

Prospectus Supplement No. 6
(To prospectus dated June 14, 2013)



Warrants to Purchase up to 28,097,500 Shares of Common Stock

This Prospectus Supplement No. 6 (the "Prospectus Supplement") supplements our Prospectus dated June 14, 2013 and Prospectus Supplements No. 1 through 5, dated June 26, 2013, August 5, 2013, August 9, 2013, October 30, 2013 and November 4, 2013, respectively (together, the "Prospectus"), relating to the issuance of up to 28,097,500 shares of our common stock issuable upon exercise of outstanding warrants issued in connection with our registered offering which closed on June 19, 2013. We cannot predict when or if the warrants will be exercised, and it is possible that the warrants may expire and never be exercised.

Recent Developments

This Prospectus Supplement is being filed to update and supplement the information in the Prospectus with the information contained in our Current Report on Form 8-K filed with the Securities and Exchange Commission on January 8, 2014 (the "Current Report"). Accordingly, we have attached the Current Report to this Prospectus Supplement. Any statement contained in the Prospectus shall be deemed to be modified or superseded to the extent that information in this Prospectus Supplement modifies or supersedes such statement. Any statement that is modified or superseded shall not be deemed to constitute a part of the Prospectus except as modified or superseded by this Prospectus Supplement.

This Prospectus Supplement should be read in conjunction with, and may not be delivered or utilized without, the Prospectus.

In reviewing this Prospectus Supplement, you should carefully consider the matters described under the caption "Risk Factors" beginning on page 4 of the Prospectus.

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

This Prospectus Supplement does not constitute an offer to sell or the solicitation of an offer to buy any securities.

The date of this Prospectus Supplement is January 8, 2014

**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): January 6, 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.

On January 6, 2014, Mast Therapeutics, Inc. (the “Company”) announced positive data from a nonclinical study of MST-188 in a model of chronic heart failure. The objective of the study was to determine the effect of acute intravenous administration of MST-188 on left ventricular systolic and diastolic cardiac function in a model of chronic heart failure produced by multiple sequential intracoronary microembolizations. A single dose of MST-188 (low or high dose) or placebo was administered over two hours. Hemodynamic, ventriculographic, echocardiographic and electrocardiographic measurements were taken at baseline (prior to study drug administration) and at the following time-points after the start of study drug administration: 2 hours (end of administration), 24 hours, 1 week and 2 weeks. Peripheral venous blood samples were obtained at the same time-points. The Company reported that MST-188 demonstrated a statistically significant improvement in parameters of heart function, including left ventricular ejection fraction and end-systolic volume, stroke volume and cardiac output, and that a single, two-hour infusion of MST-188 resulted in improvements that were significant immediately (at the end of MST-188 administration) and remained significant at one week (and, in some cases, at two weeks) after MST-188 administration. The improvements described above were calculated as the difference between baseline and mean values of each study group at each time-point using a one-way analysis of variance, with $p < 0.05$ considered significant. The study was conducted under the supervision of Dr. Hani N. Sabbah at Henry Ford Health System, a Michigan non-profit corporation. The Company will provide an update on its plans for MST-188 in heart failure later in 2014.

On January 8, 2014, the Company announced the following updates related to EPIC, its pivotal phase 3 study of MST-188 in sickle cell disease:

- The Company had opened 40 clinical sites in the U.S. by year-end 2013.
- The Company expects to open clinical sites in at least three countries outside the U.S. during the first quarter of 2014 and plans to have a total of approximately 30 ex-U.S. sites open by the end of 2014.
- Overall study enrollment is consistent with internal projections and the Company continues to expect to complete full enrollment for the trial by the end of 2015.
- The Company has decided to amend the study’s entry criteria to expand the genotype and age range. In parallel, the Company will add a limited number of investigational sites with an adult patient focus to the 40 pediatric-focused sites that already are open to generate additional safety and efficacy data on MST-188 in the adult population. Given that the majority of the study investigators will be pediatric hematologists, the Company expects that the majority of enrolled subjects will be children and young adults.

The Company’s cash, cash equivalents and investment securities as of December 31, 2013 were over \$44 million.

The information contained in this report 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 19, 2013, its Quarterly Report on Form 10-Q filed on November 4, 2013, and other public announcements that the Company makes, by press release or otherwise, from time to time. The Company makes no admission as to the materiality of any information in this report. 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.

Forward Looking Statements

Mast Therapeutics cautions you that this report includes forward-looking statements within the meaning of Section 21E of the Securities Exchange Act of 1934, as amended (the “Exchange Act”). All statements in this report, other than statements of historical fact, are forward-looking statements that are based on the Company’s current expectations and assumptions. The words “expect,” “believe,” “will,” “may,” “plan,” “intend,” “continues,” and similar forward-looking expressions are intended to identify forward-looking statements. Such forward-looking statements include, but are not limited to, statements related to progress with, completion and potential success of the EPIC study, prospects for MST-188 in sickle cell disease and heart failure, and the Company’s development plans for MST-188 in sickle cell disease, heart failure and acute limb ischemia, including the timing of initiation of any clinical studies. 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 MST-188 and the risk that MST-188 may not demonstrate adequate safety, efficacy or tolerability in one or more such studies, including EPIC; 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 sufficient quantities of clinical trial material, being subject to a “clinical hold,” and/or suspension or termination of a clinical study, including due to patient safety concerns or lack of funding; the potential for institutional review boards or the FDA or other regulatory agencies to require additional nonclinical or clinical studies prior to initiation of any planned phase 2 clinical study of MST-188; 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 risk that, even if clinical studies are successful, the FDA or other regulatory agencies may determine they are not sufficient to support a new drug application; 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 MST-188, including clinical studies, and regulatory activities for MST-188, 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 MST-188 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, even if the Company successfully develops MST-188 in one or more indications, it may not realize commercial success with its products and may never generate revenue sufficient to achieve profitability; the risk that the Company is not able to adequately protect its intellectual property rights relating to the MAST platform and MST-188 and prevent competitors from duplicating or developing equivalent versions of its product candidates, including MST-188; and other risks and uncertainties more fully described in the Company’s press releases and periodic filings with the SEC.

You are cautioned not to place undue reliance on forward-looking statements, which speak only as of the date when 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 Exchange Act.

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.

January 8, 2014

By: /s/ Patrick L. Keran

Name: Patrick L. Keran

Title: President and Chief Operating Officer