October 15, 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 September 20, 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

License Agreements and Intellectual Property, page 5

1. **With respect to your agreements with each of The University of Texas M.D. Anderson Cancer Center and the Texas A&M University System, DEKK-Tec and Baxter, please provide proposed revised disclosure for inclusion in future filings that expands your discussion to include a range of royalty payments (e.g. low single digits or a range not to exceed ten percent) and the term and termination provisions for each agreement.**

Set forth below is revised disclosure regarding the Company's license agreements and intellectual property that the Company proposes to include in its future filings. The disclosure below has been expanded from that included in the Form 10-K to include a range of royalty payments and the term and termination provisions for each agreement. The proposed future disclosure is marked below to show additions to the corresponding disclosure in the Form 10-K.

Patent and Technology License Agreement — The University of Texas M. D. Anderson Cancer Center and the Texas A&M University System.

On August 24, 2004, the Company entered into a patent and technology license agreement with The Board of Regents of the University of Texas System, acting on behalf of The University of Texas M. D. Anderson Cancer Center and the Texas A&M University System (collectively, the "Licensors"). Under this agreement, the Company was granted an exclusive, worldwide license to rights (including rights to U.S. and foreign patent and patent applications and related improvements and know-how) for the manufacture and commercialization of two classes of organic arsenicals (water- and lipid-based) for human and animal use. The class of water-based organic arsenicals includes darinaparsin.

As partial consideration for the license rights obtained, the Company made an upfront payment in 2004 of $125 thousand and granted the Licensors 250,487 shares of the Company's common stock. In addition, the Company issued options to purchase an additional 50,222 shares outside the 2003 Stock Option Plan for $0.002 per share following the successful completion of certain clinical milestones, which vested with respect to 12,555 shares upon the filing of an Investigation New Drug application ("IND") for darinaparsin in 2005 and vested with respect to another 25,111 shares upon the completion of dosing of the last patient for both Phase I clinical trials in 2007. The Company recorded $120 thousand of stock based compensation expense related to the vesting in 2007. The remaining 12,556 shares will vest upon enrollment of the first patient in a multi-center pivotal clinical trial, i.e., a human clinical trial intended to provide the substantial evidence of efficacy necessary to support the filing of an approvable New Drug Application ("NDA"). In addition, the Licensors are entitled to receive certain milestone payments, including $100 thousand that was paid in 2005 upon the commencement of Phase I clinical trial and $250 thousand that was paid in 2006 upon the dosing of the first patient in the Registrant-sponsored Phase II clinical trial for darinaparsin. The Company may be required to make additional payments upon achievement of certain other milestones, in varying amounts which on a cumulative basis could total up to $4.85 million. In addition, the Licensors are entitled to receive **single digit percentage** royalty payments on sales of a licensed product should such a product be approved for commercial sale and sales of a licensed product be effected in the United States, Canada, the European Union or Japan. The Licensors also will be entitled to receive a portion of any fees that the Company may receive from a possible sublicense under certain circumstances. The Company also paid the Licensors $100 thousand in 2006 and 2007 to conduct scientific research with the Company obtaining exclusive right to all resulting intellectual property rights. The sponsored research agreements governing this research and any related extensions expired in February 2008 with no payments being made in 2008 or 2009.

The license agreement also contains other provisions customary and common in similar agreements within the industry, such as the right to sublicense the Company rights under the agreement. However, if the Company sublicenses its rights prior to the commencement of a pivotal study, i.e., a human clinical trial intended to provide the substantial evidence of efficacy necessary to support the filing of an approvable NDA, the Licensors will be entitled to receive a share of the payments received by the Company in exchange for the sublicense (subject to certain exceptions). **The term of the license agreement extends until the expiration of all claims under patents and patent applications associated with the licensed technology, subject to earlier termination in the event of defaults by the Company or the Licensors under the license agreement, or if the Company becomes bankrupt or insolvent.**

License Agreement with DEKK-Tec, Inc.

On October 15, 2004, the Company entered into a license agreement with DEKK-Tec, Inc., pursuant to which it was granted an exclusive, worldwide license for palifosfamide. As part of the signing of license agreement with DEKK-Tec, the Company expensed an upfront $50 thousand payment to DEKK-Tec in 2004.

