Filed with the registrant s Amendment No. 1 to Current Report on Form 8-K/A on May 1, 2006 (SEC file number 001-32157-06796248)
- (2) Filed with the registrant s Current Report on Form 8-K on April 11, 2011 (SEC file number 001-32157-11752769)
- (3) Filed with the registrant s Annual Report on Form 10-K on March 16, 2006 (SEC file number 001-32157-06693266)
- (4) Filed with the registrant s Current Report on Form 8-K on March 1, 2013 (SEC file number 001-32157-13657723)
- (5) Filed with the registrant s Current Report on Form 8-K on June 8, 2009 (SEC file number 001-32157-09878961)
- (6) Filed with the registrant s Current Report on Form 8-K on June 30, 2009 (SEC file number 001-32157-09917820)
- (7) Filed with the registrant s Current Report on Form 8-K on August 5, 2009 (SEC file number 001-32157-09989205)
- (8) Filed with the registrant s Amendment No. 3 to the Registration Statement on Form S-1 on October 5, 2009 (SEC file number 333-160778-091107945)
- (9) Filed with the registrant s Current Report on Form 8-K on January 4, 2010 (SEC file number 001-32157- 10500379)
- (10) Filed with the registrant s Current Report on Form 8-K on May 3, 2010 (SEC file number 001-32157-10790486)
- (11) Filed with the registrant s Current Report on Form 8-K on January 7, 2011 (SEC file number 001-32157-11515655)
- (12) Filed with the registrant s Current Report on Form 8-K on November 14, 2011 (SEC file number 001-32157-111203681)
- (13) Filed with registrant s Annual Report on Form 10-K on March 17, 2008 (SEC file number 001-32157-08690952)
- (14) Filed with the registrant s Quarterly Report on Form 10-Q on May 15, 2009 (SEC file number 001-32157-09878961)
- (15) Filed with the registrant s Annual Report on Form 10-K on March 15, 2007 (SEC file number 001-32157-07697283)

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(16) Filed with the registrant's Registration Statement on Form S-8 on July 13, 2005 (SEC file number 333-126551-05951362)

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- (17) Filed with the registrant s Quarterly Report on Form 10-Q on May 12, 2008 (SEC file number 001-32157-08820541)
- (18) Filed with the registrant s Current Report on Form 8-K on June 2, 2008 (SEC file number 001-32157-08874724)
- (19) Filed with the registrant s Current Report on Form 8-K on February 2, 2009 (SEC file number 001-32157- 09561715)
- (20) Filed with the registrant s Quarterly Report on Form 10-Q on August 11, 2008 (SEC file number 001-32157-081005744)
- (21) Filed with the registrant s Current Report on Form 8-K on July 22, 2009 (SEC file number 001-32157-09957353)
- (22) Filed with the registrant s Current Report on Form 8-K on January 26, 2010 (SEC file number 001-32157- 10547818)
- (23) Filed with the registrant s Quarterly Report on Form 10-Q on May 9, 2011 (SEC file number 001-32157-11823538)
- (24) Filed with the registrant s Form S-8 Registration Statement on June 16, 2011 (SEC file number 333-174940-11914946)
- (25) Filed with the registrant s Quarterly Report on Form 10-Q on November 8, 2011 (SEC file number 001-32157-111186142)
- (26) Filed with the registrant s Annual Report on Form 10-K on March 8, 2012 (SEC file number 001-32157- 12677367)
- (27) Filed with the registrant s Quarterly Report on Form 10-Q on November 5, 2012 (SEC file number 001-32157-121180752)
- (28) Filed with the registrant s Annual Report on Form 10-KSB on March 31, 2005 (SEC file number 001-32157-05719975)
- (29) Filed with the registrant s Current Report on Form 8-K on March 22, 2011 (SEC file number 001-32157-11704394)
- (30) Filed with the registrant s Current Report on Form 8-K on December 7, 2012 (SEC file number 001-32157- 121250022)
- (31) Filed with the registrant s Current Report on Form 8-K on February 27, 2012 (SEC file number 001-32157-12642097)
- (32) Filed with the registrant s Current Report on Form 8-K on February 8, 2013 (SEC file number 001-32157-13587943)
- (33) Filed with the registrant s Current Report on Form 8-K on October 23, 2006 (SEC file number 001-32157-061156993)
- (34) Filed with the registrant s Annual Report on Form 10-K on March 19, 2013 (SEC file number 001-32157-13702619)
- (35) Filed with the registrant s Quarterly Report on Form 10-Q on May 15, 2013 (SEC file number 001-32157-13847400)
- (36) Filed with the registrant s Registration Statement on Form S-1 on May 24, 2013 (SEC file number 333-188870-13873232)