Mail Stop 4720 December 3, 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
Filed November 6, 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

General

1. Please provide us proofs of all graphic, visual, or photographic information you will provide in the printed prospectus prior to its use, for example in a preliminary prospectus. Please note we may have comments regarding these materials.

2. Please note that where we provide examples to illustrate what we mean by our comments, they are examples and not complete lists. If our comments are applicable

to portions of the filing that we have not cited as examples, please make the appropriate changes in accordance with our comments.

3. Please update the discussion in your prospectus to the most recent date practicable.

4. Please note that our comments on your request for confidential treatment will be provided under separate cover.

5. Please note that when you file a pre-effective amendment containing pricing-related information, we may have additional comments. As you are likely aware, you must file this amendment prior to circulating the prospectus.

6. Please note that when you file a pre-effective amendment that includes your price range, it must be bona fide. We interpret this to mean that your range may not exceed $2 if you price below $20 and 10% if you price above $20.

Cover Page

7. Please delete the term "Sole Book-Running Manager."

Prospectus Summary
Overview, page 1

8. Please define "second generation" and "gram-positive" the first time you use the terms.

9. The summary should provide a balanced presentation of the information presented in the body of the filing. As currently written, the overview focuses only on your positive attributes. Please balance the discussion of your challenges and risks. In this regard, we note:
   - The overview refers to your preparation for initiation of Phase 3 clinical trials for torezolid phosphate, however you do not disclose that you have no products approved for commercial sale until page 5;
   - The overview may tend to suggest that Zyvox is the only drug with which you may compete, however the discussion on page 2 indicates there are several products approved for sale which may compete with the product you are currently developing;
   - The discussion of the advantages of torezolid phosphate is not balanced with a description of the disadvantages, if any, of the product or any advantages competing products may have over the use of torezolid phosphate. Please consider whether a discussion of the advantages and disadvantages of your product relative to competing products is too complicated to be addressed in an overview section;

- You state you are developing torezolid phosphate for acute bacterial skin and skin structure infections, which represents the largest commercial opportunity for antibiotics that treat gram positive infections. If Zyvox is sold for purposes beyond the use you will initially concentrate your efforts, the reference to the amount of worldwide sales of Zyvox may tend to create an unwarranted impression of the size of the market you are targeting; and
- The reference to the NIH contract in the last sentence of the first paragraph of this section may suggest that your development of torezolid phosphate as an alternative to Zyvox is funded by, and at the direction of NIH. If retained in the Overview section, please consider relocating the discussion to the end of the section and expanding the discussion to clarify whether the NIH contract you refer to is for the development of competing products or to support the discovery platform you are developing as described in the section entitled "Our Research and Preclinical Programs."

10. Please briefly discuss when you submitted application(s) to the FDA for your product(s) and the current status of such application(s) in the FDA review process.

Development Program Table, page 2

11. In view of the discussion in your overview section and the lack of an adequate context reference for potential investors to understand the presentation, consideration should be given to deleting the table from the summary.

The Market Opportunity for Torezolid Phospate, page 2

12. We note your reference to the sales growth of antibiotics labeled for MRSA. The use of "compound annual growth rate" is inappropriate without balanced, accompanying disclosure, in the context of such compounded rates, of the actual rates of growth on a year to year basis. An explanation of "compound annual growth rate" should be provided which clearly discloses the nature of the term and that such term should not be confused with growth rates on a year to year basis. Any anomalies in annual growth rates or other factors affecting the compounded rates should also be discussed. In this regard, we are of the opinion that such disclosure is inappropriate in the summary, but may be provided elsewhere in the registration statement. Please provide us with the computation of the compound annual growth rates used. Please clarify whether and the extent to which the sales data has been adjusted for price changes, i.e. to what extent has the increase been attributed to unit sales or price increases. We may have further comment upon receipt of your response.

Torezolid Phospate, page 3

13. Please provide us with support for the statement that your product is the most advanced of its kind in clinical development.

14. Please clarify whether by using the phrase “most advanced” you are referring to your product’s current stage in the process of product development or you are comparing the attributes of your product with those of your competitors.

15. Briefly identify the competing products under development and their current stage in the development process.

16. Please expand the discussion to provide a balanced discussion of the positive and negative characteristics of torezolid phosphate compared to competing existing products and products under development, to the extent known.

Our Strategy, page 4

17. Please expand the discussion in the second sentence of the last paragraph to indicate the number of individuals that comprise your senior management team.

18. Please delete the last sentence of the last paragraph of this section. In this regard, we note your management background discussion contains no reference to these products or the extent of involvement of the named individuals in the development of the products identified.

Risk Factors

“We have limited sources of revenues…,” page 9

19. Please revise the discussion, if true, to state you do not anticipate revenues, if any, from the sales of torezolid phosphate for at least ___ years.

“To raise additional funds to support our business operations…,” page 11

20. Please revise the heading and related discussion to indicate sales of additional equity will result in dilution to your stockholders.

“The timing of the milestone and royalty payments…,” page 11

21. It appears your principal product, torezolid phosphate, was originally developed by Dong-A Pharmaceutical Co., Ltd. and you have acquired a license for patent applications and intellectual property related to this product. If true, please expand the discussion in your prospectus summary to disclose this information.

22. We note the possible effects on your development activities in the event you lack the funds to make a required milestone payment. Please clarify whether Dong-A or its assignee has any recourse in the event you fail to make a required payment in a timely

manner or otherwise delay the development or commercialization of torezolid phosphate.