In consideration for the license rights, DEKK-Tec is entitled to receive milestone payments upon the occurrence of certain achievements of certain milestones in varying amounts which on a cumulative basis may total $3.9 million. Of the aggregate milestone payments, most of the total amount will be creditable against future royalty payments as referenced below. The Company expensed a $100 thousand milestone payment upon achieving Phase II milestones during the year ended December 31, 2006. Additionally, in 2004 the Company issued DEKK-Tec an option to purchase 27,616 shares of the Company’s common stock for $0.02 per share. Upon the execution of the license agreement, 6,904 shares vested and were subsequently exercised in 2005 and the remaining options will vest upon certain milestone events, culminating with final FDA approval of the first NDA submitted by the Company (or by its sublicensee) for palifosfamide. None of the remaining options have vested as of December 31, 2009. DEKK-Tec is entitled to receive **single digit percentage** royalty payments on the sales of palifosfamide should it be approved for commercial sale. There were no payments during 2008 or 2009. **The Company’s obligation to pay royalties will terminate on a country-by-country basis upon the expiration of all valid claims of patents in such country covering licensed product, subject to earlier termination in the event of defaults by the parties under the license agreement.**

License Agreement with Baxter Healthcare Corporation

On November 3, 2006, the Company entered into a definitive Asset Purchase Agreement (for indibulin) and License Agreement (to Baxter's proprietary nanosuspension technology) with affiliates of Baxter. Indibulin is a novel anti-cancer agent that binds to tubulin, one of the essential proteins for chromosomal segregation, and targets mitosis like the taxanes and vinca alkaloids. It is being developed as an oral form. Among the more well known antimitotic drugs are the taxanes (paclitaxel, docetaxel) and the vinca alkaloids (vincristine, vinblastine). The purchase included the entire indibulin intellectual property portfolio as well as existing drug substance and capsule inventories. The terms of the Asset Purchase Agreement included an upfront cash payment of approximately $1.1 million and an additional $100 thousand payment for existing inventory, both of which were expensed in 2006. In addition to the upfront costs, the Asset Purchase Agreement includes additional milestone payments that could amount to approximately $8 million in the aggregate and royalties on net sales of products covered by a valid claim of a patent for the life of the patent on a country-by-country basis. The Company expensed a $625 thousand milestone payment upon the successful U.S. IND application for indibulin in 2007. The License Agreement requires payment of a $15 thousand annual patent and license prosecution/maintenance fee through the expiration of the last to expire of the licensed patents**,** which is expected to expire in 2025**,** and **single digit percentage** royalties on net sales of licensed products covered by a valid claim of a patent for the life of the patent on a country-by-country basis. **The term of the license agreement extends until the expiration of the last to expire of the patents covering the licensed products, subject to earlier termination in the event of defaults by the parties under the license agreement.**

In October 2009, the Baxter License Agreement was amended to allow the Company to manufacturer indibulin.

2. **We note your disclosure on pages 25-27 that your product candidates are covered by certain issued patents and patent applications in the U.S. and foreign countries. Please provide proposed revised disclosure for inclusion in future filings that expands your disclosure to identify the number of material patents and patent applications for each of your products, including the jurisdiction and, as applicable, the expiration of such patents.**

Set forth below is proposed disclosure regarding the issued patents and patent applications in the U.S. and in foreign countries, which cover the Company's product candidates:

Patents and Other Proprietary Rights

Our goal is to obtain, maintain, and enforce patent protection for our products, formulations, processes, methods, and other proprietary technologies in order to preserve our trade secrets and to operate without infringing upon the proprietary rights of other parties, both in the United States and in other countries. Our policy is to actively seek the broadest possible intellectual property protection for our product candidates through a combination of contractual arrangements and patents, both in the United States and abroad.

Patents extend for varying periods according to the date of patent filing or grant and the legal term of patents in the various countries where patent protection is obtained. The actual protection offering by a patent, which can vary from country to country, depends of the type of patent, the scope of its coverage and the availability of legal remedies in the country.

