ZIOPHARM ONCOLOGY INC
Form S-3/A
July 01, 2011

As filed with the Securities and Exchange Commission
July 1, 2011

Registration No. 333-174292

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

Amendment No. 1 to

FORM S-3
REGISTRATION STATEMENT UNDER THE SECURITIES ACT OF 1933

ZIOPHARM Oncology, Inc.
(Exact name of registrant as specified in its charter)

Delaware	84-1475642
(State or jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)

1180 Avenue of the Americas, 19th Floor
New York, NY 10036
(646) 214-0700
(Address and telephone number of registrant's principal executive offices and principal place of business)

Dr. Jonathan Lewis	Copies to:
Chief Executive Officer	Alan M. Gilbert, Esq.
ZIOPHARM Oncology, Inc.	Maslon Edelman Borman & Brand, LLP
1180 Avenue of the Americas, 19th Floor	90 South 7th Street, Suite 3300
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(Name, address and telephone number of agent for service)

Approximate date of proposed sale to the public: From time to time after the effective date of this Registration Statement.

If the only securities being registered on this form are being offered pursuant to dividend or interest reinvestment plans, please check the following box. ¨

If any of the securities being registered on this form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, other than securities offered only in connection with dividend or interest reinvestment plans, check the following box: þ

If this form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective

registration statement for the same offering. o

If this form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ¨

If this form is a registration statement pursuant to General Instruction I.D. or a post-effective amendment thereto that shall become effective upon filing with the Commission pursuant to Rule 462(e) under the Securities Act, check the following box. ¨

If this form is a post-effective amendment to a registration statement filed pursuant to General Instruction I.D. filed to register additional securities or additional classes of securities pursuant to Rule 413(b) under the Securities Act, check the following box. ¨

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a smaller reporting company. See definition of “large accelerated filer,” “accelerated filer” and “smaller reporting company” in Rule 12b-2 of the Exchange Act. (Check one):

Large accelerated filer ¨	Accelerated filer þ
Non-accelerated filer ¨ (Do not check if a smaller reporting company)	Smaller reporting company ¨

CALCULATION OF REGISTRATION FEE

Title of Each Class of Securities to be Registered	Amount to be Registered (1)	Proposed Maximum Offering Price Per Unit (2)	Proposed Maximum Aggregate Offering Price (2)	Amount of Registration Fee (3)
Common stock, par value $.001 per share	6,036,161 shares	$6.455	$38,963,419.26	$4,523.65

(1) There is also being registered hereunder an indeterminate number of additional shares of common stock as shall be issuable pursuant to Rule 416 to prevent dilution resulting from stock splits, stock dividends or similar transactions.

(2) Estimated solely for the purpose of calculating the registration fee in accordance with Rule 457 of the Securities Act based upon a $6.455 per share average of high and low prices of the registrant's common stock on the Nasdaq Capital Market on May 16, 2011.

(3) Previously paid.

The registrant hereby amends this registration statement on such date or dates as may be necessary to delay its effective date until the registrant shall file a further amendment which specifically states that this registration statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933 or until the registration statement shall become effective on such date as the Commission, acting pursuant to said Section 8(a), may determine.

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 July 1, 2011

PROSPECTUS

ZIOPHARM Oncology, Inc.

6,063,161 Shares

Common Stock

This prospectus covers a total of 6,063,161 shares of our common stock. The shares covered by this prospectus may be disposed of by the selling stockholder set forth herein, or its transferees. We will not receive any proceeds from the disposition of such shares.

Our common stock is listed on the Nasdaq Capital Market under the symbol "ZIOP." On June 27, 2011, the closing price of our common stock, as reported on the Nasdaq Capital Market, was $6.00. We urge prospective purchasers of our common stock to obtain current information about the market prices of our common stock.

The securities offered by this prospectus involve a high degree of risk.
See "Risk Factors" beginning on page 6.

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. Any representation to the contrary is a criminal offense.

The date of this prospectus is , 2011.

