

Mail Stop 4720

May 7, 2010

Dr. Jonathan Lewis  
Chief Executive Officer  
ZIOPHARM Oncology, Inc.  
1180 Avenue of the Americas  
19th Floor  
New York, NY 10036

**Re: ZIOPHARM Oncology, Inc.  
Registration Statement on Form S-3  
Filed April 30, 2010  
File Number 333-166444**

Dear Dr. Lewis:

We have reviewed your filing and have the following comment. Where indicated, we think you should revise your document in response to this comment. 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.

Form S-3

Incorporation of Certain Information by Reference, page 20

1. We note that you filed a Form 8-K on January 27, 2010 and a Form 10-K/A on April 30, 2010, both of which are not incorporated by reference into your Form S-3. Please amend your Form S-3 to incorporate by reference these two filings. Please see Item 12(a) of Form S-3 for additional information.

\* \* \*

We urge all persons who are responsible for the accuracy and adequacy of the disclosure in the filings reviewed by the staff to be certain that they have provided all information investors require for an informed 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.

Dr. Jonathan Lewis  
ZIOPHARM Oncology, Inc.  
May 7, 2010  
Page 2

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 this action 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 a 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.

Please contact Rose Zukin at (202) 551-3239 or me at (202) 551-3710 with any questions.

Sincerely,

Jeffrey P. Riedler  
Assistant Director

cc: Alan M. Gilbert, Esq.  
Maslon Edelman Borman & Brand, LLP  
90 South 7th Street, Suite 3300  
Minneapolis, MN 55402