The information in this prospectus is not complete and may be changed. We may not sell these securities until the registration statement filed with the Securities and Exchange Commission is effective. This prospectus is not an offer to sell these securities and it is not soliciting offers to buy these securities in any jurisdiction where the offer or sale is not permitted.

Subject to Completion, Dated December 3, 2009

PROSPECTUS SUPPLEMENT
(To Prospectus dated September 21, 2009)

Filed Pursuant to Rule 424(b)(5)
File No. 333-161453

ZIOPHARM Oncology, Inc.

Shares
Warrants to Purchase Shares

Common Stock

We are offering shares of our common stock, par value $0.001 per share, and warrants to purchase up to shares of our common stock pursuant to this prospectus supplement and the accompanying prospectus. The common stock and warrants will be sold in units, with each unit consisting of one share of common stock and a warrant to purchase 0.50 of a share of our common stock at an exercise price of $ per share. Each unit will be sold at a purchase price of $. Units will not be issued or certificated. The shares of common stock and warrants are immediately separable and will be issued separately. We are also issuing warrants to purchase up to an aggregate of shares of our common stock at an exercise price of $ per share to the underwriters as underwriting compensation. See "Underwriting" beginning on page S-12 of this prospectus supplement for more information regarding these arrangements.

Our common stock is listed on the NASDAQ Capital Market under the symbol "ZIOP." On December 2, 2009, the last reported sale price of our common stock on the NASDAQ Capital Market was $3.72 per share. There is no established public trading market for the offered warrants and we do not expect a market to develop. In addition, we do not intend to apply for listing of the warrants on any national securities exchange.

Investing in our securities involves risks. See "Risk Factors" beginning on page S-7 of this prospectus supplement.

	Per Unit	Total
Public offering price	$	$
Underwriting discounts and commissions	$	$
Proceeds, before expenses, to us	$	$

Delivery of the shares of the securities offered hereby is expected to be made on or about , 2009.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus supplement or the accompanying prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

JMP Securities **Rodman & Renshaw, LLC**

The date of this prospectus supplement is , 2009.

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Prospectus Supplement

Prospectus

ABOUT THIS PROSPECTUS

This prospectus supplement is part of a registration statement that we filed with the Securities and Exchange Commission (the "SEC"), using a "shelf" registration process. This document has two parts. The first part is the prospectus supplement, which describes the specific terms of the offering. The second part is the accompanying prospectus, which describes more general information, some of which may not apply to the offering. You should read both this prospectus supplement and the accompanying prospectus, together with the additional information described under the heading "Where You Can Find More Information."

You should rely only on the information contained or incorporated by reference in this prospectus supplement, in the accompanying prospectus, in any other prospectus supplement and in any free writing prospectus filed by us with the SEC. We have not, and the underwriters have not, authorized any other person to provide you with different information. If anyone provides you with different or inconsistent information, you should not rely on it. We are not, and the underwriters are not, making an offer to sell these securities in any jurisdiction where the offer or sale is not permitted. You should assume that the information appearing in this prospectus supplement, the accompanying prospectus and the documents incorporated by reference is accurate only as of each of their respective dates. Our business, financial condition, results of operations and prospects may have changed since those dates. To extent that any statement that we make in this prospectus supplement differs from or is inconsistent with statements made in the accompanying prospectus or any documents incorporated by reference therein, the statements made in this prospectus supplement will be deemed to modify or supersede those made in the accompanying prospectus and such documents incorporated by reference therein.

Unless the context otherwise requires, references in this prospectus supplement to "ZIOPHARM Oncology," "ZIOPHARM," "we," "us," and "our" refer to ZIOPHARM Oncology, Inc.

This prospectus supplement, the accompanying prospectus, and the information incorporated herein and therein by reference includes trademarks, service marks and trade names owned by us or other companies. All trademarks, service marks and trade names included or incorporated by reference into this prospectus supplement or the accompanying prospectus are the property of their respective owners.

PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights certain information about us, this offering and information appearing elsewhere in this prospectus supplement, in the accompanying prospectus and in the documents we incorporate by reference. This summary is not complete and does not contain all of the information that you should consider before investing in our securities. You should read this entire prospectus supplement and the accompanying prospectus carefully, including the information referred to under the heading "Risk Factors" in this prospectus supplement beginning on page S-7, and the risk factors and the financial statements and other information contained in our filings with the SEC which have been incorporated by reference in this prospectus supplement and the accompanying prospectus, when making an investment decision.

Our Company

ZIOPHARM Oncology, Inc. is a biopharmaceutical company that is seeking to develop and commercialize a diverse, risk-sensitive portfolio of in-licensed cancer drugs that can address unmet medical needs through enhanced efficacy and/or safety and quality of life. Our principal focus is on the licensing and development of proprietary small molecule drug candidates that are related to cancer therapeutics already on the market or in development and can be administered by intravenous ("IV") and/or oral capsule forms. We believe this strategy will result in lower risk and expedited drug development programs with product candidates having a low cost of manufacturing to address changing reimbursement requirements around the world. While we may commercialize our products on our own in North America, we recognize that favorable clinical trial results can be better addressed by partnering with companies with the requisite financial resources and commercialization bandwidth. The Company could also negotiate the right to complete development and to enter into commercialization arrangements in certain other geographies. Our three product candidates are darinaparsin (Zinapar™, ZIO-101), palifosfamide (Zymafos™, ZIO-201), and indibulin (Zybulin™, ZIO-301), with both darinaparsin and palifosfamide having completed phase II clinical trials in refractory hematological malignancies and advanced sarcoma respectively, and with favorable interim results also reported on the palifosfamide randomized phase II trial (PICASSO) in the front- and second-line setting of soft tissue sarcoma (STS). The interim results were subsequently reported at the Connective Tissue Oncology Society's (CTOS) annual meeting after enrollment in the PICASSO trial was terminated early at 67 patients. The Company's focus had been on completing enrollment in the palifosfamide randomized Phase II trial in support of a planned registration trial for palifosfamide in combination with doxorubicin versus doxorubicin alone in the front- and second-line setting of STS. We anticipate the initiation of such a trial as early as the first half of 2010. Our more recent focus includes having requested an end of Phase II meeting with the U.S. Food and Drug Administration (FDA) not only for palifosfamide but also for darinaparsin, the latter with regard to a potential registration trial in the first half of 2010 of darinaparsin in combination with CHOP versus CHOP alone in the front-line setting of peripheral T-cell lymphoma, while at the same time progressing with the initiation the indibulin Phase I portion of a Phase I-II trial in breast cancer involving a dosing schedule developed preclinically by the Company's consultant Dr. Larry Norton, also expected in the first half of 2010.

- ZIO-101, or darinaparsin (Zinapar™), is an anti-mitochondrial (organic arsenic) compound covered by issued patents and pending patent applications in the U.S. and in foreign countries. A form of commercially available inorganic arsenic (arsenic trioxide [Trisenox ®]; "ATO") has been approved in the United States, the European Union and Japan for the treatment of acute promyelocytic leukemia ("APL"), a precancerous condition. In the United States, ATO is on the compendia listing for the therapy of multiple myeloma, and has been studied for the treatment of various other cancers. Nevertheless, ATO has been shown to be toxic to the heart, liver, and brain, which limits its use as an anti-cancer agent. ATO carries a "black box" warning for ECG abnormalities since arsenic trioxide has been shown to cause QT interval prolongation and complete atrioventricular block. QT prolongation can lead to a torsade de pointes-type ventricular arrhythmia, which can be fatal. Inorganic arsenic has also been shown to cause cancer of the skin and lung in humans. The toxicity of arsenic is generally correlated to its accumulation in organs and tissues. Our preclinical and clinical studies to date have demonstrated that darinaparsin is considerably less toxic than inorganic arsenic, particularly with regard to cardiac toxicity. In vitro testing of darinaparsin using the National Cancer Institute's human cancer cell panel demonstrated activity against a series of tumor cell lines including lung, colon, brain, melanoma, ovarian, and kidney cancer. Moderate activity was shown against breast and prostate cancer tumor cell lines. In addition to solid tumors, in vitro testing in both the National Cancer Institute's cancer cell panel and in vivo testing in a leukemia animal model demonstrated substantial activity against hematological cancers (cancers of the blood and blood-forming tissues) such as leukemia, lymphoma, myelodysplastic syndromes, and multiple myeloma. Results indicate significant activity against the HuT 78 cutaneous T-cell lymphoma, the NK-G2MI natural killer-cell NHL, KARPAS-299 T-cell NHL, SU-DHL-8 B-cell NHL, SU-DHL-10 B-cell NHL and SU-DHL-16 B-cell NHL cell lines. Preclinical studies have also established anti-angiogenic properties of darinaparsin and provided support for the development of an oral capsule form of the drug, and established synergy of darinaparsin in combination with other approved anti-cancer agents.

Phase I testing of the intravenous (IV) form of darinaparsin in solid tumors and hematological cancers has been completed. The Company reported clinical activity and, importantly, a safety profile from these studies as predicted by preclinical results. The Company subsequently completed Phase II studies in advanced myeloma and primary liver cancer and is nearing completion of a Phase II study in certain other hematological cancers. In addition, the Company is completing two Phase I studies with an oral capsule form of darinaparsin. At the May 2009 annual meeting of the American Society of Clinical Oncology ("ASCO"), the Company reported favorable results from the trial with IV-administered darinaparsin in lymphoma, particularly peripheral T-cell lymphoma ("PTCL"). In the ongoing Phase I trials, also reported at the ASCO annual meeting, preliminary data primarily in solid tumors indicate the oral form is active and well tolerated. The Company is presently initiating data collection for completing the IV Phase II trial with intention of meeting with the U.S. Food and Drug Administration ("FDA") to progress the IV program into a potentially pivotal trial in PTCL as early as the first half of 2010. The Company intends to fund that trial most likely from potential partnering and other third party arrangements. We expect that the oral Phase I program will continue to completion with establishment of a maximum tolerated dose ("MTD").

- ZIO-201, or palifosfamide (Zymafos™), is the active metabolite of ifosfamide, a compound chemically related to cyclophosphamide. Patent applications covering proprietary forms of palifosfamide for pharmaceutical composition and method of use have been filed in the U.S. and internationally. Like cyclophosphamide, ifosfamide and bendamustine, palifosfamide is a DNA alkylating agent, a form of cancer therapy to treat a wide range of solid tumors and hematological malignancies. The Company believes that cyclophosphamide is the most widely used alkylating agent in cancer therapy, with significant use in the treatment of breast cancer and non-Hodgkin's lymphoma. Bendamustine has been recently approved and successfully launched by Cephalon in the U.S. and Europe to treat certain hematological malignancies. Ifosfamide has been shown to be effective at high doses in the treatment of sarcoma and lymphoma, either by itself or in combination with other anticancer agents. Ifosfamide is approved by the FDA as a treatment for testicular cancer while ifosfamide-based treatment is a standard of care for sarcoma, although it is not licensed for this indication by the FDA. Preclinical studies have shown that palifosfamide has activity against leukemia and solid tumors. These studies also indicate that palifosfamide may have a better safety profile than ifosfamide or cyclophosphamide because it does not appear to produce known toxic metabolites of ifosfamide, such as acrolein and chloroacetaldehyde. Acrolein, which is toxic to the kidneys and bladder, can mandate the administration of a protective agent called mesna, which is inconvenient and expensive. Chloroacetaldehyde is toxic to the central nervous system, causing "fuzzy brain" syndrome for which there is currently no protective measure. Similar toxicity concerns pertain to high-dose cyclophosphamide, which is widely used in bone marrow and blood cell transplantation. Palifosfamide has evidenced activity against ifosfamide- and/or cyclophosphamide-resistant cancer cell lines. Also in preclinical cancer models, palifosfamide was shown to be orally active and encouraging results have been obtained with palifosfamide in combination with doxorubicin, an agent approved to treat sarcoma.

