
**UNITED STATES
SECURITIES AND EXCHANGE COMMISSION**

Washington, D.C. 20549

FORM 8-K

**CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934**

Date of Report (Date of earliest event reported): May 9, 2014

Mast Therapeutics, Inc.

(Exact name of registrant as specified in its charter)

Delaware
(State or other jurisdiction
of incorporation)

001-32157
(Commission
File Number)

84-1318182
(IRS Employer
Identification No.)

**12390 El Camino Real, Suite 150,
San Diego, California**
(Address of principal executive offices)

92130
(Zip Code)

Registrant's telephone number, including area code: (858) 552-0866

Not Applicable

Former name or former address, if changed since last report

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

- Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
 - Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
 - Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
 - Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))
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Item 8.01. Other Events.

The information attached as Exhibit 99.1 to this report relating to Mast Therapeutics, Inc. (the “Company”) and its lead product candidate, MST-188, may be presented from time to time by the Company at various investor and analyst meetings.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits.

The list of exhibits called for by this Item is incorporated by reference to the Exhibit Index filed with this report.

By filing this report, including the information contained in Exhibit 99.1 attached hereto, the Company makes no admission as to the materiality of any information in this report. The information contained in Exhibit 99.1 hereto is summary information that is intended to be considered in the context of the Company’s filings with the U.S. Securities and Exchange Commission (the “SEC”), including its Annual Report on Form 10-K filed on March 26, 2014, Quarterly Report on Form 10-Q filed on May 5, 2014 and other public announcements that the Company makes, by press release or otherwise, from time to time. The Company undertakes no duty or obligation to publicly update or revise the information contained in this report, although it may do so from time to time as it believes is appropriate. Any such updating may be made through the filing of other reports or documents with the SEC, through press releases, or through other public disclosure.

Forward-Looking Statements

Mast Therapeutics cautions you that statements included in this report, including in Exhibit 99.1 attached hereto, that are not a description of historical facts are forward-looking statements that are based on the Company’s current expectations and assumptions. Such forward-looking statements include, but are not limited to, statements regarding the Company’s development, regulatory and commercialization strategies and plans for MST-188 in sickle cell disease, arterial disease and heart failure, as well as the timing of activities related to those plans. Among the factors that could cause or contribute to material differences between the Company’s actual results and the expectations indicated by the forward-looking statements are risks and uncertainties that include, but are not limited to: the uncertainty of outcomes in ongoing and future studies of its product candidates and the risk that its product candidates may not demonstrate adequate safety, efficacy or tolerability in one or more such studies, including MST-188 in the EPIC study and the phase 2 clinical study in acute lower limb ischemia; the potential for delays in the commencement or completion of clinical studies, including as a result of difficulties in obtaining regulatory agency agreement on clinical development plans or clinical study design, opening trial sites, enrolling study subjects, manufacturing clinical trial material, completing manufacturing process development activities, and being subject to a “clinical hold”; the risk of suspension or termination of a clinical study, including due to lack of adequate funding or patient safety concerns; the potential for institutional review boards or the FDA or regulatory agencies outside of the U.S. to require additional nonclinical or clinical studies prior to initiation of phase 2 clinical studies of MST-188 in any particular indication in which the Company determines to develop MST-188, including heart failure, which likely would increase the total time and cost of development in the indication; the risk that clinical studies of the Company’s product candidates are not successfully executed and/or do not successfully demonstrate the drug’s safety or efficacy; the risk that, even if clinical studies are successful, the FDA or a regulatory agency outside of the U.S. determines they are not sufficient to support a new drug application; the risk that even if clinical studies of a product candidate in one indication are successful, clinical studies in another indication may not be successful; the Company’s reliance on contract research organizations (CROs), contract manufacturing organizations (CMOs), and other third parties to assist in the conduct of important aspects of development of its product candidates, including clinical studies, and regulatory activities for its product candidates and that such third parties may fail to perform as expected; the Company’s ability to obtain additional funding on a timely basis or on acceptable terms, or at all; the potential for the Company to delay, reduce or discontinue current and/or planned development activities, including clinical studies, partner its product candidates at inopportune times or pursue less expensive but higher-risk and/or lower return development paths if it is unable to raise sufficient additional capital as needed; the risk that the FDA and regulatory agencies outside of the U.S. do not grant marketing approval of a product candidate, on a timely basis, or at all; the risk that the Company is not able to adequately protect its intellectual property rights relating to the MAST platform or MST-188 and prevent competitors from duplicating or developing equivalent versions of its product candidates; the risk that, even if the Company successfully develops and obtains marketing approval for its product candidates, it may not realize commercial success with its products and may never generate revenue sufficient to achieve profitability; and other risks and uncertainties more fully described in the Company’s periodic filings with the SEC and press releases.

