



DIVISION OF
CORPORATION FINANCE

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

June 2, 2011

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 limited our review of your registration statement to those issues we have addressed in our comments.

Please respond to this letter by providing the requested information or amending your registration statement. Where you do not believe our comment applies to your facts and circumstances, please tell us why in your response.

After reviewing the information you provide in response to this comment, we may have additional comments.

We note that you are seeking to register the resale of 3,636,926 shares of ZIOPHARM Oncology, Inc.'s common stock comprising the Second Tranche Shares which are issuable upon dosing of the first patient in a ZIOPHARM-conducted U.S. Phase II clinical trial of a product candidate created, produced or developed by us using Intrexon technology. As the Second Tranche Shares issuable upon achievement of this milestone are not currently outstanding and may never be issued, please provide us with a detailed analysis underlying your conclusion that it is appropriate to register the resale of these shares before they are outstanding.

Alternatively, please amend your registration statement to remove these 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.

Notwithstanding our comments, in the event you request acceleration of the effective date of the pending registration statement please provide a written statement from the company 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 staff comments and the declaration of effectiveness as a defense in any proceeding initiated by the Commission or any person under the federal securities laws of the United States.

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.

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,

Jeffrey Riedler
Assistant Director

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