



DIVISION OF  
CORPORATION FINANCE

UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION  
WASHINGTON, D.C. 20549

June 21, 2011

Via E-mail

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 May 18, 2011  
File No. 333-174292**

Dear Dr. Lewis:

We have reviewed your analysis presented in your letter filed June 8, 2011 and have the following comment.

Please respond to this letter by amending your registration statement.

After reviewing any amendment to your registration statement and any information you provide in response to these comments, we may have additional comments.

We disagree with your analysis underlying your conclusion that you may rely on Securities Act Forms C&DI 116.05 (February 27, 2009) in the instant transaction to register the Second Tranche Shares at this time. Accordingly, please amend your registration statement to remove the Second Tranche Shares. Once the milestone has been achieved and the Second Tranche Shares are outstanding, you may register the resale of those shares.

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 the information the Securities Act of 1933 and all applicable Securities Act rules require. 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.

Please refer to Rules 460 and 461 regarding requests for acceleration. 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. Please allow adequate time for us to review any amendment prior to the requested effective date of the registration statement.

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Please contact Karen Ubell, Staff Attorney, at (202) 551-3873, Dan Greenspan, Branch Chief, at (202) 551-3623 or me at (202) 551-3715 with any questions.

Sincerely,

/s/ Daniel Greenspan for

Jeffrey Riedler  
Assistant Director

cc: Alan M. Gilbert, Esq.  
Maslon Edelman Borman & Brand, LLP