"We rely on third parties to conduct our clinical trials…," page 15
"Our dependence upon third parties for the manufacture and supply…," page 15

23. We note you may be substantially dependent on one or more of these agreements. If you are, please file copies of these agreements as exhibits and discuss them in greater detail in your business section. If you do not believe you are substantially dependent upon these agreements, please provide an analysis supporting your determination. See Item 601(b)(10)(ii)(B) of Regulation S-K.

"If approved, torezolid phosphate will face competition…," page 18

24. To the extent practicable, please quantify the anticipated price differential referred to in the discussion.

"If we are not successful in attracting and retaining highly qualified personnel…," page 21

25. Please identify the employees upon whom you are dependent.

"Product liability lawsuits could divert our resources…," page 26

26. Please expand the discussion to indicate the amount of insurance coverage you presently have for general liability and product liability claims.

"We do no intend to pay dividends…," page 38

27. Please revise the last sentence of this discussion to insert "appreciation" for the term "value."

Use of Proceeds, page 41

28. Please expand the discussion to indicate the approximate amount of the proceeds that will be allocated to fund clinical, research and development costs for torezolid phosphate and the anticipated additional costs and expenses associated with being a public company.

Management's Discussion and Analysis of Financial Condition and Results of Operations, page 48

29. Please include a caption in this section to address the impact that the material weakness over internal controls discussed on pages 35 and 36 had on the financial

reporting process covered in this period. Please include how the material weakness was identified, whether the material weakness was corrected and the steps the company has taken to remedy the material weakness.

Business, page 65

30. Please define the terms “pharmacokinetic” and “pharmacodynamic” which appear on page 76 and the terms “cross activity” and “down regulated” which appear on page 77.

Our Strategy, page 66

31. Please consider expanding the discussion to provide a timeline for the components of your strategy.

Torezolid Phosphate, a Second Generation Oxazolidinone, page 70

32. Please expand the discussion to also address any disadvantages of the use of torezolid phosphate.

Our Nonclinical Studies of Torezolid Phosphate, page 75

33. In the tables on page 76, please clarify the meaning of the different values in the columns for Torezolid Phosphate and Linezolid, as well as the meaning of “50% effective dose” and “90% effective dose.”

Dong-A Pharmaceutical Co., Ltd. License Agreement, page 77

34. We note Dong-A Pharmaceutical retained the right to develop and commercialize products in Korea with respect to oral and injectable forms of torezolid phosphate. Please expand the discussion to briefly describe the extent of Dong-A Pharmaceutical’s activities to date in this regard.

NIAID Contract, page 78

35. Please expand the discussion to provide more specific information as to how the contract was “valued at $27.7 million.”

36. Please define the term “march-in rights” and explain whether and how you may be compensated in the event such rights are exercised.

Lawrence Livermore Cooperative Research and Development Agreement, page 78

37. Please expand the discussion to further describe the nature of the license you may obtain for any invention developed under the CRADA.

38. Please explain whether and how you may be compensated in the event march-in rights are exercised.

Employees, page 89

39. Please state the number of your full-time employees.

Facilities, page 89

40. We note your lease expires in January 2010. Please update the discussion to reflect the current status of your lease or describe your new facilities.

Setting Executive Compensation, page 96

41. Please state when the compensation committee was formed and when it began reviewing the compensation paid to your executive officers.

42. We note your reference on page 96 and 97 to the consideration given by the board and compensation committee to compensation paid by similarly situated biotechnology companies in connection with the setting of executive compensation. It appears these companies constitute a peer group. Yet, you disclose on page 97 that neither the board nor the compensation committee "benchmarks" executive compensation against comparable companies. This appears to be contradictory. Please delete your statement that you do not benchmark, identify the members of the peer group(s) considered in setting executive compensation and also disclose how your compensation levels are set in relation to the compensation levels of such peer group(s) regarding the various components of your compensation package. Alternatively, please explain how the comparable company information is used and why this should not be deemed benchmarking and delete your statements on pages 96 and 97 suggesting otherwise.

Summary Compensation Table, page 99

43. Please update your disclosure to provide your executive compensation disclosure for your last completed fiscal year, i.e. the fiscal year ended December 31, 2009. We may have further comments based upon your response.

44. If applicable, after the compensation committee determines the amounts, if any, earned for 2009 awards, please disclose those amounts in the Compensation Discussion and Analysis and in the Summary Compensation Table.

Principal Stockholders, page 117

45. Please expand the discussion in footnotes 3, 4 and 5 to identify the natural person(s) with voting or investment control over the securities held by the respective 5% or greater stockholders. In addition, it would appear the identification of the natural person(s) with voting and investment authority currently presented in footnotes 6 and 8 should be presented in footnotes 1 and 2, respectively.

Notes to Financial Statements

Note 3 – Significant Agreements and Contracts, page F-16

46. Please expand your disclosure to include the length of and termination provisions for all of your material agreements.

Note 6 – Convertible Preferred Stock and Stockholders' Equity (Deficit)

47. Please provide us with an analysis of whether the conversion option should be a derivative liability.

Note 7 – Stock-based Compensation, page F-21

48. We may have comments on your accounting for stock compensation and related disclosure once you have disclosed an estimated offering price. In addition, please provide quantitative and qualitative disclosures explaining the difference between the estimated offering price and the fair value of your recent stock sales.

* * *

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.

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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