

Mail Stop 4720

December 29, 2009

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
Amendment no. 1 filed December 10, 2009
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

Cover Page

1. We note your response to comment 7 and reissue the comment. In this regard, it appears your concerns can be addressed by revising the "Underwriting" section to include a definition of "sole book-running manager" and the significance of direct contact with such entity.

Prospectus Summary
Overview, page 1

2. We note your response to comment 8 and reissue the comment. The presentation does not define the term gram-positive and the distinction between a first generation and second generation product is not clear.
3. We note the disclosure regarding the filing of a request for a Special Protocol Assessment related to a Phase 3 trial of Torezolid Phosphate for oral administration. Please expand your disclosure to disclose the nature of all communications received from the FDA regarding this request since you have made it.

The Market Opportunity for Torezolid Phosphate, page 2

4. Please expand the discussion to indicate the source of the sales data provided.

Use of Proceeds, page 41

5. Please expand the first bullet in the second paragraph to explain the extent to which the registrant's research objectives are expected to be accomplished with the expenditure of the proceeds (i.e. completion of one Phase 3 trial for oral administration of Torezolid Phosphate for ABSSI, completion of one Phase 3 trial and the partial completion of the second Phase 3 trial for oral administration of Torezolid Phosphate for ABSSI, advancement of oral Torezolid Phosphate for ABSSI for oral administration through the filing of an NDA, completion of one Phase 3 trial for oral administration of Torezolid Phosphate for ABSSI and completion of a Phase 1 trial of Torezolid Phosphate for IV administration for ABSSI, etc.).

Principal Stockholders, pages 120-123

6. Please expand Footnote 5 on page 122 to identify the five Managers referred to in that footnote.

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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.

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.

Dr. Jeffrey Stein
Trius Therapeutics, Inc.
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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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