Following Phase I study, Phase II testing of the intravenous form of palifosfamide as a single agent to treat advanced sarcoma has been completed. In both Phase I and Phase II testing, palifosfamide has been administered without the "uroprotectant" mesna, and the toxicities associated with acrolein and chloroacetaldehyde have not been observed. The Company reported clinical activity of palifosfamide when used alone in the Phase II study addressing advanced sarcoma. Following review of the preclinical combination studies, clinical data, and discussion with sarcoma experts, the Company initiated a Phase I dose escalation study of palifosfamide in combination with doxorubicin in patients with metastatic or unresectable soft tissue sarcoma. The Company reported favorable results and safety profile from this study at this year's ASCO annual meeting. In light of reported favorable Phase II clinical activity data and with the combination of palifosfamide with doxorubicin well tolerated in the Phase I trial and evidencing activity, the Company initiated a Phase II randomized controlled trial in the second half of last year to compare doxorubicin plus palifosfamide to doxorubicin alone in patients with front and second-line metastatic or unresectable soft tissue sarcoma. With regard to an interim analysis of this trial and as a result of reaching a pre-specified efficacy milestone and following safety and efficacy data review by the Data Committee, sarcoma experts, and the Company's Medical Advisory Board, the decision was reached to formally stop enrollment in the trial on October 13, 2009. Subsequently, further positive interim data from the trial was presented at the 15th Annual Connective Tissue Oncology Society ("CTOS") meeting held on November 6, 2009. The Company plans to initiate a registration trial following and end of phase II meeting with FDA and further regulatory review of the palifosfamide program to date. The Company is also developing an oral capsule form of palifosfamide to be studied clinically following further data from the IV trials and subject to partnering or the availability of other sources of funding. The Company is also considering additional Phase II trials in other solid tumors as funding becomes available. Orphan Drug Designation for palifosfamide has been obtained in both the United States and the European Union for the treatment of soft tissue sarcomas.

- ZIO-301, or indibulin (Zybulin™), is a novel, orally available small molecular-weight inhibitor of tubulin polymerization that was acquired from Baxter Healthcare and is the subject of numerous patents worldwide, including the United States, the European Union and Japan. The microtubule component, tubulin, is one of the more well established drug targets in cancer. Microtubule inhibitors interfere with the dynamics of tubulin polymerization, resulting in inhibition of chromosome segregation during mitosis and consequently inhibition of cell division. A number of marketed IV anticancer drugs target tubulin, such as the taxane family members, paclitaxel (Taxol®), docetaxel (Taxotere®) , the Vinca alkaloid family members, vincristine and vinorelbine, and the new class of epothilones with IxempraTM marketed. This class of agents is typically the mainstay of therapy in a wide variety of indications. In spite of their effectiveness, the use of these drugs is associated with significant toxicities, notably peripheral neurotoxicity.

  Preclinical studies with indibulin demonstrate significant and broad antitumor activity, including activity against taxane-refractory cell lines. The cytotoxic activity of indibulin was demonstrated in several rodent and human tumor cell lines derived from prostate, brain, breast, pancreas, lung, ovary, and cervical tumor tissues and in rodent tumor and human tumor xenograft models. In addition, indibulin was effective against multidrug resistant tumor cell lines (breast, lung, and leukemia) both in vitro and in vivo. Indibulin is potentially safer than other tubulin inhibitors. No neurotoxicity has been observed at therapeutic doses in rodents and in the ongoing Phase I trials. Indibulin has also demonstrated synergy with approved anti-cancer agents in preclinical studies. The availability of an oral capsule formulation of indibulin creates significant commercial opportunity because no oral capsule formulations of microtubulin inhibitors are currently on the market in the United States.

  Indibulin, as a single agent, has completed a Phase I trial in Europe and additional Phase I trials are nearing completion in the U.S. in patients with advanced solid tumors and the Company has reported clinical activity at well-tolerated doses using a continuous dosing scheme without the development of clinically relevant peripheral neuropathy. Following encouraging results obtained with indibulin in combination with erlotinib, and 5-FU in preclinical models, two Phase I combination studies were initiated with Tarceva® in one and Xeloda® in another and are reaching completion. Favorable activity and safety profile of oral indibulin with oral Xeloda® were reported at ASCO's annual meeting in May 2009. Preclinical work with consultant Dr. Larry Norton to explore dose scheduling for the clinical setting have been completed and were also reported at the ASCO meeting, supporting the Company's plan to initiate the Phase I portion of a Phase I/II breast cancer trial using a dose schedule established preclinically.

Subject to obtaining appropriate funding, we intend to continue with clinical development of IV palifosfamide for soft tissue sarcoma and as the appropriate circumstances would dictate, to initiate a clinical study with the oral form following the United States Food and Drug Administration approval; with IV darinaparsin, for PTCL and with the further development of the oral form; and with oral indibulin, for solid tumors and in particular breast cancer. However, the successful development of our product candidates is highly uncertain. Product development costs and timelines can vary significantly for each product candidate, are difficult to accurately predict, and will require us to obtain additional funding, either alone or in connection with partnering arrangements. Various statutes and regulations also govern or influence the manufacturing, safety, labeling, storage, record keeping and marketing of each product. The lengthy process of seeking approval and the subsequent compliance with applicable statutes and regulations require the expenditure of substantial resources. Any failure by us to obtain, or any delay in obtaining, regulatory approvals could materially, adversely affect our business. To date, we have not received approval for the sale of any drug candidates in any market and, therefore, have not generated any revenues from our drug candidates.

Corporate Information

We were originally incorporated in Colorado in September 1998 (under the name Net Escapes, Inc.) and later changed our name to "EasyWeb, Inc." in February 1999. We were re-incorporated in Delaware on May 16, 2005 under the same name. On September 13, 2005, we completed a "reverse" acquisition of privately held ZIOPHARM, Inc., a Delaware corporation. To effect this transaction, we caused ZIO Acquisition Corp., our wholly-owned subsidiary, to merge with and into ZIOPHARM, Inc., with ZIOPHARM, Inc. surviving as our wholly owned subsidiary. In accordance with the terms of the merger, the outstanding common stock of ZIOPHARM, Inc. automatically converted into the right to receive an aggregate of approximately 97.3% of our outstanding common stock (after giving effect to the transaction). Following the merger, we caused ZIOPHARM, Inc. to merge with and into us and we changed our name to "ZIOPHARM Oncology, Inc." Although EasyWeb, Inc. was the legal acquirer in the transaction, we accounted for the transaction as a reverse acquisition under generally accepted accounting principles. As a result, ZIOPHARM, Inc. became the registrant with the Securities and Exchange Commission and the historical financial statements of ZIOPHARM, Inc. became our historical financial statements.

Our executive offices are located at 1180 Avenue of the Americas, 19th Floor, New York, NY 10036, and our telephone number is (646) 214-0700. Our internet site is www.ziopharm.com. None of the information on our internet site is part of this prospectus supplement or the accompanying prospectus.

The Offering

We are offering shares of our common stock and warrants to purchase shares of our common stock to purchasers pursuant to this prospectus supplement and the accompanying prospectus. The common stock and warrants will be sold in units, with each unit consisting of one share of common stock and a warrant to purchase 0.50 of a share of common stock.

Common stock offered	shares
Warrants	Warrants to purchase up to shares of our common stock will be offered in this offering, including warrants to purchase up to an aggregate of shares of our common stock as part of the units offered hereby and warrants to purchase up to an additional shares as underwriter compensation. The warrants will have a term of five years and will be exercisable at any time after the date of issuance at an exercise price of $ per share. This prospectus supplement also relates to the offering of the shares of common stock issuable upon exercise of the warrants. For additional information regarding the warrants, see "Description of Securities We are Offering – Warrants " below.
Common stock outstanding after this offering	shares (assuming none of the warrants issued in the offering are exercised)
Use of Proceeds	We expect to use the net proceeds from this offering for general corporate purposes, which may include the initiation of pivotal clinical trials for some of our drug candidates, and general and administrative expenses.
Risk Factors	See "Risk Factors" and other information included or incorporated by reference in this prospectus supplement and the accompanying prospectus for a discussion of factors you should carefully consider before deciding to invest in our securities.
Listing	Our common stock is listed on the NASDAQ Capital Market under the symbol "ZIOP." The last reported price of our common stock on December 2, 2009 was $3.72 per share. There is no established public trading market for the offered warrants and we do not expect a market to develop. In addition, we do not intend to apply for listing of the warrants on any national securities exchange.

The amounts above are based on 25,708,287 common shares outstanding as of December 2, 2009 and assume no exercise of outstanding options or warrants since that date. The number of common shares expected to be outstanding after this offering excludes:

- 3,151,249 shares of our common stock issuable upon the exercise of outstanding stock options as of December 2, 2009, including those issued under our 2003 Stock Option Plan, having a weighted average exercise price of $2.74 per share;
- 1,246,068 shares of our common stock reserved for future issuance under our 2003 Stock Option Plan;
- 7,813,627 shares of our common stock issuable upon the exercise of outstanding warrants as of December 2, 2009 with a weighted-average exercise price of $4.22 per share; and
- shares of common stock issuable upon the exercise of the warrants to be issued in this offering, including those to be issued as underwriting compensation, at an exercise price of $ per share.

RISK FACTORS

In considering whether to purchase the securities, you should carefully consider all the information we have included or incorporated by reference in this prospectus supplement and the accompanying prospectus. In particular, you should carefully consider the following risk factors, the factors listed in "Forward-Looking Statements" and those commencing on page 7 of the accompanying prospectus, as well as those incorporated by reference into this prospectus supplement and the accompanying prospectus from the reports we file with the Securities and Exchange Commission .. You should carefully review all the information in this prospectus supplement and the accompanying prospectus about these securities.

Since we have broad discretion in how we use the proceeds from this offering, we may use the proceeds in ways with which you disagree.

We have not allocated specific amounts of the net proceeds from this offering for any specific purpose. Accordingly, our management will have significant flexibility in applying the net proceeds of this offering. You will be relying on the judgment of our management with regard to the use of these net proceeds, and you will not have the opportunity, as part of your investment decision, to assess whether the proceeds are being used appropriately. It is possible that the net proceeds will be invested in a way that does not yield a favorable, or any, return for us. The failure of our management to use such funds effectively could have a material adverse effect on our business, financial condition, operating results and cash flow.

There is no minimum offering amount required to consummate this offering.

There is no minimum offering amount which must be raised in order for us to consummate this offering. Accordingly, the amount of money raised may not be sufficient for us to meet our business objectives. Moreover, if only a small amount of money is raised, all or substantially all of the offering proceeds may be applied to cover the offering expenses and we will not otherwise benefit from the offering. In addition, because there is no minimum offering amount required, investors will not be entitled to a return of their investment if we are unable to raise sufficient proceeds to meet our business objectives.

Investors in this offering will pay a much higher price than the book value of our stock.

If you purchase units in this offering, you will incur an immediate and substantial dilution in net tangible book value of $ per share, after giving effect to the sale by us of shares of common stock in this offering and assuming no exercise of the warrants offered hereby.

There is no public market for the warrants to purchase common stock in this offering.

There is no established public trading market for the warrants being offered in this offering, and we do not expect a market to develop. In addition, we do not intend to apply for listing the warrants on any securities exchange or other trading market. Without an active market, the liquidity of the warrants will be limited.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement and the accompanying prospectus contain, and the documents incorporated by reference herein and therein may contain, forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended (the "Securities Act"), and Section 21E of the Securities Exchange Act of 1934, as amended (the "Exchange Act"). These statements relate to future events or to our future financial performance and involve known and unknown risks, uncertainties and other factors which may cause our actual results, performance or achievements to be materially different from any future results, performances or achievements expressed or implied by the forward-looking statements. Forward-looking statements may include, but are not limited to statements about:

- the progress of preclinical and clinical trials involving our drug candidates;
- the progress of our research and development programs;
- the risk that final trial data may not support interim analysis of the viability of our drug candidates;
- the benefits to be derived from relationships with our collaborators;
- the receipt or anticipated receipt of regulatory clearances and approvals;
- our ability to adequately protect our intellectual property rights;
- our estimates of future revenues and profitability; and
- our estimates regarding our capital requirements and our need for additional financing.

In some cases, you can identify forward-looking statements by terms such as "may," "will," "should," "could," "would," "expects," "plans," "anticipates," "believes," "estimates," "projects," "predicts," "potential" and similar expressions intended to identify forward-looking statements. These statements reflect our current views with respect to future events and are based on assumptions and subject to risks and uncertainties. Given these uncertainties, you should not place undue reliance on these forward-looking statements. We discuss many of these risks in greater detail under the heading "Risk Factors" in this prospectus supplement and the accompanying prospectus and in our reports filed from time to time under the Securities Act and/or the Exchange Act. We encourage you to read these filings as they are made.

Further, any forward-looking statement speaks only as of the date on which it is made, and we undertake no obligation to update any forward-looking statement or statements to reflect events or circumstances after the date on which such statement is made or to reflect the occurrence of unanticipated events. New factors emerge from time to time, and it is not possible for us to predict which factors will arise. In addition, we cannot assess the impact of each factor on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements.

USE OF PROCEEDS

We expect the net proceeds from this offering to be up to approximately $ million, after deducting the underwriting discounts and commissions, as described in "Underwriting," and other estimated offering expenses payable by us, which include legal, accounting and printing fees.

We intend to use the net proceeds from the sale of the securities under this prospectus supplement for general corporate purposes, including the initiation of pivotal clinical trials for our drug candidates, darinaparsin and palifosfamide, working capital, and general operating and administrative expenses. However, as of the date of this prospectus supplement, we cannot specify with certainty all of the particular uses of the proceeds from this offering. Accordingly, we will retain broad discretion over the use of such proceeds. Pending the use of the net proceeds from this offering as described above, we intend to invest the net proceeds in investment-grade, interest-bearing instruments.