We also depend upon the skills, knowledge, and experience of our scientific and technical personnel, as well as those of our advisors, consultants, and other contractors, none of which is patentable. To help protect proprietary know-how, which is not patentable, and for inventions for which patents may be difficult to enforce, we currently rely, and in the future will continue to rely, on trade secret protection and confidentiality agreements to protect our interests. To this end, we generally require employees, consultants, advisors and other contractors to enter into confidentiality agreements that prohibit the disclosure of confidential information and, where applicable, require disclosure and assignment to us of the ideas, developments, discoveries and inventions important to our business.

Our patent position and proprietary rights are subject to certain risks and uncertainties. Please read the “Risk Factors” section of this report for information about certain risks and uncertainties that may affect our patent position and proprietary rights.

Additional information about material patents and other proprietary rights covering our product candidates is set forth below.

Darinaparsin

The patent estate covering darinaparsin compositions, methods of use and methods of manufacture includes three issued United States patents, as well as issued patents in certain foreign jurisdictions, all of which are scheduled to expire in 2023. We license these patents, as well as pending applications in various foreign jurisdictions, from The University of Texas M. D. Anderson Cancer Center and the Texas A&M University System pursuant to an Agreement dated August 24, 2004. We have also filed pending applications in the United States and various foreign jurisdictions.

Palifosfamide

The patent estate covering palifosfamide compositions, methods of use and methods of manufacture includes one issued United States patent that is scheduled to expire in 2029, as well as pending applications in the United States and various foreign jurisdictions. We license the issued patent and the patent applications from DEKK-Tec, Inc. pursuant to an Agreement dated October 15, 2004. We have also filed pending applications in the United States and various foreign jurisdictions.

Indibulin

The patent estate covering indibulin compositions, methods of use and methods of manufacture includes pending applications in the United States, and various foreign jurisdictions, all of which we license from affiliates of Baxter Healthcare Corporation pursuant to an agreement dated November 6, 2006. We also have five issued United States patents that are scheduled to expire at varying times between 2017 and 2019, as well as issued patents in various foreign jurisdictions, and have filed pending applications in the United States and various foreign jurisdictions.

Management Discussion and Analysis of Financial Condition and Results of Operation

Results of Operations for the Fiscal Year Ended December 31, 2009 versus December 31, 2008

Research and Development Expenses, page 30

3. **Please refer to the Division of Corporation Finance "Current Issues and Rulemaking Projects Quarterly Update" under section VIII-Industry Specific Issues – Accounting and Disclosure by Companies Engaged in Research and Development Activities. You can find it at the following website address: http://www.sec.gov/divisions/corpfin/cfcrq032001.htm#secviii.**

Please provide us proposed disclosure to be included in your future filings beginning with your September 30, 2010 Form 10-Q of the following information for each of your major research and development projects:

a. **The costs incurred during each period presented and to date on the project;**
b. **The nature, timing and estimated costs of the efforts necessary to complete the project;**
c. **The anticipated completion dates;**
d. **The risks and uncertainties associated with completing development on schedule, and the consequences to operations, financial position and liquidity if the project is not completed timely; and finally**
e. **The period in which material net cash inflows from significant projects are expected to commence.**

Regarding b., if you do not maintain any research and development costs by project, disclose that fact and explain why management does not maintain and evaluate research and development costs by project. Provide other quantitative or qualitative disclosure that indicates the amount of the company's resources being used on the project.

Regarding c. and d., disclose the amount or range of estimated costs and timing to complete the phase in process and each future phase. To the extent that information is not estimable , disclose those facts and circumstances indicating the uncertainties that preclude you from making a reasonable estimate.

Set forth below is disclosure that the Company proposes to include in future filings, beginning with its Form 10-Q for the quarter ended September 30, 2010, which includes expanded information for each of the Company's major research and development projects.

Overview

Our research and development expense consists primarily of salaries and related expenses for personnel, costs of contract manufacturing services, costs of facilities and equipment, fees paid to professional service providers in conjunction with our clinical trials, fees paid to research organizations in conjunction with pre-clinical animal studies, costs of materials used in research and development, consulting, license and milestone payments and sponsored research fees paid to third parties.

We have not accumulated and tracked our internal historical research and development costs or our personnel and personnel-related costs on a program-by-program basis. Our employee and infrastructure resources are allocated across several projects, and many of our costs are directed to broadly applicable research endeavors. As a result, we cannot state or accurately estimate the costs incurred for each of our oncology programs on a program-by-program basis.