You are cautioned not to place undue reliance on forward-looking statements, which speak only as of the date they are made. Mast Therapeutics does not intend to revise or update any forward-looking statement set forth in this report to reflect events or circumstances arising after the date hereof, except as may be required by law. This caution is made under the safe harbor provisions of Section 21E of the Securities Exchange Act of 1934, as amended, and Section 27A of the Securities Act of 1933, as amended.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Mast Therapeutics, Inc.

May 9, 2014

By: /s/ Patrick L. Keran

Name: Patrick L. Keran

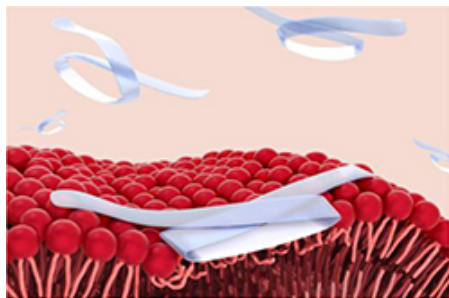
Title: President and Chief Operating Officer

Exhibit Index

<u>Exhibit No.</u>	<u>Description</u>
99.1	Summary of the development history of MST-188, May 2014



A Brief History of MST-188



MST-188 binds to damaged membranes, restoring the cell's natural, hydrated, non-adhesive surface.

Definitions

RheothRx – A first-generation product with unpurified, excipient-grade poloxamer 188 as the active ingredient. Associated with elevated serum creatinine.

MST-188 (formerly known as ANX-188, FLOCOR and CRL-5861) – A second-generation product with purified poloxamer 188 as the active ingredient. Certain low molecular weight substances present in excipient-grade poloxamer 188 that are associated with elevated serum creatinine are not present in MST-188. No clinically significant elevations in creatinine have been observed in clinical studies conducted with the purified material (>300 administrations).

Early Development: The CytRx Corporation/Burroughs Wellcome Alliance

Poloxamer 188 is a well-studied compound. It was originally used as an emulsifying agent in topical wound cleansers and parenteral nutrition products. However, the therapeutic use of poloxamer 188 was largely conceived by Dr. Robert Hunter, MD, PhD (Distinguished Professor and Chairman, Department of Pathology and Laboratory Medicine, University of Texas Medical School at Houston). Dr. Hunter (then at Emory University) identified the compound's rheologic, cytoprotective and antithrombotic activities through an extensive series of laboratory studies. His work led to the formation of CytRx Corporation, a start-up company that licensed Dr. Hunter's inventions from Emory. CytRx conducted a wide range of pre-clinical and clinical studies with first-generation poloxamer 188, then known as RheothRx. These studies led to a major alliance with Burroughs Wellcome (today, GSK). Burroughs also performed an extensive series of nonclinical studies and 8 clinical trials, primarily focused on acute myocardial infarction (AMI). Early studies investigating RheothRx were promising. The largest AMI trial planned to enroll approximately 20,000 patients. However, during the 3,000-patient lead-in phase of this study, elevations in serum creatinine were observed, particularly in those patients aged 65 years and older and in subjects with elevated creatinine at baseline. This phenomenon was referred to as "acute renal dysfunction" and resulted in the discontinuation of the program by Glaxo, which had recently merged with Burroughs Wellcome.

Addressing Renal Toxicity and Pursuing Sickle Cell Disease

After Glaxo returned the RheothRx program, CytRx investigated the source of the renal dysfunction and determined the elevation in serum creatinine was attributable to preferential absorption of certain low molecular weight substances by the proximal tubule epithelial cells in the kidney. CytRx developed a proprietary method of manufacture based on supercritical fluid chromatography that reduced the level of these low molecular weight substances present in poloxamer 188, creating what is now known as *purified* poloxamer 188. Nonclinical testing of *purified* poloxamer 188 (now known as MST-188), demonstrated less accumulation in kidney tissue, less pronounced vacuolization of proximal tubular epithelium, more rapid recovery from vacuolar lesions, and less effect on serum creatinine. A full report of the differential effects of commercial-grade and purified poloxamer 188 on renal function has been published.¹

