

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

POST-EFFECTIVE AMENDMENT NO. 1
TO
FORM S-3
REGISTRATION STATEMENTS
UNDER THE SECURITIES ACT OF 1933
(Registration Nos. 333-159376 and 333-164177)

Mast Therapeutics, Inc.

(Exact name of registrant as specified in its charter)

Delaware (State or other jurisdiction of incorporation or organization) **84-1318182** (I.R.S. employer identification number)

3611 Valley Centre Drive, Suite 500
San Diego, CA 92130
(858) 552-0866
(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

Brandi L. Roberts
Chief Financial Officer and Senior Vice President
Mast Therapeutics, Inc.
3611 Valley Centre Drive, Suite 500
San Diego, California 92130
(858) 552-0866
(Name, address, including zip code, and telephone number, including area code, of agent for service)

Approximate date of commencement of proposed sale to the public: From time to time after the effective date of the registration statement.

If the only securities being registered on this Form are being offered pursuant to dividend or interest reinvestment plans, please check the following box.

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, other than securities offered only in connection with dividend or interest reinvestment plans, 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 registration statement pursuant to General Instruction I.D. or a post-effective amendment thereto that shall become effective upon filing with the Commission pursuant to Rule 462(e) under the Securities Act, check the following box.

If this Form is a post-effective amendment to a registration statement filed pursuant to General Instruction I.D. filed to register additional securities or additional classes of securities pursuant to Rule 413(b) under the Securities Act, check the following box.

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 Smaller reporting company
(Do not check if a smaller reporting company)

Deregistration of Securities

This Post-Effective Amendment relates to the following registration statements on Form S-3 (collectively, the "Registration Statements") filed by Mast Therapeutics, Inc. (the "Company"):

- the registration Statement on Form S-3 originally filed with the Securities and Exchange Commission (the "SEC") on May 21, 2009 (File No. 333-159376); and
- the registration Statement on Form S-3 originally filed with the SEC on January 4, 2010 (File No. 333-164177).

The Company is filing this Post-Effective Amendment to withdraw and remove from registration the unissued and unsold shares of the Company's common stock, par value \$0.001 per share, shares of the Company's preferred stock, par value \$0.001 per share, the Company's debt securities and the Company's warrants, issuable by the Company pursuant to the Registration Statements.

In accordance with an undertaking made by the Company in the Registration Statements to remove from registration, by means of a post-effective amendment, any shares of its common stock, its preferred stock, its debt securities or its warrants which remain unsold at the termination of the offering, the Company hereby removes from registration all shares of its common stock, its preferred stock, its debt securities and its warrants registered under the Registration Statements that remain unsold as of the date hereof.

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, the registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-3 and 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, on May 6, 2016.

MAST THERAPEUTICS, INC.

By: /s/ Brian M. Culley

Brian M. Culley
Chief Executive Officer

Note: No other person is required to sign this Post-Effective Amendment to the Registration Statements in reliance on Rule 478 of the Securities Act of 1933, as amended.