In 2010, our clinical projects consisted primarily of a Phase 3 project for our lead product candidate palifosfamide. This project was initiated during 2010. The expenses incurred by us to third parties were $2.5 million and $3.1 million for the three and nine months ended September 30, 2010, respectively and $3.1 million for project to date.

Our future research and development expenses in support of our current and future programs will be subject to numerous uncertainties in timing and cost to completion. We test potential products in numerous pre-clinical studies for safety, toxicology and efficacy. We may conduct multiple clinical trials for each product. As we obtain results from trials, we may elect to discontinue or delay clinical trials for certain products in order to focus our resources on more promising products or indications. Completion of clinical trials may take several years or more, and the length of time generally varies substantially according to the type, complexity, novelty and intended use of a product. It is not unusual for pre-clinical and clinical development of each of these types of products to require the expenditure of substantial resources.

We estimate that clinical trials of the type generally needed to secure a new drug approval are typically completed over the following timelines:

Clinical Phase	Estimated Completion Period
Phase 1	1 - 2 years
Phase 2	2 - 3 years
Phase 3	2-4 years

The duration and the cost of clinical trials may vary significantly over the life of a project as a result of differences arising during clinical development, including, among others, the following:

- the number of clinical sites included in the trials;
- the length of time required to enroll suitable patents;
- the number of patients that ultimately participate in the trials;
- the duration of patient follow-up to ensure the absence of long-term product-related adverse events; and
- the efficacy and safety profile of the product.

As a result of the uncertainties discussed above, we are unable to determine or accurately estimate the duration and completion costs of our programs or when and to what extent we will receive cash inflows from the commercialization and sale of a product. Our inability to complete our programs in a timely manner or our failure to enter into appropriate collaborative agreements could significantly increase our capital requirements and could inversely impact our liquidity. These uncertainties could force us to seek additional, external sources of financing from time-to-time in order to continue with our product development strategy. Our ability to raise additional capital, or to do so on terms reasonably acceptable to us, would jeopardize the future success of our business.

Contractual Obligations, page 33

4. **Please provide us proposed revised disclosure to be included in your future filings beginning with your September 30, 2010 Form 10-Q of your table of contractual obligations to include the annual patent and license prosecution/maintenance fee due to Baxter Healthcare Corporation and any other obligations resulting from your license agreements.**

Set forth below is proposed disclosure to be included in the Company's future filings, beginning with the September 30, 2010 Form 10-Q, of the Company's table of contractual obligations. As proposed, the table of contractual obligations includes the annual patent and license prosecution/maintenance fee due to Baxter Healthcare Corporation and any other obligations resulting from the Company's license agreements.

Contractual obligations

The following table summarizes our outstanding obligations as of September 30, 2010 and the effect those obligations are expected to have on our liquidity and cash flows in future periods:

($ in thousands)	Total	Less than 1 year	2 - 3 years	4 - 5 years	More than 5 years
Operating leases	$ 1,051	$ 410	$ 536	$ 105	$ -
Royalty and license fees	1,625	25	300	800	500
Total	$ 2,676	$ 435	$ 836	$ 905	$ 500

Our commitments for operating leases relate to the lease for our corporate headquarters in New York, New York and our operations center in Boston, Massachusetts. Our commitments for royalty and license fees relate to our patent agreement with Baxter Healthcare Corporation and our royalty agreements with Southern Research Institute and Baxter Healthcare Corporation.

Notes to Financial Statements

Note 8. Warrants, page F-26

5. **With regard to the warrants issued in connection with your December 2009 public offering, you state that you classified these warrants as derivative liabilities as they were not indexed to the Company's own stock. It appears in the agreement that this may be a result of anti-dilution provisions. Please provide us proposed revised disclosure to be included in future filings beginning with your September 30, 2010 Form 10-Q that discusses the key terms of the warrants that led to the derivative classification. Regarding the valuation of your warrants using the Black-Scholes model, this model does not appear to take into account the warrants down-round protection. It appears to us that the price adjustment feature would add value to the warrant. Please explain to us why you use the Black-Scholes option pricing model, instead of a binomial or lattice pricing model to value your warrants. It appears that binomial or lattice models are better suited to handle the potential changes to your warrant exercise price.**

