



DIVISION OF
CORPORATION FINANCE

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

December 3, 2010

Richard E. Bagley
President and Chief Financial Officer
ZIOPHARM Oncology, Inc.
1180 Avenue of the Americas, 19th Floor,
New York, NY 10036

Re: ZIOPHARM Oncology, Inc.
Form 10-K for the Fiscal Year Ended December 31, 2009
Filed March 17, 2010
Form 10-K/A for the Fiscal Year Ended December 31, 2009
Filed April 30, 2010
File Number: 001-33038

Dear Mr. Bagley:

We have reviewed your October 15, 2010 response to our September 20, 2010 letter and have the following comments. In our comments, we ask you to provide us with information so we may better understand your disclosure.

Please respond to this letter within ten business days by providing us the requested information or by advising us when you will provide the requested response. Please furnish us a letter on EDGAR under the form type label CORRESP that keys your responses to our comments. If you do not believe a comment applies to your facts and circumstances, please tell us why in your response.

After reviewing the information provided, we may have additional comments.

Form 10-K for the Fiscal Year Ended December 31, 2009

Notes to Financial Statements

Note 8. Warrants, page F-26

1. We acknowledge your response to comment 5. It remains unclear how you determined that the "down-round" antidilution features have a "negligible" effect on the valuation of the warrants and that the Black-Scholes option pricing model is appropriate to value these warrants. You further indicate in your response that you have undertaken a valuation using the binomial model and will use this method to value the warrants if the variance between the two methods, in the future, is significant. Please provide us with an analysis of the warrant valuation using both methodologies at December 31, 2009 and each 2010 interim valuation date. To the extent there is a significant variance, please explain why

using the Black-Scholes model to calculate the fair value of the warrant liability for the above periods is reasonable.

Form 10-K/A filed April 30, 2010

Item 13. Certain Relationships and Related Transactions, and Director Independence
Related Party Transactions, page 18

2. We have reviewed your response to prior comment 7. Please confirm that in future filings you will disclose in this section that Riverbank allocated warrants to purchase 40,298 shares of your common stock to Mr. McInerney from its sub-placement agent compensation.

You may contact Melissa Rocha, Accounting Branch Chief, at (202) 551-3854 if you have any questions regarding the processing of your response as well as any questions regarding comments on the financial statements and related matters. You may contact Karen Ubell, Staff Attorney, at (202) 551-3873 or Jennifer Riegel, Staff Attorney, at (202) 551-3575 with questions on any of the other comments. In this regard, do not hesitate to contact me, at (202) 551-3679.

Sincerely,

Jim B. Rosenberg
Senior Assistant Chief Accountant