Subsequently, CytRx sought to re-introduce MST-188 into the clinic. However, CytRx lacked the resources to conduct a 20,000-patient heart attack study. Instead, they focused the development of MST-188 in sickle cell disease (SCD), a rare disease with a huge unmet need and in which RheothRx had demonstrated positive results in a pilot Phase 2 study conducted by Burroughs Wellcome. In that Phase 2 study (n=50), RheothRx significantly reduced the duration of crisis, pain intensity, and total analgesic use and showed trends to shorter days of hospitalization in the subgroup of patients who received the full dose of study drug (n=31). These data were reported more fully by Adams-Graves et al.² Notably, CytRx conducted safety studies in both adult and pediatric sickle cell patients and, even at significantly higher levels of exposure than anticipated therapeutic doses, there were no clinically significant changes in serum creatinine observed and no acute kidney failure reported. Based on these promising Phase 1 and 2 results, CytRx subsequently launched a randomized, double-blind, placebo-controlled Phase 3 study of MST-188 in 350 patients with sickle cell disease. The primary endpoint was a reduction in the duration of a painful crisis. However, CytRx concluded the study at 255 patients, in part due to capital constraints. Nonetheless, the study demonstrated treatment benefits in favor of MST-188. However, it did not achieve statistical significance in the primary study endpoint (p=0.07). Mast believes that enrolling fewer than the originally-planned number of patients and key features of the study's design negatively affected the outcome of the primary endpoint. In particular, the study assumed that most patients would resolve their crisis within one week (168 hours). However, a substantial number of patients did not achieve crisis resolution within 168 hours and were assigned a "default" value of 168 hours, which had a potentially significant effect on the primary endpoint. Notably, in a post hoc "responder's analysis" of the intent-to-treat population (n=249), which analyzed the proportion of patients who achieved crisis resolution at 168 hours (excluding those who had been assigned the default of 168 hours), over 50% of subjects receiving MST-188 achieved crisis resolution within 168 hours, compared to 37% in the control group (p=0.02). Data from the Phase 3 study are reported more fully by Orringer et al.³ Following conclusion of the Phase 3 study, CytRx merged with a private company and modified its business strategy by discontinuing development of all of its existing programs (including MST-188) to focus on assets held by the private company with which it merged.

SynthRx

After the corporate reorganization at CytRx, a group of individuals, including Dr. Hunter, formed a private entity, which they named SynthRx, Inc., to acquire rights to the data, know-how, and extensive clinical and pre-clinical and manufacturing information necessary to continue development of MST-188. SynthRx developed new intellectual property and conducted additional analyses of the existing data. However, they were unable to raise capital to fund development of MST-188 during the "great recession."

Mast Therapeutics

In 2010, Mast Therapeutics met with Dr. Hunter and his colleagues to negotiate the acquisition of SynthRx and continue the development of MST-188. The merger was finalized in April 2011.

Since April 2011, Mast Therapeutics has re-established the unique manufacturing process through a partnership with Pierre Fabre (FRA) and met with the FDA multiple times to discuss a pivotal study protocol for MST-188 in sickle cell disease. In 2013, Mast initiated the EPIC study, a 388-patient pivotal Phase 3 trial of MST-188 in sickle cell disease, and, in 2014, Mast initiated its second MST-188 clinical program with a Phase 2, proof-of-concept study of MST-188 in combination with rt-PA in patients with acute limb ischemia. In addition, based on recent nonclinical study data showing improvements in cardiac ejection fraction and key biomarkers and prior studies showing MST-188 improved cardiac function without increasing cardiac energy requirements, Mast has announced its intent to pursue clinical development of MST-188 in heart failure.

1 Emanuele, M. and Balasubramaniam, B. Differential Effects of Commercial-Grade and Purified Poloxamer 188 on Renal Function. *Drugs in R&D* April 2014. Available at <http://link.springer.com/article/10.1007/s40268-014-0041-0>.

2 Adams-Graves P, Kedar A, Koshy M, et al. RheothRx (Poloxamer 188) Injection for the Acute Painful Episode of Sickle Cell Disease: A Pilot Study. *Blood* 1997;90:2041-6

3 Orringer EP, Casella JF, Ataga KI, et al. Purified poloxamer 188 for treatment of acute vaso-occlusive crisis of sickle cell disease: A randomized controlled trial. *JAMA* 2001;286(17):2099-106