



DIVISION OF
CORPORATION FINANCE

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

March 31, 2015

Via E-mail

Brandi L. Roberts
Chief Financial Officer and Senior Vice President
Mast Therapeutics, Inc.
3611 Valley Centre Drive, Suite 500
San Diego, CA 92130

**Re: Mast Therapeutics, Inc.
Registration Statement on Form S-3
Filed March 24, 2015
File No. 333-202960**

Dear Ms. Roberts:

We have limited our review of your registration statement to the issue addressed in our comment. Please respond to this letter by providing the requested information. If you do not believe our comment applies to your facts and circumstances, please tell us why in your response.

After reviewing the information you provide in response to these comments, we may have additional comments.

Information Incorporated by Reference, page 26

1. We note that you are incorporating your annual report on Form 10-K for the fiscal year ended December 31, 2014 by reference to your registration statement. As of the date of this letter, you have yet to file Part III of that report. Please be advised that we will not be in a position to grant effectiveness to your registration statement until such time as you have amended your annual report to include Part III or you have filed your definitive proxy statement.

We urge all persons who are responsible for the accuracy and adequacy of the disclosure in the filing to be certain that the filing includes the information the Securities Act of 1933 and all applicable Securities Act rules require. Since the company and its management are in possession of all facts relating to a company's disclosure, they are responsible for the accuracy and adequacy of the disclosures they have made.

Brandi L. Roberts
Mast Therapeutics, Inc.
March 31, 2015
Page 2

Notwithstanding our comment, in the event you request acceleration of the effective date of the pending registration statement, please provide a written statement from the company acknowledging that:

- should the Commission or the staff, acting pursuant to delegated authority, declare the filing effective, it does not foreclose the Commission from taking any action with respect to the filing;
- the action of the Commission or the staff, acting pursuant to delegated authority, in declaring the filing effective, does not relieve the company from its full responsibility for the adequacy and accuracy of the disclosure in the filing; and
- the company may not assert staff comments and the declaration of effectiveness as a defense in any proceeding initiated by the Commission or any person under the federal securities laws of the United States.

Please refer to Rules 460 and 461 regarding requests for acceleration. We will consider a written request for acceleration of the effective date of the registration statement as confirmation of the fact that those requesting acceleration are aware of their respective responsibilities under the Securities Act of 1933 and the Securities Exchange Act of 1934 as they relate to the proposed public offering of the securities specified in the above registration statement. Please allow adequate time for us to review any amendment prior to the requested effective date of the registration statement.

Please contact Scot Foley at (202) 551-3383 or Daniel Greenspan at (202) 551-3623 with any questions.

Sincerely,

/s/ Daniel Greenspan for

Jeffrey P. Riedler
Assistant Director

cc: Michael S. Kagnoff, Esq.
DLA Piper LLP (US)
4365 Executive Drive, Suite 1100
San Diego, CA 92121