

Mail Stop 6010

January 31, 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. 1 to the Registration Statement on Form S-1  
Filed January 30, 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. 1

Manufacturing, page 78

1. We note your response to comment 19 and your revised disclosure on page 78. Please revise your description of your agreement with PharmaDirections to explain what you mean by "certain initiatives" and also disclose that they receive fees on a per-project basis as approved.

Note 1. Organization and Basis of Presentation, page F-7  
Revenue Recognition, page F-9

2. We note your response to comment 44 and your revised disclosures. Please revise your disclosure to clarify whether research and development revenues were recognized over the term of the agreement in which services were performed.

Note 3. Commitments and Contingencies, page F-13  
Technology and License Agreements, page F-13

3. We note your response to comment 46 and your revised disclosures. Please clarify in your disclosure when you will be required to provide future clinical support under the agreement. In addition, please clarify how recognizing the upfront fee over the estimated life of the patent reflects the obligation period for future clinical support under the agreement.

Operating Lease, page F-16

4. We note your response to comment 47 and your revised disclosure. However, it is still not clear whether there are any withdrawal restrictions on the certificate of deposit. Please disclose the withdrawal restrictions, if any, for the certificate of deposit.

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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 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  
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