

Mail Stop 6010

May 15, 2008

Paul K. Laikind, Ph.D.  
President and Chief Executive Officer  
Metabasis Therapeutics, Inc.  
11119 North Torrey Pines Road  
La Jolla, CA 92037

**Re: Metabasis Therapeutics Inc.  
Registration Statement on Form S-3  
Filed May 9, 2008  
File No. 333-150806**

Dear Mr. Laikind:

We have limited our review of your filing to those issues we have addressed in our 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.

General

1. We are monitoring your filing for the resolution of your pending confidential treatment request.

Selling Stockholders, page 28

2. We note that several of the entities listed as selling stockholders are controlled by three members of your board of directors: David F. Hale, Arnold L. Oronsky, and Luke B. Evnin. Please revise your disclosure to identify these entities as underwriters or provide an analysis as to why you believe these entities are not underwriters.

\* \* \*

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 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.

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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.

Please contact Bryan Pitko at (202) 551-3203 or me at (202) 551-3715 with any questions.

Sincerely,

Jeffrey P. Riedler  
Assistant Director

cc: Frederick T. Muto, Esq.  
Jason L. Kent, Esq.  
Cooley Godward Kronish LLP  
4401 Eastgate Mall  
San Diego, CA 92121