DILUTION

The net tangible book value of our common stock on September 30, 2009 was approximately $3.9 million, or approximately $0.15 per share, based on 25,571,301 shares of our common stock outstanding as of September 30, 2009. Net tangible book value per share represents the amount of our total tangible assets, less our total liabilities, divided by the total number of shares of our common stock outstanding. Dilution in net tangible book value per share to new investors represents the difference between the amount per unit paid by purchasers of securities in this offering and the net tangible book value per share of our common stock immediately afterwards. Without taking into account any other changes in net tangible book value after September 30, 2009, other than the sale of units offered by us hereby at a price of $ per unit and after deducting underwriting discounts and commissions and our estimated offering expenses, our net tangible book value at September 30, 2009 would have been approximately $ million, or approximately $ per share. This represents an immediate increase in net tangible book value of approximately $ per share to existing shareholders and an immediate dilution in net tangible book value of $ per share to investors in this offering. Our net tangible book value calculation assumes no exercise of the warrants offered hereby.

The following table illustrates this per share dilution:

Public offering price per unit		$
Net tangible book value per share as of September 30, 2009	$ 0.15	
Increase in net tangible book value per share attributable to this offering	$	
Net tangible book value per share as of September 30, 2009, after giving effect to this offering		$
Dilution per share to new investors in the offering		$

Investors that purchase common stock upon exercise of the warrants offered hereby may experience dilution depending on our net tangible book value at the time of exercise.

The amounts above are based on 25,571,301 common shares outstanding as of September 30, 2009 and assume no exercise of outstanding options or warrants since that date. The number of common shares expected to be outstanding after this offering excludes:

- 3,151,249 shares of our common stock issuable upon the exercise of outstanding stock options, including those issued under our 2003 Stock Option Plan, having a weighted average exercise price of $2.74 per share;
- 1,246,068 shares of our common stock reserved for future issuance under our 2003 Stock Option Plan;
- 7,950,613 shares of our common stock issuable upon the exercise of warrants outstanding at September 30, 2009 with a weighted-average exercise price of $4.22 per share; and
- shares of common stock issuable upon the exercise of warrants to be issued to purchasers in this offering, including those to be issued as underwriting compensation, at an exercise price of $ per share.

To the extent options or warrants outstanding as of September 30, 2009 have been or may be exercised or other shares have been issued, there may be further dilution to investors.

DESCRIPTION OF SECURITIES WE ARE OFFERING

In this offering, we are offering units, consisting of shares of common stock and warrants to purchase shares of common stock. Each unit consists of one share of common stock and warrants to purchase 0.50 of a share of common stock at an exercise price of $ per share. We are also issuing warrants to purchase up to an aggregate of shares of our common stock at an exercise price of $ per share to the underwriters as underwriting compensation. This prospectus supplement also relates to the offering of shares of our common stock upon exercise, if any, of the warrants.

Common Stock

The material terms and provisions of our common stock are described under the caption "Description of Capital Stock" starting on page 7 of the accompanying prospectus.

Warrants

The material terms and provisions of the warrants being offered pursuant to this prospectus supplement are summarized below. This summary is subject to, and qualified in its entirety by, the form of warrant included as an exhibit to our Current Report on Form 8-K that will be filed with the SEC in connection with this offering.

Exercisability. The warrants will have a term of five years and will be exercisable at any time following the date of issuance at an exercise price of $ per share. The warrants will be exercisable, at the option of each holder, upon the surrender of the warrants to us and the payment in cash, or in the case of a cashless exercise described below, by delivery of shares of common stock by the holder equal in value to the exercise price of the shares being acquired upon exercise of the warrants. The holder will not have the right to exercise any portion of the warrant if the holder, together with its affiliates, would beneficially own in excess of 9.99% (the "Maximum Percentage") of the number of shares of our common stock outstanding immediately after the exercise, provided however, that upon 61 days' prior written notice, the holder may increase the Maximum Percentage to 19.99%. If shares are not delivered to the holder of any warrant within three trading days of such holder's due exercise thereof, and prior to the time such shares are received, the holder purchases shares of our common stock to deliver in satisfaction of a sale by the holder of shares to be issued upon such exercise (a "Buy-in"), then we will be required to pay the holder the amount by which the total purchase price paid for common stock as a result of the Buy-in (including brokerage commissions, if any) exceeds the proceeds received by such holder as a result of the sale to which such Buy-in relates.

Cashless Exercise. If there is no effective registration statement registering the issuance of shares of common stock issuable upon exercise of the warrants issued to purchasers in this offering, then such warrants may be exercised by means of a "cashless exercise" in which the holder will be entitled to surrender a portion of the shares of common stock subject to the warrant in lieu of cash for the exercise price. The warrants to be issued in this offering as underwriting compensation may be exercised by means of a "cashless exercise" at any time during which such warrants are exercisable.

Exercise Price. The exercise price per share of common stock purchasable upon exercise of the warrants is $ with respect to warrants being issued as part of the units offered hereby, and $ with respect to warrants being issued as underwriting compensation. In either case, the exercise price is subject to appropriate adjustment in the event of stock dividends, stock splits, stock combinations, reclassifications or similar events affecting our common stock.

If, any time prior to the four year anniversary of the warrants' initial issue date, we sell or issue shares of our common stock, rights, options or warrants to purchase shares of our common stock, other rights for shares of our common stock, or securities convertible or exchangeable into shares of our common stock, in any case at a price per share less than the than applicable warrant exercise price, then in each such case the warrant exercise price will be reduced to the price determined by multiplying the exercise price in effect immediately prior to such issuance by a fraction, (A) the numerator of which will be the number of shares of our common stock outstanding immediately prior to such issuance plus the number of shares which the aggregate consideration received for such issuance would purchase at the exercise price in effect immediately prior to such issuance, and (B) the denominator of which will be the number of shares of our common stock outstanding immediately after such issuance; provided, however, that no such sale or issuance will reduce the warrant exercise price to an amount less than $0.50 (which $0.50 floor is subject to appropriate adjustment in the event of stock dividends, stock splits, stock combinations, reclassifications or similar events affecting our common stock). In determining whether a sale or issuance is at a price per share less than the than applicable warrant exercise price, we will take into account any consideration received by us for such sale or issuance, any consideration required to be paid upon the exercise, conversion, or exchange, as applicable, of the issued securities and the fair market value of all other consideration (if other than cash). Any adjustment to the warrant exercise price made upon the issuance of convertible securities, and any subsequent adjustments based thereon, will be recomputed upon any expiration or termination of conversion rights in order to reflect the issuance of only the number of shares actually issued upon the conversion and the actual consideration received. Notwithstanding the foregoing, the following issuances will not trigger adjustments in the warrant exercise price: (i) the issuance of securities upon the exercise or conversion of any convertible securities issued by us prior to the date hereof (unless the conversion price, exercise price or number of shares issuable thereunder is amended, modified or changed), (ii) the grant of options, warrants, common stock or other convertible securities (but not including any amendments to such instruments) under any stock option, restricted stock plan or stock purchase plan approved by us and our stockholders, and the issuance of common stock in respect thereof, or (iii) the issuance of securities in a transaction that otherwise results in an adjustment to the warrant exercise price.

Transferability. The warrants issued in the offering may be transferred at the option of the warrant holder upon surrender of the warrants to the Company with the appropriate instruments of transfer.

Effect of Fundamental Transaction. If (i) we merge or consolidate with or into another entity, in which our stockholders as of immediately prior to the transaction own less than a majority of the outstanding stock of the surviving entity, (ii) we sell of all or substantially all of our assets in one or a series of related transactions, (iii) a tender or exchange offer is completed pursuant to which all or substantially all of our stockholders are permitted to tender or exchange their shares for other securities, cash or property and would result in our stockholders immediately prior to such offer owning less than a majority of the outstanding stock thereafter, (iv) if we reclassify our common stock or effect any compulsory share exchange pursuant to which our common stock is effectively converted into or exchanged for other securities, cash or property, (v) we consummate a stock purchase transaction or other business combination with a third party whereby that third party acquires more than the 50% of our outstanding common stock, or (vi) we consummate a transaction in which any "person" or "group" (as these terms are used for purposes of Sections 13(d) and 14(d) of the Securities Exchange Act of 1934, as amended) is or becomes the "beneficial owner" (as defined in Rule 13d-3 under the Securities Exchange Act of 1934, as amended) of a majority of the voting power represented by our outstanding common stock (each a "Fundamental Transaction"), then the holder of any warrants will thereafter receive upon exercise of the warrants the same amount and kind of securities, cash or property to which a holder of the number of shares of common stock then issuable upon the exercise or conversion of such warrants would have been entitled upon such transaction. Notwithstanding the foregoing, in the event of a Fundamental Transaction, we or the surviving company (as applicable) will be required, at the warrant holder's option, exercisable at any time within 90 days after the Fundamental Transaction, to purchase the warrant from such holder by paying to such holder an amount of cash equal to the Black Scholes Value of the remaining unexercised portion of such holder's warrant as of the date that the Fundamental Transaction is consummated. As used herein, "Black Scholes Value" means the value of such holder's warrant based on the Black and Scholes Option Pricing Model obtained from the "OV" function on Bloomberg determined as of the day of the closing of the applicable Fundamental Transaction for pricing purposes and reflecting (i) a risk-free interest rate corresponding to the U.S. Treasury rate for a period equal to the remaining term of the warrant as of such date of request, (ii) an expected volatility equal to the greater of 100% and the 100 day volatility obtained from the HVT function on Bloomberg as of the day immediately following the public announcement of the applicable Fundamental Transaction, (iii) the underlying price per share used in such calculation shall be the sum of the price per share being offered in cash, if any, plus the value of any non cash consideration, if any, being offered in the Fundamental Transaction, and (iv) a 365 day annualization factor.

Rights Upon Distribution of Assets. If at any time while the warrant is outstanding, we declare or make any dividend or other distribution of our assets (or rights to acquire our assets) to holders of our common stock, by way of return of capital or otherwise, then in each such case we shall will distribute such assets pro rata to the warrant holder on the record date or date of effectiveness, as the case may be, fixed for determining the holders of common stock entitled to participate therein, in an amount equal to the amount that such holder would have been entitled to receive had such holder's warrants been exercised in full (without regard to any limitations on the exercise of the warrants) immediately prior to the time for determination of the holders of common stock entitled to participate in such distribution.

UNDERWRITING

We are offering the securities described in this prospectus supplement through underwriters. JMP Securities LLC and Rodman & Renshaw, LLC are acting as co-lead managers of the offering. We have entered into a firm commitment underwriting agreement with the underwriters. Subject to the terms and conditions of the underwriting agreement, we have agreed to sell to the underwriters, and each underwriter has severally agreed to purchase, at the public offering price less the underwriting discount set forth on the cover page of this prospectus supplement, the number of units listed next to its name in the following table:

Underwriter	Number of Units
JMP Securities LLC	$
Rodman & Renshaw, LLC	$
Total	

The underwriting agreement provides that the obligations of the underwriters to pay for and accept delivery of the units offered by this prospectus supplement are subject to the approval of certain legal matters by their counsel and certain other conditions. The underwriters are committed to purchase all the units offered by us if they purchase any units. The underwriting agreement also provides that if an underwriter defaults, the purchase commitments of non-defaulting underwriter(s) may also be increased or the offering may be terminated.

Commission and Expenses

The underwriters have advised us that they propose to offer the units to the public at the public offering price set forth on the cover page of this prospectus supplement and to certain dealers at that price less a concession not in excess of $ per share.

The following table shows the per unit and total underwriting discount to be paid to the underwriters.

Underwriting discount per unit	$
Total underwriting discount	$

We estimate that the total fees and expenses payable by us, excluding underwriting discounts, will be approximately $, which includes up to $100,000 that we have agreed to reimburse the underwriters for the fees incurred by them in connection with the offering.

In compliance with the guidelines of FINRA, the maximum consideration or discount to be received by any FINRA member or independent broker dealer may not exceed 8% of the aggregate amount of the securities offered pursuant to this prospectus supplement.

Lock –up Agreements

We and each of our directors and executive officers are subject to lock-up agreements that prohibit us and them, subject to certain exceptions, from offering for sale, selling, contracting to sell, pledging, granting any option, right or warrant to purchase, or otherwise transferring or disposing of, any shares of our common stock or any securities convertible into or exercisable or exchangeable for shares of our common stock for a period of 90 days from the date of this prospectus supplement without the prior written consent of JMP Securities LLC as the representative of the underwriters. The lock-up agreement does not prohibit our executive officers from transferring shares of our common stock to us to cover taxes payable upon the lapse of restrictions on previously awarded restricted stock grants and permits our directors to sell limited amounts of shares for the same purpose. The lock-up agreement does not prohibit us from issuing shares upon the exercise or conversion of securities outstanding on the date of this prospectus supplement. The lock-up provisions do not prevent us from selling shares to the underwriters pursuant to the underwriting agreement, or from granting options to acquire securities under our existing stock option plans or issuing shares upon the exercise or conversion of securities outstanding on the date of this prospectus supplement.