The warrants issued in connection with the Company's December 2009 public offering are classified as derivative liabilities not indexed to the Company's own stock. This classification is due to warrant provisions that provide for anti-dilution protection. In its future filings, beginning with its September 30, 2010 Form 10-Q, the Company will discuss the key terms of the warrants that led to the derivative classification. In that regard, proposed revised disclosure is set forth below:

Also, in connection with the December 2009 public offering, the Company issued warrants to purchase an aggregate of 8,206,520 shares of common stock (including the investor warrants and 464,520 warrants issued to the Underwriters). The investor warrants are exercisable immediately and the underwriter warrants exercisable six months after the date of issuance. The warrants have an exercise price of $4.02 per share and have a five year term. Subject to certain exceptions, these warrants provide for anti-dilution protection should common stock or common stock equivalents be subsequently issued at a price less than the exercise price of the warrants then in effect.

The Company assessed whether the warrants require accounting as derivatives and, based on the anti-dilution protection provided to the warrantholders, determined that the warrants were not indexed to the Company's own stock in accordance with accounting standards codification Topic 815, Derivatives and Hedging. As such, the Company has concluded the warrants did not meet the scope exception for determining whether the instruments require accounting as derivatives and should be classified in liabilities. The fair value of the warrants was estimated at $22.9 million using a Black-Scholes model with the following assumptions: expected volatility of 105%, risk free interest rate of 2.14%, expected life of five years and no dividends.

The Company believes that the "down-round" antidilution protection to which warrantholders are entitled has a negligible effect on the valuation of the warrants. The Company has therefore elected to use the Black-Scholes option pricing model to value the warrants. However, the Company has undertaken a valuation of the warrants using a binomial pricing model and will use such pricing model to value the warrants going forward if the variance in warrant value resulting from the two pricing models proves to be significant.

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

Item 11. Executive Compensation

Summary Compensation Table, page 9

6. **You disclose that you are reporting the bonus amounts for your named executive officers in 2007 and 2008 in the year in which such amounts were paid, rather than in the year in which such bonus was earned. Your summary compensation table should reflect in each year's bonus column the amount of year-end bonus earned during such year even if the payment was made in the subsequent year. Please confirm that in future filings you will report the year-end cash and equity bonuses as paid in the year during which such bonuses were earned and that you will revise the compensation for prior years accordingly.**

In its future filings, the Company will report the year-end cash and equity bonuses as paid in the year during which such bonuses were earned, rather than the year in which such bonuses were paid (if different), and the Company will revise the compensation for prior years accordingly.

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

7. **You disclose that Riverbank may allocate or may have allocated to Mr. McInerney a portion of the compensation that it received for serving as a sub-placement agent. Please advise us whether Riverbank directly allocated a portion of the consideration for service as a sub-placement agent in connection with your September 15, 2009 private placement and, if so, the amount allocated to Mr. McInerney. In addition, please file a copy of the placement agent agreement as an exhibit.**

As set forth in the 10-K, the Company paid Riverbank Capital Securities, Inc. ("Riverbank") approximately $185,000 and issued to Riverbank and its designees warrants to purchase a total of 65,843 shares of the Company's common stock, as compensation for serving as a sub-placement agent in connection with the Company's September 15, 2009 private placement. Of such compensation, Riverbank allocated warrants to purchase 40,298 shares of common stock to Mr. McInerney.

In connection with the private placement, the Company entered into a placement agency agreement with Rodman & Renshaw, LLC, a subsidiary of Rodman & Renshaw Capital Group, Inc. ("Rodman"), whereby Rodman agreed to serve as placement agent. Rodman, in turn, engaged Riverbank to serve as a sub-agent under an agreement to which the Company was not a party. The Company will file a copy of the placement agency agreement with Rodman as an exhibit to its Form 10-Q for the quarter ending September 30, 2010.

In connection with this response, the Company hereby acknowledges that:

- that it is responsible for the adequacy and accuracy of the disclosure in its filings with the Commission;
- staff comments or changes to disclosure in response to staff comments do not foreclose the Commission from taking any action with respect to the filings; and
- The Company may not assert staff comments as a defense in any proceeding initiated by the Commission or any person under the federal securities laws of the United States.

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