

June 8, 2011

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SUBMITTED VIA EDGAR

Jeffrey P. Reidler
Assistant Director
Division of Corporation Finance
Securities and Exchange Commission
Judiciary Plaza
450 Fifth Street, N.W.
Washington, DC 20549

Re: ZIOPHARM Oncology, Inc. (the "**Company**")
Registration Statement on Form S-3
Filed May 18, 2011
File Number 333-174292

Dear Mr. Riedler:

This letter will respond on behalf of the Company to your comment letter dated June 2, 2011 (the "**Comment Letter**") with respect to the Registration Statement on Form S-3, SEC File No. 333-174292, filed by the Company on May 18, 2011 (the "**Registration Statement**"). In the Comment Letter, you note that the Company is seeking to register the resale of 3,636,926 shares that are not currently outstanding. These shares, referred to as the "Second Tranche Shares," are shares that the Company will be required to issue to Intrexon Corporation, the selling stockholder listed in Registration Statement, subject to the satisfaction of a milestone set forth in a Stock Purchase Agreement between the Company and Intrexon Corporation. You have asked the Company to provide an analysis underlying its conclusion that it is appropriate to register the resale of the Second Tranche Shares before they are outstanding.

Although the Second Tranche Shares are not currently outstanding, the Company concluded that it is appropriate to register the resale of the Second Tranche Shares on the Registration Statement based on the instruction and guidance provided by Question 116.05 of the Securities Act Forms Compliance & Disclosure Interpretations, which provides as follows:

Question 116.05

Question: In reliance on Securities Act Section 4(2), a merger transaction will not be registered. May resales of earnout shares to be issued in connection with the merger be registered on Form S-3 pursuant to General Instruction I.B.3 after the consummation of the merger, even though the shares have not been earned and are not outstanding at the time the registration statement is filed?

Answer: Yes. [Feb. 27, 2009]

This C&DI supports the ability of an issuer to register the resale of earn-out shares offered and sold in a private placement pursuant to General Instruction I.B.3 of Form S-3, even though they have not been earned and are not outstanding at the time the registration statement is filed. Although the private placement in the C&DI occurred in the context of a merger, an issuer's ability to register the resale of yet-to-be issued earn-out shares on Form S-3 should apply equally to shares issued as consideration in an acquisition transaction not involving an actual merger.

Consistent with yet-to-be issued earn-out shares in a transaction involving a merger, the Second Tranche Shares represent contingent earn-out shares that may be issued as additional consideration for the Company's acquisition of assets from Intrexon. The Stock Purchase Agreement between the Company and Intrexon was entered into as part of an overall transaction in which the Company, which is engaged in the development and commercialization of cancer therapeutics, acquired rights under patents and other intellectual property of Intrexon for use in connection with the development and commercialization of product candidates for the treatment of cancer. As partial consideration for acquiring these rights, the Company issued 3,636,926 shares of its common stock to Intrexon on January 12, 2011 (the "First Tranche Shares"). As part of the same transaction, the Company agreed to issue the Second Tranche Shares to Intrexon as "earn-out" consideration subject to satisfying a specified milestone (namely, dosing of a patient in a Company-conducted U.S. Phase II clinical trial of a product candidate that uses the Intrexon technology). The number of Second Tranche Shares was determined in part based on the perceived additional value that rights to Intrexon's technology may provide if the Company is able to progress the development of oncologic product candidates using that technology. In light of the structure of the overall transaction, the Company considers the Second Tranche Shares to be contingent earn-out consideration in an acquisition transaction and, based on the C&DI referred to above, the Company has concluded that it is appropriate to register the resale of the Second Tranche on the Registration Statement before they are outstanding.

Jeffrey P. Reidler
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Securities and Exchange Commission
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Should you have additional comments or questions regarding the Registration Statement, please direct them to the undersigned by telephone at (612) 672-8381, or by facsimile at (612) 642-8381; or to Richard E. Bagley, the Company's President, Chief Operating Officer and Chief Financial Officer by telephone at (617) 259-1978, or by facsimile at (617) 241-2855.

Regards,

/s/ Alan M. Gilbert
Alan M. Gilbert, Esq.

cc: via email): Dr. Jonathan Lewis
Richard E. Bagley
Tyler Cook
Kevin Lafond