The lock-up period in all of the lock-up agreements is subject to extension if (i) during the last 17 days of the lock-up period we issue an earnings release or material news or a material event relating to us occurs or (ii) prior to the expiration of the lock-up period, we announce that we will release earnings results during the 16-day period beginning on the last day of the lock-up period, in which case the restrictions imposed in these lock-up agreements shall continue to apply until the expiration of the 18-day period beginning on the issuance of the earnings release or the occurrence of the material news or material event, unless JMP Securities LLC waives the extension in writing.

Price Stabilization; Short Positions and Penalty Bids

Until the distribution of the units of common stock and warrants is completed, SEC rules may limit the underwriters from bidding for and purchasing shares of our common stock.

In connection with this offering, the underwriters may engage in transactions that stabilize, maintain or otherwise make short sales of our common stock and may purchase our common stock on the open market to cover positions created by short sales. Short sales involve the sale by the underwriters of a greater number of shares than they are required to purchase in this offering. The underwriters may close out any short position by purchasing shares in the open market.

A short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the shares in the open market after pricing that could adversely affect investors who purchase in this offering. A “stabilizing bid” is a bid for or the purchase of common stock on behalf of the underwriters in the open market prior to the completion of this offering for the purpose of fixing or maintaining the price of the shares of common stock. A “syndicate covering transaction” is the bid for or purchase of common stock on behalf of the underwriters to reduce a short position incurred by the underwriters in connection with the offering.

Similar to other purchase transactions, the underwriters’ purchases to cover the syndicate short sales may have the effect of raising or maintaining the market price of our shares or preventing or retarding a decline in the market price of our shares. As a result, the price of our shares may be higher than the price that might otherwise exist in the open market.

In connection with this offering, the underwriters may also engage in passive market making transactions in our common stock on the Nasdaq Capital Market in accordance with Rule 103 of Regulation M during a period before the commencement of offers or sales of shares of our common stock in this offering and extending through the completion of distribution. A passive market maker must display its bid at a price not in excess of the highest independent bid of that security. However, if all independent bids are lowered below the passive market maker's bid, that bid must then be lowered when specified purchase limits are exceeded.

Neither we, nor the underwriters make any representation or prediction as to the direction or magnitude of any effect that the transactions described above may have on the price of our common stock. In addition, neither we nor the underwriters make any representation that the representative will engage in these transactions or that any transaction, if commenced, will not be discontinued without notice.

Indemnification

We have agreed to indemnify the underwriters against certain liabilities, including liabilities under the Securities Act, and liabilities arising from breaches of representations and warranties contained in the underwriting agreement. We have also agreed to contribute to payments the underwriters may be required to make in respect of such liabilities.

WHERE YOU CAN FIND MORE INFORMATION

We are a reporting company and file annual, quarterly and current reports, proxy statements and other information with the SEC. You may read and copy these reports, proxy statements and other information at the SEC's public reference room at 100 F. Street, N.E., Washington, D.C. 20549 or at the SEC's other public reference facilities. Please call the SEC at 1-800-SEC-0330 for more information about the operation of the public reference rooms. You can request copies of these documents by writing to the SEC and paying a fee for the copying costs. In addition, the SEC maintains an Internet site at http://www.sec.gov that contains reports, proxy and information statements and other information regarding issuers that file electronically with the SEC. Our SEC filings are available on the SEC's Internet site.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

We are allowed to incorporate by reference information contained in documents that we file with the SEC. This means that we can disclose important information to you by referring you to those documents and that the information in this prospectus supplement is not complete and you should read the information incorporated by reference for more detail. We incorporate by reference in two ways. First, we list certain documents that we have already filed with the SEC. The information in these documents is considered part of this prospectus supplement. Second, the information in documents that we file in the future will update and supersede the current information in, and incorporated by reference in, this prospectus supplement.

We incorporate by reference the documents listed below and any future filings we will make with the SEC under Section 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934, as amended, or the Exchange Act (other than information furnished in Current Reports on Form 8-K filed under Item 2.02 or 7.01 of such form):

- Annual Report on Form 10-K for the fiscal year ended December 31, 2008, filed on March 23, 2009;
- Quarterly Reports on Form 10-Q for the quarters ended March 31, 2009, June 30, 2009, and September 30, 2009, filed on May 15, 2009, August 14, 2009, and November 11, 2009, respectively;
- Current Reports on Form 8-K filed on June 1, 2009, June 4, 2009, September 15, 2009, October 14, 2009, and November 6, 2009; and
- The description of our common stock set forth in the registration statement on Form 8-A registering our common stock under Section 12 of the Exchange Act, which was filed with the SEC on September 20, 2006.

We will provide to each person, including any beneficial owner, to whom a prospectus supplement is delivered, a copy of any or all of the information that has been incorporated by reference in this prospectus supplement but not delivered with this prospectus supplement. You may request a copy of this information at no cost, by writing or telephoning us at the following address or telephone number:

ZIOPHARM Oncology, Inc.
1180 Avenue of the Americas, 19th Floor
New York, NY 10036

Attention: President
Telephone: (646) 214-0700

You should rely only on the information incorporated by reference or provided in this prospectus supplement or the accompanying prospectus. We have not authorized anyone else to provide you with different information. You should not assume that the information in this prospectus supplement is accurate as of any date other than the date on the front of this prospectus supplement.

LEGAL MATTERS

The validity of the issuance of the securities offered hereby will be passed upon by our counsel, Maslon Edelman Borman & Brand, LLP, Minneapolis, Minnesota. The underwriters are being represented in connection with this offering by Goodwin Procter LLP, New York, New York.

EXPERTS

The financial statements incorporated in this prospectus supplement by reference from the Company's Annual Report on Form 10-K for the year ended December 31, 2008 have been audited by Vitale, Caturano & Company, P.C., (whose name has been changed to Caturano and Company, P.C. effective May 1, 2009), as stated in their report incorporated in this prospectus supplement by reference, and have been so incorporated in reliance upon the report of such firm given upon their authority as experts in accounting and auditing.

PROSPECTUS

$75,000,000

ZIOPHARM Oncology, Inc.

Common Stock, Preferred Stock,
Warrants and Debt Securities

We may offer and sell any combination of common stock, preferred stock, warrants and debt securities, with a total initial offering price of up to $75,000,000.

This prospectus provides a general description of securities we may offer and sell from time to time. Each time we sell these securities, we will provide their specific terms in a supplement to this prospectus. This prospectus supplement may also add, update or change information contained in this prospectus. You should read this prospectus and the applicable prospectus supplement carefully before you invest in any securities. This prospectus may not be used to consummate a sale of securities unless accompanied by the applicable prospectus supplement.

We may offer and sell these securities, from time to time, to or through one or more underwriters, dealers and agents, or directly to purchasers, on a continuous or delayed basis, at prices and on other terms to be determined at the time of offering. If we use agents, underwriters or dealers to sell the securities, we will name them and describe their compensation in a prospectus supplement.

Our common stock is listed on the Nasdaq Capital Market under the symbol "ZIOP." On September 10, 2009, the closing price of our common stock, as reported on the Nasdaq Capital Market, was $1.71. We urge prospective purchasers of our common stock to obtain current information about the market prices of our common stock.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved these securities or determined if this prospectus is truthful or complete. A representation to the contrary is a criminal offense.

The date of this Prospectus is September 21, 2009.

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the Securities and Exchange Commission, or SEC, using a "shelf" registration process. Under this shelf registration process, from time to time, we may sell any combination of the securities described in this prospectus in one or more offerings, up to a total dollar amount of $75,000,000. This prospectus provides you with a general description of the securities we may offer. Each time we offer and sell securities under this prospectus, we will provide a prospectus supplement that will contain more specific information about the terms of the applicable offering. We may also add, update or change in the prospectus supplement any of the information contained in this prospectus. This prospectus, together with the applicable prospectus supplement(s) and the documents incorporated by reference into this prospectus and such supplement(s), includes all material information relating to this offering. To the extent there is a conflict between the information contained in this prospectus and the prospectus supplement, you should rely on the information in the prospectus supplement; provided that, if any statement in one of these documents is inconsistent with a statement in another document having a later date — for example, a document incorporated by reference in this prospectus or any prospectus supplement — the statement in the document having the later date modifies or supersedes the earlier statement. Please carefully read both this prospectus and any prospectus supplement, together with the additional information described below under "Where You Can Find More Information," before buying securities in this offering.

You should rely only on the information contained or incorporated by reference in this prospectus or a prospectus supplement. We have not authorized any other person to provide you with different information. If anyone provides you with different or inconsistent information, you should not rely on it. This prospectus and the accompanying supplement to this prospectus do not constitute an offer to sell or the solicitation of an offer to buy any securities other than the registered securities to which they relate, nor do this prospectus and the accompanying supplement to this prospectus constitute an offer to sell or the solicitation of an offer to buy securities in any jurisdiction to any person to whom it is unlawful to make such offer or solicitation in such jurisdiction. You should not assume that the information contained in this prospectus and the accompanying prospectus supplement is accurate on any date subsequent to the date set forth on the front cover of this document or that any information we have incorporated by reference is correct on any date subsequent to the date of the document incorporated by reference, even though this prospectus and any accompanying prospectus supplement is delivered or securities sold on a later date.

This prospectus may not be used to consummate a sale of our securities unless it is accompanied by a prospectus supplement.

PROSPECTUS SUMMARY

The following is a summary of this prospectus. Because it is only a summary, it does not contain all of the detailed information contained elsewhere in this prospectus or in the documents incorporated by reference into this prospectus or included as exhibits to the registration statement that contains this prospectus. Accordingly, you are urged to carefully review this prospectus (including all documents incorporated by reference into this prospectus) in its entirety. Unless otherwise indicated, "ZIOPHARM," our "Company," "we," "us," "our" and similar terms refer to ZIOPHARM Oncology, Inc.

Our Company

ZIOPHARM Oncology, Inc. is a biopharmaceutical company that is seeking to develop and commercialize a diverse, risk-sensitive portfolio of in-licensed cancer drugs that can address unmet medical needs through enhanced efficacy and/or safety and quality of life. Our principal focus is on the licensing and development of proprietary small molecule drug candidates that are related to cancer therapeutics already on the market or in development and can be administered by intravenous ("IV") and/or oral capsule forms. We believe this strategy will result in lower risk and expedited drug development programs with product candidates having a low cost of manufacturing to address changing reimbursement requirements around the world. While we may commercialize our products on our own in North America, we recognize that favorable clinical trial results can be better addressed by partnering with companies with the requisite financial resources. The Company could also negotiate the right to complete development and marketing in certain geographies especially for certain limited (niche) indications. Although we are currently in Phase I and/or II studies for three product candidates identified as darinaparsin (ZinaparTM, ZIO-101), palifosfamide (ZymafosTM, ZIO-201), and indibulin (ZybulinTM, ZIO-301), the Company's current focus is on palifosfamide and more specifically on completing initial enrollment of the ongoing randomized Phase II trial with palifosfamide to support a registration trial for palifosfamide in combination with doxorubicin in the front- and second-line setting of soft tissue sarcoma. We anticipate the initiation of such a trial as early as the first half of 2010.

- ZIO-101, or darinaparsin (ZinaparTM), is an anti-mitochondrial (organic arsenic) compound covered by issued patents and pending patent applications in the U.S. and in foreign countries. A form of commercially available inorganic arsenic (arsenic trioxide [Trisenox ®]; "ATO") has been approved in the United States and the European Union for the treatment of acute promyelocytic leukemia ("APL"), a precancerous condition. ATO is on the compendia listing for the therapy of multiple myeloma, and has been studied for the treatment of various other cancers. Nevertheless, ATO has been shown to be toxic to the heart, liver, and brain, which limits its use as an anti-cancer agent. ATO carries a "black box" warning for ECG abnormalities since arsenic trioxide has been shown to cause QT interval prolongation and complete atrioventricular block. QT prolongation can lead to a torsade de pointes-type ventricular arrhythmia, which can be fatal. Inorganic arsenic has also been shown to cause cancer of the skin and lung in humans. The toxicity of arsenic is generally correlated to its accumulation in organs and tissues. Our preclinical and clinical studies to date have demonstrated that darinaparsin is considerably less toxic than inorganic arsenic, particularly with regard to cardiac toxicity. In vitro testing of darinaparsin using the National Cancer Institute's human cancer cell panel detected activity against a series of tumor cell lines including lung, colon, brain, melanoma, ovarian, and kidney cancer. Moderate activity was detected against breast and prostate cancer. In addition to solid tumors, in vitro testing in both the National Cancer Institute's cancer cell panel and in vivo testing in a leukemia animal model demonstrated substantial activity against hematological cancers (cancers of the blood and blood-forming tissues) such as leukemia, lymphoma, myelodysplastic syndromes, and multiple myeloma. Results indicate significant activity against the HuT 78 cutaneous T-cell lymphoma, the NK-G2MI natural killer-cell NHL, KARPAS-299 T-cell NHL, SU-DHL-8 B-cell NHL, SU-DHL-10 B-cell NHL and SU-DHL-16 B-cell NHL cell lines. Preclinical studies have also established anti-angiogenic properties of darinaparsin and provided support for the development of an oral capsule form of the drug, and established synergy of darinaparsin in combination with other approved anti-cancer agents.

