

December 10, 2010

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SUBMITTED VIA EDGAR

Jim B. Rosenberg
Senior Assistant Chief Accountant
Division of Corporation Finance
United States Securities and Exchange Commission
100 F Street, N.E.
Washington, D.C. 20549

**Re: ZIOPHARM Oncology, Inc. (the "Company")
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. Rosenberg:

This letter will respond on behalf of the Company to your comment letter dated December 3, 2010 (the "**Comment Letter**") with respect to the above referenced documents filed by the Company with the Securities and Exchange Commission (the "**Commission**") (collectively, the "**Form 10-K**"). To facilitate your review, we have included in this letter your original comments (in bold) followed by our response, which has been numbered to correspond to your letter.

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. 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 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.**
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The Commission's original request was prospective in nature, requesting that we examine the applicability of using a binomial model to value the Company's warrants moving forward. Accordingly, the Company prepared a binomial valuation model at September 30, 2010, which it compared to its Black-Scholes valuation model at September 30, 2010. The result of the comparison showed a difference of \$0.01 per warrant share, or \$77,906 in the aggregate, between the two models. Based on an assessment of both quantitative and qualitative factors under a SAB 99 materiality analysis, the Company concluded that the difference at September 30, 2010 was not material to its financial statements as a whole.

Because the Commission's original request was prospective in nature, and based on the cost and timing involved in preparing warrant valuations using a binomial valuation model at multiple points in time, the Company has not prepared such valuations in connection with this response. However, differences in warrant valuation under the two models employed will not vary considerably so long as the Company utilizes the same input assumptions. As such, the Company believes that the difference in warrant valuation at December 31, 2009 and each 2010 interim valuation date will also be immaterial to its financial statements as a whole.

Similarly, the Company believes that the difference will continue to be immaterial to the Company's financial statements as a whole so long as the Company utilizes the same input assumptions. As a result, the Company believes that its continued use of the Black-Scholes valuation model, which is considerably more cost-effective than employing a binomial valuation model, is appropriate. The Company will continue to monitor its input assumptions and the quantitative and qualitative factors utilized under its SAB 99 materiality analysis, and will again re-calculate the difference in warrant valuation between the two models if warranted based on changes in such inputs or assumptions.

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.

In the "Certain Relationships and Related Transactions, and Director Independence Related Party Transactions" section of its future filings, the Company will disclose that Riverbank Capital Securities, Inc. allocated warrants to purchase 40,298 shares of the Company's common stock that it received as sub-placement agent compensation to Mr. McInerney.

Should you have any questions or comments regarding the foregoing, 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 mail): Dr. Jonathan Lewis
Richard Bagley
Tyler Cook
Kevin Lafond
