

Mail Stop 6010

February 20, 2007

Gary D. Tollefson, M.D., Ph.D.  
President and Chief Executive Officer  
Orexigen Therapeutics, Inc.  
12841 High Bluff Drive, Suite 160  
San Diego, CA 92130

**Re: Orexigen Therapeutics, Inc.  
Amendment No. 2 to the Registration Statement on Form S-1  
Filed February 16, 2007  
File No. 333-139496**

Dear Dr. Tollefson:

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/Amendment No. 2

Balance Sheets, page F-3

1. Please disclose on the face of this statement the aggregate liquidation preference of the "Series C convertible preferred stock." Refer to paragraph 6 of SFAS 129.

\* \* \*

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 supplemental information. Detailed cover letters greatly facilitate our review. Please furnish your letter to us via EDGAR under the form type label CORRESP. Please understand that we may have additional comments after reviewing your amendment and responses to our comments.

You may contact Vanessa Robertson at (202) 551-3649 or Lisa Vanjoske at (202) 551-3614 if you have questions regarding comments on the financial statements and related matters. Please contact Song Brandon at (202) 551-3621, Michael Reedich, Special Counsel at (202) 551-3612, or me at (202) 551-3715 with any other questions.

Sincerely,

Jeffrey Riedler  
Assistant Director

cc: Charles K. Ruck, Esq.  
Cheston J. Larson, Esq.  
Latham & Watkins LLP  
12636 High Bluff Drive, Suite 400  
San Diego, CA 92130