  Phase I testing of the intravenous form of darinaparsin in solid tumors and hematological cancers has been completed. The Company reported clinical activity and, importantly, a safety profile from these studies as predicted by preclinical results. The Company subsequently completed Phase II studies in advanced myeloma and primary liver cancer and is nearing completion of a Phase II study in certain other hematological cancers. In addition, the Company is completing two Phase I studies with an oral capsule form of darinaparsin. At the May 2009 annual meeting of the American Society of Clinical Oncology ("ASCO"), the Company reported favorable results from the trial with IV-administered darinaparsin in lymphoma, particularly peripheral T-cell lymphoma ("PTCL"). In the ongoing Phase I trials, also reported at the ASCO annual meeting, preliminary data primarily in solid tumors indicate the oral form is active and well tolerated. The Company is actively seeking a partner or other sources of funding to progress the IV program into a potentially pivotal trial in PTCL as early as the first half of 2010 as well as to complete the oral Phase I program. If we cannot find a partner or otherwise raise the capital for continuing the darinaparsin programs, our intent is to complete the ongoing studies included in the Company's current estimate of expenses and then place the development program for darinaparsin on hold.

- ZIO-201, or palifosfamide (ZymafosTM), is the active metabolite of ifosfamide, a compound chemically related to cyclophosphamide. Patent applications covering proprietary forms of palifosfamide for pharmaceutical composition and method of use have been filed in the U.S. and internationally. Like cyclophosphamide and ifosfamide, palifosfamide is an alkylating agent. The Company believes that cyclophosphamide is the most widely used alkylating agent in cancer therapy, with significant use in the treatment of breast cancer and non-Hodgkin's lymphoma. More importantly, ifosfamide has been shown to be effective at high doses in the treatment of sarcoma and lymphoma, either by itself or in combination with other anticancer agents. Ifosfamide is approved by the U.S. Food and Drug Administration ("FDA") as a treatment for testicular cancer while ifosfamide-based treatment is a standard of care for sarcoma, although it is not licensed for this indication by the FDA. Preclinical studies have shown that palifosfamide has activity against leukemia and solid tumors. These studies also indicate that palifosfamide may have a better safety profile than ifosfamide or cyclophosphamide because it does not appear to produce known toxic metabolites of ifosfamide, such as acrolein and chloroacetaldehyde. Acrolein, which is toxic to the kidneys and bladder, can mandate the administration of a protective agent called mesna, which is inconvenient and expensive. Chloroacetaldehyde is toxic to the central nervous system, causing "fuzzy brain" syndrome for which there is currently no protective measure. Similar toxicity concerns pertain to high-dose cyclophosphamide, which is widely used in bone marrow and blood cell transplantation. Palifosfamide has evidenced activity against ifosfamide- and/or cyclophosphamide-resistant cancer cell lines. Also in preclinical cancer models, palifosfamide was shown to be orally active and encouraging results have been obtained with palifosfamide in combination with doxorubicin, an agent approved to treat sarcoma.

  Following Phase I study, Phase II testing of the intravenous form of palifosfamide as a single agent to treat advanced sarcoma has been completed. In both Phase I and Phase II testing, palifosfamide has been administered without the "uroprotectant" mesna, and the toxicities associated with acrolein and chloroacetaldehyde have not been observed. The Company reported clinical activity of palifosfamide when used alone in the Phase II study addressing advanced sarcoma. Following review of the preclinical combination studies, clinical data, and discussion with sarcoma experts, the Company initiated a Phase I dose escalation study of palifosfamide in combination with doxorubicin in patients with metastatic or unresectable soft tissue sarcoma. The Company reported favorable results and safety profile from this study at the ASCO annual meeting. In light of reported favorable Phase II clinical activity data and with the combination of palifosfamide with doxorubicin well tolerated in the Phase I trial and evidencing activity, the Company initiated a Phase II randomized controlled trial in the second half of last year to compare doxorubicin plus palifosfamide to doxorubicin alone in patients with front and second-line metastatic or unresectable soft tissue sarcoma. Data from the initial patients in this trial are expected to shape a registration trial in the same setting which is expected to initiate as early as the first half of 2010. The study is currently actively enrolling and, in conjunction with ASCO, the initial drug safety monitoring committee meeting concluded to continue enrollment as planned. The Company is also developing an oral capsule form of palifosfamide to be studied clinically following further data from the IV trials and partnering or other sources of funding. The Company is also considering additional Phase II trials in other solid tumors as funding becomes available. Orphan Drug Designation for palifosfamide has been obtained in both the United States and the European Union for the treatment of soft tissue sarcomas.

- ZIO-301, or indibulin (ZybulinTM), is a novel, orally available small molecular-weight inhibitor of tubulin polymerization that was acquired from Baxter Healthcare and is the subject of numerous patents worldwide, including the United States, the European Union and Japan. The microtubule component, tubulin, is one of the more well established drug targets in cancer. Microtubule inhibitors interfere with the dynamics of tubulin polymerization, resulting in inhibition of chromosome segregation during mitosis and consequently inhibition of cell division. A number of marketed IV anticancer drugs target tubulin, such as the taxane family members, paclitaxel (Taxol®), docetaxel (Taxotere®) , the Vinca alkaloid family members, vincristine and vinorelbine, and the new class of epothilones with IxempraTM marketed. This class of agents is typically the mainstay of therapy in a wide variety of indications. In spite of their effectiveness, the use of these drugs is associated with significant toxicities, notably peripheral neurotoxicity.

Preclinical studies with indibulin demonstrate significant and broad antitumor activity, including activity against taxane-refractory cell lines. The cytotoxic activity of indibulin was demonstrated in several rodent and human tumor cell lines derived from prostate, brain, breast, pancreas, lung, ovary, and cervical tumor tissues and in rodent tumor and human tumor xenograft models. In addition, indibulin was effective against multidrug resistant tumor cell lines (breast, lung, and leukemia) both in vitro and in vivo. Indibulin is potentially safer than other tubulin inhibitors. No neurotoxicity has been observed at therapeutic doses in rodents and in the ongoing Phase I trials. Indibulin has also demonstrated synergy with approved anti-cancer agents in preclinical studies. The availability of an oral capsule formulation of indibulin creates significant commercial opportunity because no oral capsule formulations of microtubulin inhibitors are currently on the market in the United States.

Indibulin, as a single agent, has completed a Phase I trial in Europe and additional Phase I trials are nearing completion in the U.S. in patients with advanced solid tumors and the Company has reported clinical activity at well-tolerated doses using a continuous dosing scheme without the development of clinically relevant peripheral neuropathy. Following encouraging results obtained with indibulin in combination with erlotinib, and 5-FU in preclinical models, two Phase I combination studies were initiated with Tarceva® in one and Xeloda® in another and are reaching completion. Favorable activity and safety profile of oral indibulin with oral Xeloda® were reported at ASCO's annual meeting in May 2009. Preclinical work with consultant Dr. Larry Norton to explore dose scheduling for the clinical setting have been completed and were also reported at the ASCO meeting, supporting the Company's plan, subject to the availability of additional funding, to initiate a Phase I/II breast cancer trial using a dose schedule established preclinically.

Subject to obtaining appropriate funding, we intend to continue with clinical development of IV palifosfamide for soft tissue sarcoma and to initiate a clinical study with the oral form following the United States Food and Drug Administration approval; with IV darinaparsin, for PTCL and with the further development of the oral form; and with oral indibulin, for solid tumors and in particular breast cancer. However, the successful development of our product candidates is highly uncertain. Product development costs and timelines can vary significantly for each product candidate, are difficult to accurately predict, and will require us to obtain additional funding, either alone or in connection with partnering arrangements. Various statutes and regulations also govern or influence the manufacturing, safety, labeling, storage, record keeping and marketing of each product. The lengthy process of seeking approval and the subsequent compliance with applicable statutes and regulations require the expenditure of substantial resources. Any failure by us to obtain, or any delay in obtaining, regulatory approvals could materially, adversely affect our business. To date, we have not received approval for the sale of any drug candidates in any market and, therefore, have not generated any revenues from our drug candidates.

Corporate Information

We were originally incorporated in Colorado in September 1998 (under the name Net Escapes, Inc.) and later changed our name to "EasyWeb, Inc." in February 1999. We were re-incorporated in Delaware on May 16, 2005 under the same name. On September 13, 2005, we completed a "reverse" acquisition of privately held ZIOPHARM, Inc., a Delaware corporation. To effect this transaction, we caused ZIO Acquisition Corp., our wholly-owned subsidiary, to merge with and into ZIOPHARM, Inc., with ZIOPHARM, Inc. surviving as our wholly owned subsidiary. In accordance with the terms of the merger, the outstanding common stock of ZIOPHARM, Inc. automatically converted into the right to receive an aggregate of approximately 97.3% of our outstanding common stock (after giving effect to the transaction). Following the merger, we caused ZIOPHARM, Inc. to merge with and into us and we changed our name to "ZIOPHARM Oncology, Inc." Although EasyWeb, Inc. was the legal acquirer in the transaction, we accounted for the transaction as a reverse acquisition under generally accepted accounting principles. As a result, ZIOPHARM, Inc. became the registrant with the Securities and Exchange Commission and the historical financial statements of ZIOPHARM, Inc. became our historical financial statements.

Our executive offices are located at 1180 Avenue of the Americas, 19th Floor, New York, NY 10036, and our telephone number is (646) 214-0700. Our internet site is www.ziopharm.com. None of the information on our internet site is part of this prospectus.

RISK FACTORS

As with most pharmaceutical product candidates, the development of our product candidates is subject to numerous risks, including the risk of delays in or discontinuation of development from lack of financing, inability to obtain necessary regulatory approvals to market the products, unforeseen safety issues relating to the products and dependence on third party collaborators to conduct research and development of the products. Because we are a development stage company with a limited history of operations, we are also subject to many risks associated with early-stage companies. For a more detailed discussion of the risks you should consider before purchasing shares of our common stock, you should carefully consider the specific risks discussed under "Risk Factors" in the applicable prospectus supplement and in our filings with the Securities and Exchange Commission that are incorporated by reference in this prospectus and such prospectus supplement.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus contains, and the documents incorporated by reference herein and in any prospectus supplement hereto may contain, forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended (the "Securities Act"), and Section 21E of the Securities Exchange Act of 1934, as amended (the "Exchange Act"). These statements relate to future events or to our future financial performance and involve known and unknown risks, uncertainties and other factors which may cause our actual results, performance or achievements to be materially different from any future results, performances or achievements expressed or implied by the forward-looking statements. Forward-looking statements may include, but are not limited to statements about:

- the progress of preclinical and clinical trials involving our drug candidates;
- the progress of our research and development programs;
- the benefits to be derived from relationships with our collaborators;
- the receipt or anticipated receipt of regulatory clearances and approvals;
- our estimates of future revenues and profitability; and
- our estimates regarding our capital requirements and our need for additional financing.

In some cases, you can identify forward-looking statements by terms such as "may," "will," "should," "could," "would," "expects," "plans," "anticipates," "believes," "estimates," "projects," "predicts," "potential" and similar expressions intended to identify forward-looking statements. These statements reflect our current views with respect to future events and are based on assumptions and subject to risks and uncertainties. Given these uncertainties, you should not place undue reliance on these forward-looking statements. We discuss many of these risks in greater detail under the heading "Risk Factors" in the applicable prospectus supplement and in our reports filed from time to time under the Securities Act and/or the Exchange Act. We encourage you to read these filings as they are made.

Further, any forward-looking statement speaks only as of the date on which it is made, and we undertake no obligation to update any forward-looking statement or statements to reflect events or circumstances after the date on which such statement is made or to reflect the occurrence of unanticipated events. New factors emerge from time to time, and it is not possible for us to predict which factors will arise. In addition, we cannot assess the impact of each factor on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements.

RATIO OF EARNINGS TO FIXED CHARGES

The following table shows our ratio of earnings to fixed charges for the periods indicated.

