

Mail Stop 4720

January 21, 2010

Dr. Jeffrey Stein
President and Chief Executive Officer
Trius Therapeutics, Inc.
6310 Nancy Ridge Drive, Suite 101
San Diego, California 92121

**Re: Trius Therapeutics, Inc.
Registration Statement on Form S-1
Supplemental response dated January 13, 2010
File No. 333-162945**

Dear Dr. Stein:

We have reviewed your filing and have the following comments. Where indicated, we think you should revise your document in response to these comments. If you disagree, we will consider your explanation as to why our comment is inapplicable or a revision is unnecessary. Please be as detailed as necessary in your explanation. In some of our comments, we may ask you to provide us with information so we may better understand your disclosure. After reviewing this information, we may raise additional comments.

Please understand that the purpose of our review process is to assist you in your compliance with the applicable disclosure requirements and to enhance the overall disclosure in your filing. We look forward to working with you in these respects. We welcome any questions you may have about our comments or any other aspect of our review. Feel free to call us at the telephone numbers listed at the end of this letter.

FORM S-1

Management's Discussion and Analysis of Financial Condition and Results of Operations

Critical Accounting Policies and Significant Judgments and Estimates
Stock-Based Compensation, page 52

1. Please revise your disclosure to bridge the gap between the assumed initial public offering price of \$13.00 per share and the fair value of common stock on September 17, 2009 of \$7.57. Please disclose each factor that contributed to the difference between the fair value of the options that were granted and the

estimated IPO price in more detail than you included in your correspondence dated January 13, 2010. Specifically, include an explanation for why the notice of allowance for your patent application supports a significantly higher proposed IPO price. Finally, please disclose whether any equity issuances were made subsequent to September 30, 2009 up until the date of your filing and if so, disclose the fair value along with the assumptions and methodology used.

* * *

As appropriate, please amend your registration statement in response to these comments. You may wish to provide us with marked copies of the amendment to expedite our review. Please furnish a cover letter with your amendment that keys your responses to our comments and provides any requested information. Detailed cover letters greatly facilitate our review. Please understand that we may have additional comments after reviewing your exhibits, amendment and responses to our comments.

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 all information required under the Securities Act of 1933 and that they have provided all information investors require for an informed investment decision. 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.

Notwithstanding our comments, in the event the company requests acceleration of the effective date of the pending registration statement, it should furnish a letter, at the time of such request, 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.

In addition, please be advised that the Division of Enforcement has access to all information you provide to the staff of the Division of Corporation Finance in connection with our review of your filing or in response to our comments on your filing.

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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. We will act on the request and, pursuant to delegated authority, grant acceleration of the effective date.

We direct your attention to Rules 460 and 461 regarding requesting acceleration of a registration statement. Please allow adequate time after the filing of any amendment for further review before submitting a request for acceleration. Please provide this request at least two business days in advance of the requested effective date.

You may contact Vanessa Robertson at (202) 551-3649 or Joel Parker at (202) 551-3651 if you have questions regarding comments on the financial statements and related matters. Please contact John Krug, Senior Counsel, at (202) 551-3862, Daniel Greenspan, Special Counsel, at (202) 551-3623, or me at (202) 551-3715 with any other questions.

Sincerely,

Jeffrey Riedler
Assistant Director

cc: M. Wainwright Fishburn, Jr., Esq.
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