

Prospectus Supplement No. 4
(To prospectus dated June 14, 2013)



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

This Prospectus Supplement No. 4 (the "Prospectus Supplement") supplements our Prospectus dated June 14, 2013 and Prospectus Supplements No. 1, 2 and 3 dated June 26, 2013, August 5, 2013 and August 9, 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 October 30, 2013 (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 Any statement contained in the Prospectus shall be deemed to be modified or superseded to the extent that information in this Prospectus Supplement modifies or supersedes such statement. Any statement that is modified or superseded shall not be deemed to constitute a part of the Prospectus except as modified or superseded by this Prospectus Supplement.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 October 30, 2013

**UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549**

**FORM 8-K/A
Amendment No. 1**

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

Date of Report (Date of Earliest Event Reported): June 19, 2013

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
(I.R.S. 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))
-
-

Explanatory Note

This Amendment No. 1 amends and supplements the Current Report on Form 8-K of Mast Therapeutics, Inc. (the “Company”) filed with the Securities and Exchange Commission on June 21, 2013 (the “Original Current Report”). The sole purpose for filing this Amendment No. 1 to the Original Current Report is to disclose, as required by paragraph (d) of Item 5.07 of Form 8-K, the Company’s decision as to how frequently the Company will include in its proxy materials an advisory vote on the compensation of its named executive officers. No other changes are being made to the Original Current Report.

Item 5.07. Submission of Matters to a Vote of Security Holders.

On June 19, 2013, the Company held its 2013 Annual Meeting of Stockholders (the “Annual Meeting”) and it reported the results of the Annual Meeting in the Original Current Report. One of the matters voted upon at the Annual Meeting was a non-binding advisory vote on the frequency of advisory votes on the compensation of the Company’s named executive officers.

Consistent with the preference indicated by the results of that advisory vote as reported in the Original Current Report, the Company’s board of directors (the “Board”) has determined that the Company will hold a stockholder advisory vote on the compensation of its named executive officers once every three years until the next stockholder advisory vote regarding the frequency of stockholder advisory votes on executive compensation is conducted or the Board otherwise determines that a different frequency for such votes is in the best interests of the Company’s stockholders.

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.

October 30, 2013

By: /s/ Patrick L. Keran

Name: Patrick L. Keran

Title: President and Chief Operating Officer