	Fiscal Year Ended December 31,					Six Months Ended June 30,
$ In Thousands, Except Ratio	2004	2005	2006	2007	2008	2009
Ratio of earnings to fixed charges[(1)]	-	-	-	-	-	-
Deficiency of earnings to fixed charges[(2)]	$ (5,687)	$ (9,517)	$ (17,857)	$ (26,608)	$ (25,231)	$ (5,738)

(1) In each of the periods presented, no earnings were sufficient to cover fixed charges.
(2) The deficiency of earnings is equivalent to net income (loss) before tax benefit (provision) and extraordinary gain.

USE OF PROCEEDS

We will retain broad discretion over the use of the net proceeds to us from the sale of our securities offered by this prospectus. Unless we indicate otherwise in the applicable prospectus supplement, we anticipate that any net proceeds will be used for working capital and general corporate purposes. We will set forth in the applicable prospectus supplement our intended use for the net proceeds received from the sale of securities sold pursuant to that prospectus supplement.

PLAN OF DISTRIBUTION

We may sell the securities covered by this prospectus:

- to or through one or more underwriters or dealers;
- directly to purchasers, or to purchasers through agents; or
- through a combination of any of these methods of sale.

We may distribute the securities offered hereby:

- from time to time in one or more transactions at a fixed price or prices, which may be changed from time to time;
- at market prices prevailing at the times of sale;
- at prices related to such prevailing market prices; or

- at negotiated prices.

We will describe the method of distribution of the securities in the applicable prospectus supplement.

We may determine the price or other terms of the securities offered under this prospectus by use of an electronic auction. We will describe how any auction will determine the price or any other terms, how potential investors may participate in the auction and the nature of the obligations of the underwriter, dealer or agent in the applicable prospectus supplement.

Underwriters, dealers or agents may receive compensation in the form of discounts, concessions or commissions from us or our purchasers (as their agents in connection with the sale of the securities). In addition, underwriters may sell securities to or through dealers, and those dealers may receive compensation in the form of discounts, concessions or commissions from the underwriters and/or commissions from the purchasers for whom they act as agent. These underwriters, dealers or agents may be considered to be underwriters under the Securities Act. As a result, discounts, commissions, or profits on resale received by the underwriters, dealers or agents may be treated as underwriting discounts and commissions. Each applicable prospectus supplement will identify any such underwriter, dealer or agent, and describe any compensation received by them from us. Any initial public offering price and any discounts or concessions allowed or re-allowed or paid to dealers may be changed from time to time.

We may enter into agreements that provide for indemnification against certain civil liabilities, including liabilities under the Securities Act, or for contribution with respect to payments made by the underwriters, dealers or agents and to reimburse these persons for certain expenses.

We may grant underwriters who participate in the distribution of the securities an option to purchase additional securities to cover over-allotments, if any, in connection with the distribution. Underwriters or agents and their associates may be customers of, engage in transactions with, or perform services for us in the ordinary course of business.

In connection with the offering of the securities, certain underwriters and selling group members and their respective affiliates, may engage in transactions that stabilize, maintain or otherwise affect the market price of the securities. These transactions may include stabilization transactions effected in accordance with Rule 104 of Regulation M promulgated by the SEC pursuant to which these persons may bid for or purchase securities for the purpose of stabilizing its market price.

The underwriters in the offering may engage in overallotment, stabilizing transactions, short covering transactions and penalty bids in accordance with rules and regulations under the Securities Exchange Act of 1934, as amended (the “Exchange Act”). Overallotment involves sales in excess of the offering size, which create a short position. Stabilizing transactions permit bids to purchase the underlying security so long as the stabilizing bids do not exceed a specified maximum. Short covering transactions involve purchases of the securities in the open market after the distribution is completed to cover short positions. Penalty bids permit the underwriters to reclaim a selling concession from a dealer when the securities originally sold by the dealer are purchased in a covering transaction to cover short positions. Those activities may cause the price of the securities to be higher than it would otherwise be. If commenced, the underwriters may discontinue any of these activities at any time.

DESCRIPTION OF CAPITAL STOCK

Pursuant to our certificate of incorporation, as amended and restated to date, our authorized capital stock consists of 280,000,000 shares, comprised of 250,000,000 shares of common stock, par value $.001 per share, and 30,000,000 shares of preferred stock, par value $.001 per share. As of September 10, 2009, there were 21,790,964 shares of common stock and no shares of preferred stock issued and outstanding. Our common stock is traded on the Nasdaq Capital Market under the symbol “ZIOP”.

The following description summarizes the material terms of our capital stock. This summary is, however, subject to the provisions of our certificate of incorporation and bylaws. For greater detail about our capital stock, please refer to our certificate of incorporation and bylaws.

Common Stock

Voting. The holders of our common stock are entitled to one vote for each outstanding share of common stock owned by such stockholder on every matter properly submitted to the stockholders for their vote. Stockholders are not entitled to vote cumulatively for the election of directors. At any meeting of the stockholders, a quorum as to any matter shall consist of a majority of the votes entitled to be cast on the matter, except where a larger quorum is required by law, by our certificate of incorporation or by our bylaws.

Dividend Rights. Holders of our common stock are entitled to receive ratably dividends and other distributions of cash or any other right or property as may be declared by the registrant’s Board of Directors out of our assets or funds legally available for such dividends or distributions. The dividend rights of holders of common stock are subject to the dividend rights of the holders of any series of preferred stock that may be issued and outstanding from time to time.

Liquidation Rights. In the event of any voluntary or involuntary liquidation, dissolution or winding up of our affairs, holders of our common stock would be entitled to share ratably in our assets that are legally available for distribution to stockholders after payment of liabilities. If we have any preferred stock outstanding at such time, the holders of such preferred stock may be entitled to distribution and/or liquidation preferences that require us to pay the applicable distribution to the holders of preferred stock before paying distributions to the holders of common stock.

Conversion, Redemption and Preemptive Rights. Holders of our common stock have no conversion, redemption, preemptive, subscription or similar rights.

The transfer agent and registrar for our common stock is American Stock Transfer and trust Company.

See “Certain Provisions of Delaware Law, the Company’s Certificate of Incorporation and Bylaws and the Company’s Stockholder Rights Plan” for a description of provisions of the Company’s certificate of incorporation and bylaws which may have the effect of delaying, deferring or preventing changes in the Company’s control.

Preferred Stock

The following description of preferred stock and the description of the terms of any particular series of preferred stock that we choose to issue hereunder and that will be set forth in the related prospectus supplement are not complete. These descriptions are qualified in their entirety by reference to the certificate of designation relating to that series. The rights, preferences, privileges and restrictions of the preferred stock of each series will be fixed by the certificate of designation relating to that series.

The board of directors has the authority, without stockholder approval, subject to limitations prescribed by law, to provide for the issuance of the shares of preferred stock in one or more series, and by filing a certificate pursuant to the applicable law of the State of Delaware, to establish from time to time the number of shares to be included in each such series, and to fix the designation, powers, preferences and rights of the shares of each series and the qualifications, limitations or restrictions, including, but not limited to, the following:

- the number of shares constituting that series;
- dividend rights and rates;
- voting rights;
- conversion terms;
- rights and terms of redemption (including sinking fund provisions); and
- rights of the series in the event of liquidation, dissolution or winding up.

All shares of preferred stock offered hereby will, when issued, be fully paid and nonassessable and will not have any preemptive or similar rights. Our board of directors could authorize the issuance of shares of preferred stock with terms and conditions that could have the effect of discouraging a takeover or other transaction that might involve a premium price for holders of the shares or which holders might believe to be in their best interests.

We will set forth in a prospectus supplement relating to the series of preferred stock being offered the following items:

- the title and stated value of the preferred stock;
- the number of shares of the preferred stock offered, the liquidation preference per share and the offering price of the preferred stock;
- the dividend rate(s), period(s) and/or payment date(s) or method(s) of calculation applicable to the preferred stock;
- whether dividends are cumulative or non-cumulative and, if cumulative, the date from which dividends on the preferred stock will accumulate;
- the procedures for any auction and remarketing, if any, for the preferred stock;
- the provisions for a sinking fund, if any, for the preferred stock;
- the provision for redemption, if applicable, of the preferred stock;
- any listing of the preferred stock on any securities exchange;
- the terms and conditions, if applicable, upon which the preferred stock will be convertible into common stock, including the conversion price (or manner of calculation) and conversion period;
- voting rights, if any, of the preferred stock;
- a discussion of any material and/or special United States federal income tax considerations applicable to the preferred stock;
- the relative ranking and preferences of the preferred stock as to dividend rights and rights upon the liquidation, dissolution or winding up of our affairs;
- any limitations on issuance of any class or series of preferred stock ranking senior to or on a parity with the class or series of preferred stock as to dividend rights and rights upon liquidation, dissolution or winding up of our affairs; and
- any other specific terms, preferences, rights, limitations or restrictions of the preferred stock.

The transfer agent and registrar for any series of preferred stock will be set forth in the applicable prospectus supplement.

DESCRIPTION OF DEBT SECURITIES

This description is a summary of the material provisions of the debt securities and the related indenture. We urge you to read the form of indenture filed as an exhibit to the registration statement of which this prospectus is a part because the indenture, and not this description, governs your rights as a holder of debt securities. References in this prospectus to an "indenture" refer to the particular indenture under which we may issue a series of debt securities.

General

The terms of each series of debt securities will be established by or pursuant to a resolution of our board of directors and set forth or determined in the manner provided in an officers' certificate or by a supplemental indenture. Debt securities may be issued in separate series without limitation as to aggregate principal amount. We may specify a maximum aggregate principal amount for the debt securities of any series. The particular terms of each series of debt securities will be described in a prospectus supplement relating to such series, including any pricing supplement. The prospectus supplement will set forth specific terms relating to some or all of the following:

- the offering price;
- the title;
- any limit on the aggregate principal amount;
- the person who shall be entitled to receive interest, if other than the record holder on the record date;
- the date the principal will be payable;
- the interest rate, if any, the date interest will accrue, the interest payment dates and the regular record dates;
- the place where payments may be made;
- any mandatory or optional redemption provisions;
- if applicable, the method for determining how the principal, premium, if any, or interest will be calculated by reference to an index or formula;
- if other than U.S. currency, the currency or currency units in which principal, premium, if any, or interest will be payable and whether we or the holder may elect payment to be made in a different currency;
- the portion of the principal amount that will be payable upon acceleration of stated maturity, if other than the entire principal amount;
- any defeasance provisions if different from those described below under "Satisfaction and Discharge; Defeasance";
- any conversion or exchange provisions;
- any obligation to redeem or purchase the debt securities pursuant to a sinking fund;
- whether the debt securities will be issuable in the form of a global security;
- any subordination provisions, if different from those described below under "Subordination";
- any deletions of, or changes or additions to, the events of default or covenants; and
- any other specific terms of such debt securities.

Unless otherwise specified in the prospectus supplement, the debt securities will be registered debt securities. Debt securities may be sold at a substantial discount below their stated principal amount, bearing no interest or interest at a rate which at the time of issuance is below market rates.

Exchange and Transfer

Debt securities may be transferred or exchanged at the office of the security registrar or at the office of any transfer agent designated by us.

We will not impose a service charge for any transfer or exchange, but we may require holders to pay any tax or other governmental charges associated with any transfer or exchange.

In the event of any potential redemption of debt securities of any series, we will not be required to:

- issue, register the transfer of, or exchange, any debt security of that series during a period beginning at the opening of business 15 days before the day of mailing of a notice of redemption and ending at the close of business on the day of the mailing; or

- register the transfer of or exchange any debt security of that series selected for redemption, in whole or in part, except the unredeemed portion being redeemed in part.

We may initially appoint the trustee as the security registrar. Any transfer agent, in addition to the security registrar, initially designated by us will be named in the prospectus supplement. We may designate additional transfer agents or change transfer agents or change the office of the transfer agent. However, we will be required to maintain a transfer agent in each place of payment for the debt securities of each series.

Global Securities

The debt securities of any series may be represented, in whole or in part, by one or more global securities. Each global security will:

- be registered in the name of a depositary that we will identify in a prospectus supplement;

- be deposited with the depositary or nominee or custodian; and

- bear any required legends.

No global security may be exchanged in whole or in part for debt securities registered in the name of any person other than the depositary or any nominee unless:

- the depositary has notified us that it is unwilling or unable to continue as depositary or has ceased to be qualified to act as depositary;

- an event of default is continuing; or

- the Company executes and delivers to the trustee an officers' certificate stating that the global security is exchangeable.

As long as the depositary, or its nominee, is the registered owner of a global security, the depositary or nominee will be considered the sole owner and holder of the debt securities represented by the global security for all purposes under the indenture. Except in the above limited circumstances, owners of beneficial interests in a global security:

- will not be entitled to have the debt securities registered in their names;

- will not be entitled to physical delivery of certificated debt securities; and

- will not be considered to be holders of those debt securities under the indentures.

