

Via Facsimile and U.S. Mail
Mail Stop 6010

June 29, 2007

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

Re: Metabasis Therapeutics, Inc.
Form 10-K for Fiscal Year Ended December 31, 2006
Form 10-Q for the Quarterly Period Ended March 31, 2007
File No. 0-50785

Dear Dr. Laikind:

We have limited our review of your filing to the issues we have addressed in our comments. In our comments, we ask you to provide us with more 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 filings. 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 10-K for the fiscal year ended December 31, 2006

Notes to Financial Statements

Note 1: Organization and Summary of Significant Accounting Policies

Warrants, page F-16

1. You disclose that your warrants are generally required to be settled in cash, but under rare and certain circumstances, such as in a default of funding by the investor, may require the Company to repurchase common stock obtained through the exercise of the warrant. It is unclear whether your use of "settled in cash" is a net cash or physical settlement. It is also unclear why you would be required to repurchase the common stock underlying a warrant exercise if the investor,

presumably the warrant holder, defaults on funding its obligations or why you would have issued common stock to this investor if it did not pay the exercise proceeds. Please provide us in a disclosure-type format revised disclosure that clearly indicates:

- a. whether your warrants provide for physical settlement, net-share settlement or net-cash settlement;
- b. what funding obligations are subject to the default provisions triggering your obligation to repurchase common stock;
- c. the business purpose for being obligated to reacquire your common stock if an investor defaults on its obligation to contribute funds to you; and
- d. your accounting for the repurchase obligation or any net-cash settlement feature.

In addition, please separately reference for us the authoritative literature you rely upon to support your accounting.

Exhibits 31: Certifications

2. Please represent to us that in future periodic report filings you will provide the wording of the certifications exactly as presented in Item 601(b)(31) of Regulation S-K. In this regard, your most recent certifications include the adjectives “annual” and “quarterly” when identifying the report covered by the certifications. Please remove these adjectives in future filings.

Form 10-Q for the quarterly period ended March 31, 2007

Notes to Financial Statements

Note 5: Collaborative Research and Development Agreement, page 8

3. You disclose the receipt of a \$1.8 million non-refundable license fee related to the assignment of a license for pradefovir from Valeant Pharmaceuticals to Schering-Plough. In MD&A you indicate that you recognized this license fee immediately, presumably in accordance with your revenue recognition policy when you have no continuing involvement or no future performance obligations. Please explain to us how the obligations of Sections 2.4 and 5.1 of your Amended and Restated Development and License Agreement with Schering Corporation, filed as Exhibit 10.19 to your 2006 Form 10-K, do not represent future performance obligations requiring the deferral of the up-front license fee over the life of your agreement. In this regard, it appears that Section 2.4(b) of the agreement requires you to continue to provide updated information on the Licensed Technology and to provide reasonable assistance to Schering in connection with understanding and using this information. It appears that Section 5.1 requires you to participate in a Development Steering Committee. Please reference the authoritative literature you rely upon to support your accounting.

Please respond to these comments within 10 business days or tell us when you will provide us with a response. Please furnish a letter that keys your responses to our comments and provides the requested information. Detailed letters greatly facilitate our review. Please furnish your letter on EDGAR under the form type label CORRESP.

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 Exchange Act of 1934 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.

In connection with responding to our comments, please provide, in your letter, a statement from the company acknowledging that:

- the company is responsible for the adequacy and accuracy of the disclosure in the filing;
- staff comments or changes to disclosure in response to staff comments do not foreclose the Commission from taking any action with respect to the filing; and
- the company may not assert staff comments 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 our review of your filing or in response to our comments on your filing.

If you have any questions, please contact Mark Brunhofer, Senior Staff Accountant, at (202) 551-3638. In this regard, do not hesitate to contact me, at (202) 551-3679.

Sincerely,

Jim B. Rosenberg
Senior Assistant Chief
Accountant