Payments on a global security will be made to the depositary or its nominee as the holder of the global security. Some jurisdictions have laws that require that certain purchasers of securities take physical delivery of such securities in definitive form. These laws may impair the ability to transfer beneficial interests in a global security.

Institutions that have accounts with the depositary or its nominee are referred to as “participants.” Ownership of beneficial interests in a global security will be limited to participants and to persons that may hold beneficial interests through participants. The depositary will credit, on its book-entry registration and transfer system, the respective principal amounts of debt securities represented by the global security to the accounts of its participants.

Ownership of beneficial interests in a global security will be shown on and effected through records maintained by the depositary, with respect to participants’ interests, or any participant, with respect to interests of persons held by participants on their behalf.

Payments, transfers and exchanges relating to beneficial interests in a global security will be subject to policies and procedures of the depositary.

The depositary policies and procedures may change from time to time. Neither we nor the trustee will have any responsibility or liability for the depositary’s or any participant’s records with respect to beneficial interests in a global security.

Payment and Paying Agent

The provisions of this paragraph will apply to the debt securities unless otherwise indicated in the prospectus supplement. Payment of interest on a debt security on any interest payment date will be made to the person in whose name the debt security is registered at the close of business on the regular record date. Payment on debt securities of a particular series will be payable at the office of a paying agent or paying agents designated by us. However, at our option, we may pay interest by mailing a check to the record holder. The corporate trust office will be designated as our sole paying agent.

We may also name any other paying agents in the prospectus supplement. We may designate additional paying agents, change paying agents or change the office of any paying agent. However, we will be required to maintain a paying agent in each place of payment for the debt securities of a particular series.

All moneys paid by us to a paying agent for payment on any debt security which remain unclaimed at the end of two years after such payment was due will be repaid to us. Thereafter, the holder may look only to us for such payment.

Consolidation, Merger and Sale of Assets

Except as otherwise set forth in the prospectus supplement, we may not consolidate with or merge into any other person, in a transaction in which we are not the surviving corporation, or convey, transfer or lease our properties and assets substantially as an entirety to, any person, unless:

- the successor, if any, is a U.S. corporation, limited liability company, partnership, trust or other entity;
- the successor assumes our obligations on the debt securities and under the indenture;
- immediately after giving effect to the transaction, no default or event of default shall have occurred and be continuing; and
- certain other conditions are met.

Events of Default

Unless we inform you otherwise in the prospectus supplement, the indenture will define an event of default with respect to any series of debt securities as one or more of the following events:

(1) failure to pay principal of or any premium on any debt security of that series when due;

(2) failure to pay any interest on any debt security of that series for 30 days when due;

(3) failure to deposit any sinking fund payment when due;

(4) failure to perform any other covenant in the indenture continued for 90 days after being given the notice required in the indenture;

(5) our bankruptcy, insolvency or reorganization; and

(6) any other event of default specified in the prospectus supplement.

An event of default of one series of debt securities is not necessarily an event of default for any other series of debt securities.

If an event of default, other than an event of default described in clause (5) above, shall occur and be continuing, either the trustee or the holders of at least 25% in aggregate principal amount of the outstanding securities of that series may declare the principal amount of the debt securities of that series to be due and payable immediately.

If an event of default described in clause (5) above shall occur, the principal amount of all the debt securities of that series will automatically become immediately due and payable. Any payment by us on subordinated debt securities following any such acceleration will be subject to the subordination provisions described below under "Subordinated Debt Securities."

After acceleration the holders of a majority in aggregate principal amount of the outstanding securities of that series may, under certain circumstances, rescind and annul such acceleration if all events of default, other than the non-payment of accelerated principal, or other specified amount, have been cured or waived.

Other than the duty to act with the required care during an event of default, the trustee will not be obligated to exercise any of its rights or powers at the request of the holders unless the holders shall have offered to the trustee reasonable indemnity. Generally, the holders of a majority in aggregate principal amount of the outstanding debt securities of any series will have the right to direct the time, method and place of conducting any proceeding for any remedy available to the trustee or exercising any trust or power conferred on the trustee.

A holder will not have any right to institute any proceeding under the indentures, or for the appointment of a receiver or a trustee, or for any other remedy under the indentures, unless:

(1) the holder has previously given to the trustee written notice of a continuing event of default with respect to the debt securities of that series;

(2) the holders of at least 25% in aggregate principal amount of the outstanding debt securities of that series have made a written request and have offered reasonable indemnity to the trustee to institute the proceeding; and

(3) the trustee has failed to institute the proceeding and has not received direction inconsistent with the original request from the holders of a majority in aggregate principal amount of the outstanding debt securities of that series within 90 days after the original request.

Holders may, however, sue to enforce the payment of principal or interest on any debt security on or after the due date without following the procedures listed in (1) through (3) above.

Modification and Waiver

Except as provided in the next two succeeding paragraphs, the applicable trustee and we may make modifications and amendments to the indentures (including, without limitation, through consents obtained in connection with a tender offer or exchange offer for, outstanding securities) and may waive any existing default or event of default (including, without limitation, through consents obtained in connection with a tender offer or exchange offer for, outstanding securities) with the consent of the holders of a majority in aggregate principal amount of the outstanding securities of each series affected by the modification or amendment.

However, neither we nor the trustee may make any amendment or waiver without the consent of the holder of each outstanding security of that series affected by the amendment or waiver if such amendment or waiver would, among other things:

- change the amount of securities whose holders must consent to an amendment, supplement or waiver;
- change the stated maturity of any debt security;
- reduce the principal on any debt security or reduce the amount of, or postpone the date fixed for, the payment of any sinking fund;
- reduce the principal of an original issue discount security on acceleration of maturity;
- reduce the rate of interest or extend the time for payment of interest on any debt security;
- make a principal or interest payment on any debt security in any currency other than that stated in the debt security;
- impair the right to enforce any payment after the stated maturity or redemption date;
- waive any default or event of default in payment of the principal of, premium or interest on any debt security (except certain rescissions of acceleration); or
- waive a redemption payment or modify any of the redemption provisions of any debt security;

Notwithstanding the preceding, without the consent of any holder of outstanding securities, we and the trustee may amend or supplement the indentures:

- to provide for the issuance of and establish the form and terms and conditions of debt securities of any series as permitted by the indenture;
- to provide for uncertificated securities in addition to or in place of certificated securities;
- to provide for the assumption of our obligations to holders of any debt security in the case of a merger, consolidation, transfer or sale of all or substantially all of our assets;
- to make any change that does not adversely affect the legal rights under the indenture of any such holder;
- to comply with requirements of the Commission in order to effect or maintain the qualification of an indenture under the Trust Indenture Act; or
- to evidence and provide for the acceptance of appointment by a successor trustee with respect to the debt securities of one or more series and to add to or change any of the provisions of the indenture as shall be necessary to provide for or facilitate the administration of the trusts by more than one Trustee.

The consent of holders is not necessary under the indentures to approve the particular form of any proposed amendment. It is sufficient if such consent approves the substance of the proposed amendment.

Satisfaction and Discharge; Defeasance

We may be discharged from our obligations on the debt securities of any series that have matured or will mature or be redeemed within one year if we deposit with the trustee enough cash to pay all the principal, interest and any premium due to the stated maturity date or redemption date of the debt securities.

Each indenture contains a provision that permits us to elect:

- to be discharged from all of our obligations, subject to limited exceptions, with respect to any series of debt securities then outstanding; and/or
- to be released from our obligations under the following covenants and from the consequences of an event of default resulting from a breach of certain convenants, including covenants as to payment of taxes and maintenance of corporate existence.

To make either of the above elections, we must deposit in trust with the trustee enough money to pay in full the principal and interest on the debt securities. This amount may be made in cash and/or U.S. government obligations. As a condition to either of the above elections, we must deliver to the trustee an opinion of counsel that the holders of the debt securities will not recognize income, gain or loss for federal income tax purposes as a result of the action.

If any of the above events occurs, the holders of the debt securities of the series will not be entitled to the benefits of the indenture, except for the rights of holders to receive payments on debt securities or the registration of transfer and exchange of debt securities and replacement of lost, stolen or mutilated debt securities.

Notices

Notices to holders will be given by mail to the addresses of the holders in the security register.

Governing Law

The indentures and the debt securities will be governed by, and construed under, the law of the State of New York.

Regarding the Trustee

The indenture limits the right of the trustee, should it become a creditor of us, to obtain payment of claims or secure its claims.

The trustee is permitted to engage in certain other transactions. However, if the trustee, acquires any conflicting interest, and there is a default under the debt securities of any series for which they are trustee, the trustee must eliminate the conflict or resign.

Subordination

Payment on subordinated debt securities will, to the extent provided in the indenture, be subordinated in right of payment to the prior payment in full of all of our senior indebtedness (except that holders of the notes may receive and retain (i) permitted junior securities and (ii) payments made from the trust described under “Satisfaction and Discharge; Defeasance”). Any subordinated debt securities also are effectively subordinated to all debt and other liabilities, including lease obligations, if any.

Upon any distribution of our assets upon any dissolution, winding up, liquidation or reorganization, the payment of the principal of and interest on subordinated debt securities will be subordinated in right of payment to the prior payment in full in cash or other payment satisfactory to the holders of senior indebtedness. In the event of any acceleration of subordinated debt securities because of an event of default, the holders of any senior indebtedness would be entitled to payment in full in cash or other payment satisfactory to such holders of all senior indebtedness obligations before the holders of subordinated debt securities are entitled to receive any payment or distribution, except for certain payments made by the trust described under “Satisfaction and Discharge; Defeasance.” The indenture requires us or the trustee to promptly notify holders of designated senior indebtedness if payment of subordinated debt securities is accelerated because of an event of default.

We may not make any payment on subordinated debt securities, including upon redemption at the option of the holder of any subordinated debt securities or at our option, if:

- a default in the payment of the principal, premium, if any, interest, rent or other obligations in respect of designated senior indebtedness occurs and is continuing beyond any applicable period of grace (called a “payment default”); or

- a default other than a payment default on any designated senior indebtedness occurs and is continuing that permits holders of designated senior indebtedness to accelerate its maturity, and the trustee receives notice of such default (called a “payment blockage notice) from us or any other person permitted to give such notice under the indenture (called a “non-payment default”).

If the trustee or any holder of the notes receives any payment or distribution of our assets in contravention of the subordination provisions on subordinated debt securities before all senior indebtedness is paid in full in cash, property or securities, including by way of set-off, or other payment satisfactory to holders of senior indebtedness, then such payment or distribution will be held in trust for the benefit of holders of senior indebtedness or their representatives to the extent necessary to make payment in full in cash or payment satisfactory to the holders of senior indebtedness of all unpaid senior indebtedness.

In the event of our bankruptcy, dissolution or reorganization, holders of senior indebtedness may receive more, ratably, and holders of subordinated debt securities may receive less, ratably, than our other creditors (including our trade creditors). This subordination will not prevent the occurrence of any event of default under the indenture.

We are not prohibited from incurring debt, including senior indebtedness, under the indenture. We may from time to time incur additional debt, including senior indebtedness.

We are obligated to pay reasonable compensation to the trustee and to indemnify the trustee against certain losses, liabilities or expenses incurred by the trustee in connection with its duties under the indenture. The trustee's claims for these payments will generally be senior to those of noteholders in respect of all funds collected or held by the trustee.

Certain Definitions

"indebtedness" means:

(1) all indebtedness, obligations and other liabilities for borrowed money, including overdrafts, foreign exchange contracts, currency exchange agreements, interest rate protection agreements, and any loans or advances from banks, or evidenced by bonds, debentures, notes or similar instruments, other than any account payable or other accrued current liability or obligation incurred in the ordinary course of business in connection with the obtaining of materials or services;

(2) all reimbursement obligations and other liabilities with respect to letters of credit, bank guarantees or bankers' acceptances;

(3) all obligations and liabilities in respect of leases required in conformity with generally accepted accounting principles to be accounted for as capitalized lease obligations on our balance sheet;

(4) all obligations and other liabilities under any lease or related document in connection with the lease of real property which provides that we are contractually obligated to purchase or cause a third party to purchase the leased property and thereby guarantee a minimum residual value of the leased property to the lessor and our obligations under the lease or related document to purchase or to cause a third party to purchase the leased property;

(5) all obligations with respect to an interest rate or other swap, cap or collar agreement or other similar instrument or agreement or foreign currency hedge, exchange, purchase or other similar instrument or agreement;

(6) all direct or indirect guaranties or similar agreements in respect of, and our obligations or liabilities to purchase, acquire or otherwise assure a creditor against loss in respect of, indebtedness, obligations or liabilities of others of the type described in (1) through (5) above;

(7) any indebtedness or other obligations described in (1) through (6) above secured by any mortgage, pledge, lien or other encumbrance existing on property which is owned or held by us; and

(8) any and all refinancings, replacements, deferrals, renewals, extensions and refundings of, or amendments, modifications or supplements to, any indebtedness, obligation or liability of the kind described in clauses (1) through (7) above.

"permitted junior securities" means (i) equity interests in the Company; or (ii) debt securities of the Company that are subordinated to all senior indebtedness and any debt securities issued in exchange for senior indebtedness to substantially the same extent as, or to a greater extent than the notes are subordinated to senior indebtedness under the indenture.

"senior indebtedness" means the principal, premium, if any, interest, including any interest accruing after bankruptcy, and rent or termination payment on or other amounts due on our current or future indebtedness, whether created, incurred, assumed, guaranteed or in effect guaranteed by us, including any deferrals, renewals, extensions, refundings, amendments, modifications or supplements to the above. However, senior indebtedness does not include:

- indebtedness that expressly provides that it shall not be senior in right of payment to subordinated debt securities or expressly provides that it is on the same basis or junior to subordinated debt securities;
- our indebtedness to any of our majority-owned subsidiaries; and
- subordinated debt securities.

DESCRIPTION OF WARRANTS

General

We may issue warrants for the purchase of our debt securities, preferred stock or common stock, or any combination thereof. Warrants may be issued independently or together with our debt securities, preferred stock or common stock and may be attached to or separate from any offered securities. Each series of warrants will be issued under a separate warrant agreement to be entered into between us and a bank or trust company, as warrant agent. The warrant agent will act solely as our agent in connection with the warrants. The warrant agent will not have any obligation or relationship of agency or trust for or with any holders or beneficial owners of warrants. This summary of certain provisions of the warrants is not complete. For the terms of a particular series of warrants, you should refer to the prospectus supplement for that series of warrants and the warrant agreement for that particular series.
Debt warrants

Debt Warrants

The prospectus supplement relating to a particular issue of warrants to purchase debt securities will describe the terms of the debt warrants, including the following:

- the title of the debt warrants;
- the offering price for the debt warrants, if any;
- the aggregate number of the debt warrants;
- the designation and terms of the debt securities, including any conversion rights, purchasable upon exercise of the debt warrants;
- if applicable, the date from and after which the debt warrants and any debt securities issued with them will be separately transferable;
- the principal amount of debt securities that may be purchased upon exercise of a debt warrant and the exercise price for the warrants, which may be payable in cash, securities or other property;
- the dates on which the right to exercise the debt warrants will commence and expire;
- if applicable, the minimum or maximum amount of the debt warrants that may be exercised at any one time;
- whether the debt warrants represented by the debt warrant certificates or debt securities that may be issued upon exercise of the debt warrants will be issued in registered or bearer form;

- information with respect to book-entry procedures, if any; the currency or currency units in which the offering price, if any, and the exercise price are payable;
- if applicable, a discussion of material U.S. federal income tax considerations;
- the antidilution provisions of the debt warrants, if any;
- the redemption or call provisions, if any, applicable to the debt warrants;
- any provisions with respect to the holder's right to require us to repurchase the warrants upon a change in control or similar event; and
- any additional terms of the debt warrants, including procedures, and limitations relating to the exchange, exercise and settlement of the debt warrants.

Debt warrant certificates will be exchangeable for new debt warrant certificates of different denominations. Debt warrants may be exercised at the corporate trust office of the warrant agent or any other office indicated in the prospectus supplement. Prior to the exercise of their debt warrants, holders of debt warrants will not have any of the rights of holders of the debt securities purchasable upon exercise and will not be entitled to payment of principal or any premium, if any, or interest on the debt securities purchasable upon exercise.

Equity Warrants

The prospectus supplement relating to a particular series of warrants to purchase our common stock or preferred stock will describe the terms of the warrants, including the following:

- the title of the warrants;
- the offering price for the warrants, if any;
- the aggregate number of warrants;
- the designation and terms of the common stock or preferred stock that may be purchased upon exercise of the warrants;
- if applicable, the designation and terms of the securities with which the warrants are issued and the number of warrants issued with each security;
- if applicable, the date from and after which the warrants and any securities issued with the warrants will be separately transferable;
- the number of shares of common stock or preferred stock that may be purchased upon exercise of a warrant and the exercise price for the warrants;
- the dates on which the right to exercise the warrants shall commence and expire;
- if applicable, the minimum or maximum amount of the warrants that may be exercised at any one time;
- the currency or currency units in which the offering price, if any, and the exercise price are payable;
- if applicable, a discussion of material U.S. federal income tax considerations;
- the antidilution provisions of the warrants, if any;
- the redemption or call provisions, if any, applicable to the warrants;
- any provisions with respect to holder's right to require us to repurchase the warrants upon a change in control or similar event; and
- any additional terms of the warrants, including procedures, and limitations relating to the exchange, exercise and settlement of the warrants.

Holders of equity warrants will not be entitled:

- to vote, consent or receive dividends;
- receive notice as stockholders with respect to any meeting of stockholders for the election of our directors or any other matter; or
- exercise any rights as stockholders of the Company.

CERTAIN PROVISIONS OF DELAWARE LAW, THE CERTIFICATE OF INCORPORATION AND BYLAWS

Limitations on Directors' Liability

The Certificate of Incorporation and our bylaws contain provisions indemnifying our directors and officers to the fullest extent permitted by law. In addition, as permitted by Delaware law, the Certificate of Incorporation provides that no director will be liable to us or our stockholders for monetary damages for breach of certain fiduciary duties as a director. The effect of this provision is to restrict our rights and the rights of our stockholders in derivative suits to recover monetary damages against a director for breach of certain fiduciary duties as a director, except that a director will be personally liable for:

- the benefits to be derived from relationships with our collaborators;
- any breach of his or her duty of loyalty to the registrant or its stockholders;
- acts or omissions not in good faith which involve intentional misconduct or a knowing violation of law;
- the payment of dividends or the redemption or purchase of stock in violation of Delaware law; or
- any transaction from which the director derived an improper personal benefit.

This provision does not affect a director's liability under the federal securities laws.

To the extent that our directors, officers and controlling persons are indemnified under the provisions contained in the Certificate of Incorporation, Delaware law or contractual arrangements against liabilities arising under the Securities Act, we have been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Securities Act, and is therefore unenforceable.

Provisions that May Have an Anti-Takeover Effect

Certain provisions set forth in our certificate of incorporation, bylaws and in Delaware law, which are summarized below, are intended to enhance the likelihood of continuity and stability in the composition of our Board of Directors and in the policies formulated by our Board of Directors and to discourage certain types of transactions that may involve an actual or threatened change of control. In that regard, these provisions are designed to reduce our vulnerability to an unsolicited acquisition proposal. The provisions also are intended to discourage certain tactics that may be used in proxy fights. However, such provisions could have the effect of discouraging others from making tender offers for our shares and, as a consequence, they also may inhibit fluctuations in the market price of our common stock that could result from actual or rumored takeover attempts. Such provisions also may have the effect of preventing changes in our management.

Blank Check Preferred Stock. Our certificate of incorporation contains provisions that permit our Board of Directors to issue, without any further vote or action by the stockholders, up to 30,000,000 shares of preferred stock in one or more series and, with respect to each such series, to fix the number of shares constituting the series and the designation of the series, the voting powers (if any) of the shares of the series, and the preferences and relative, participating, optional and other special rights, if any, and any qualifications, limitations or restrictions, of the shares of such series. As a result, our Board of Directors could authorize the issuance of shares of preferred stock with terms and conditions that could have the effect of delaying, deferring or preventing a transaction or a change in control that might involve a premium price for holders of the registrant's common stock or otherwise be in their best interest.

Special Meetings of Stockholders. Our bylaws provide that special meetings of stockholders may be called only by the Board of Directors. Stockholders are not permitted to call a special meeting of stockholders or to require that the Board of Directors call such a special meeting.

Delaware Takeover Statute.

In general, Section 203 of the Delaware General Corporation Law prohibits a Delaware corporation that is a public company from engaging in any "business combination" (as defined below) with any "interested stockholder" (defined generally as an entity or person beneficially owning 15% or more of the outstanding voting stock of the corporation and any entity or person affiliated with such entity or person) for a period of three years following the date that such stockholder became an interested stockholder, unless: (1) prior to such date, the board of directors of the corporation approved either the business combination or the transaction that resulted in the stockholder becoming an interested stockholder; (2) on consummation of the transaction that resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the number of shares outstanding those shares owned (x) by persons who are directors and also officers and (y) by employee stock plans in which employee participants do not have the right to determine confidentially whether shares held subject to the plan will be tendered in a tender or exchange offer; or (3) on or subsequent to such date, the business combination is approved by the board of directors and authorized at an annual or special meeting of stockholders, and not by written consent, by the affirmative vote of at least $66^{2/3}$% of the outstanding voting stock that is not owned by the interested stockholder.

Section 203 of the Delaware General Corporation Law defines "business combination" to include: (1) any merger or consolidation involving the corporation and the interested stockholder; (2) any sale, transfer, pledge or other disposition of 10% or more of the assets of the corporation involving the interested stockholder; (3) subject to certain exceptions, any transaction that results in the issuance or transfer by the corporation of any stock of the corporation to the interested stockholder; (4) any transaction involving the corporation that has the effect of increasing the proportionate share of the stock of any class or series of the corporation beneficially owned by the interested stockholder; or (5) the receipt by the interested stockholder of the benefit of any loans, advances, guarantees, pledges or other financial benefits provided by or through the corporation.

WHERE YOU CAN FIND MORE INFORMATION

We are a reporting company and file annual, quarterly and current reports, proxy statements and other information with the SEC. You may read and copy these reports, proxy statements and other information at the SEC's public reference room at 100 F. Street, N.E., Washington, D.C. 20549 or at the SEC's other public reference facilities. Please call the SEC at 1-800-SEC-0330 for more information about the operation of the public reference rooms. You can request copies of these documents by writing to the SEC and paying a fee for the copying costs. In addition, the SEC maintains an Internet site at http://www.sec.gov that contains reports, proxy and information statements and other information regarding issuers that file electronically with the SEC. Our SEC filings are available on the SEC's Internet site.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

We are allowed to incorporate by reference information contained in documents that we file with the SEC. This means that we can disclose important information to you by referring you to those documents and that the information in this prospectus is not complete and you should read the information incorporated by reference for more detail. We incorporate by reference in two ways. First, we list certain documents that we have already filed with the SEC. The information in these documents is considered part of this prospectus. Second, the information in documents that we file in the future will update and supersede the current information in, and incorporated by reference in, this prospectus.

We incorporate by reference the documents listed below and any future filings we will make with the SEC under Section 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934, as amended, or the Exchange Act (other than information furnished in Current Reports on Form 8-K filed under Item 2.02 or 7.01 of such form):

- Annual Report on Form 10-K for the fiscal year ended December 31, 2008, filed on March 23, 2009;
- Quarterly Reports on Form 10-Q for the quarters ended March 31, 2009 and June 30, 2009, filed on May 15, 2009 and August 14, 2009, respectively;
- Current Reports on Form 8-K filed on June 1, 2009 and June 4, 2009; and
- The description of our common stock set forth in the registration statement on Form 8-A registering our common stock under Section 12 of the Exchange Act, which was filed with the SEC on September 20, 2006.

We will provide to each person, including any beneficial owner, to whom a prospectus is delivered, a copy of any or all of the information that has been incorporated by reference in this prospectus but not delivered with this prospectus. You may request a copy of this information at no cost, by writing or telephoning us at the following address or telephone number:

ZIOPHARM Oncology, Inc.
1180 Avenue of the Americas, 19th Floor
New York, NY 10036
Attention: President
Telephone: (646) 214-0700

You should rely only on the information incorporated by reference or provided in this prospectus or any supplement. We have not authorized anyone else to provide you with different information. The selling stockholders will not make an offer of these shares in any state where the offer is not permitted. You should not assume that the information in this prospectus or any supplement is accurate as of any date other than the date on the front of these documents.

LEGAL MATTERS

The validity of the securities offered hereby will be passed upon by Maslon Edelman Borman & Brand, LLP, Minneapolis, Minnesota.

EXPERTS

The balance sheets of ZIOPHARM Oncology, Inc. as of December 31, 2008 and 2007 and the related statements of operations, changes in convertible preferred stock and stockholders' equity (deficit) and cash flows for each of the years in the three-year period ended December 31, 2008 and for the period from September 9, 2003 (date of inception) through December 31, 2008, included in this prospectus, have been included herein in reliance on the report, dated March 16, 2009, of Vitale, Caturano & Company, P.C., (whose name has been changed to Caturano and Company, P.C. effective May 1, 2009) independent registered public accounting firm, given on the authority of that firm as experts in auditing and accounting.