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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 of which this prospectus is a part. Accordingly, you should carefully review this prospectus, including all documents incorporated by reference into this prospectus, in its entirety. Unless otherwise indicated, "ZIOPHARM," the "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 portfolio of in-licensed cancer drugs that can address unmet medical needs. Our principal focus has been 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 that can be administered by intravenous ("IV") and/or oral dosing. Our clinical programs for our small molecule candidates include palifosfamide (ZymafosTM or ZIO-201) darinaparsin (ZinaparTM or ZIO-101) and indibulin (ZybulinTM or ZIO-301). We are also pursuing the development of novel DNA-based biotherapeutics in the field of cancer pursuant to a partnering arrangement with Intrexon Corporation ("Intrexon"). Under the arrangement, we obtained rights to Intrexon's effector platform for use in the field of oncology, which includes two existing clinical stage product candidates, ZIN-CTI-001 (or DC-RTS-IL-12 + AL) and ZIN-ATI-001 (or Ad-RTS-IL-12 + AL). We plan to leverage Intrexon's synthetic biology platform to develop products to stimulate key pathways used by the body's immune system to inhibit the growth and metastasis of cancers, adding significantly to our small molecule drug development portfolio utilizing our global capabilities to translate science to the patient setting. Descriptions of our current clinical development plans for palifosfamide, darinaparsin and indibulin, ZIN-CTI-001 and ZIN-ATI-001, are set forth below. More detailed descriptions of these product candidates and our clinical development plans for each are also set forth in our Annual Report on Form 10-K for the fiscal year ended December 31, 2010, our Quarterly Report of Form 10-Q for the quarter ended March 31, 2011 and in the other reports that we file from time to time with the Securities and Exchange Commission that are incorporated herein by reference.

We believe that our strategy will result in expedited drug development programs for product candidates with a cost of manufacturing that, upon successful commercialization, would help to address changing worldwide product reimbursement requirements. We are currently in Phase 1, 2, and/or Phase 3 studies for our product candidates with a particular emphasis on completing a global palifosfamide pivotal Phase 3 trial to support registration in combination with doxorubicin in the front-line setting of metastatic soft tissue sarcoma.

Product Candidates

ZIO-101, Darinaparsin, ZinaparTM

Darinaparsin is a novel mitochondrial-targeted agent (organic arsenic) in development with intravenous ("IV") and oral administration. Phase 1 testing of the intravenous (IV) form of darinaparsin in solid tumors and hematological cancers was completed and we reported clinical activity and, importantly, a safety profile from these studies as predicted by preclinical results. We subsequently completed Phase 2 studies in advanced myeloma, primary liver cancer and in certain other hematological cancers. At the May 2009 annual meeting of the American Society of Clinical Oncology ("ASCO"), we reported favorable results from the trial with IV-administered darinaparsin in lymphoma, particularly peripheral T-cell lymphoma ("PTCL"). Subject to further review, we would plan to initiate an adaptive, potentially pivotal trial in certain relapsed patients. With focus on the relapsed setting, a Phase 1 study of darinaparsin in combination treatment with "CHOP" in the front-line setting of PTCL was closed. A Phase 1 trial with

an oral form of darinaparsin is currently in progress and, upon completion, we anticipate conducting further study in solid tumors and/or PTCL. We have obtained Orphan Drug Designation for darinaparsin in the United States and Europe for the treatment of PTCL.

ZIO-201, Palifosfamide, ZymafosTM

Palifosfamide is a novel DNA cross-linker (stabilized active metabolite of ifosfamide) in class with bendemustine, ifosfamide, and cyclophosphamide and currently in development with IV administration (oral in late preclinical). Following Phase 1 study, we completed Phase 2 testing of the IV form of palifosfamide as a single agent to treat advanced sarcoma. In both Phase 1 and Phase 2 testing, palifosfamide has been administered without the "uroprotectant" mesna as is required with ifosfamide, and the toxicities associated with the other ifosfamide metabolites, acrolein and chloroacetaldehyde, have not been observed. We reported clinical activity of palifosfamide when used alone in the Phase 2 study addressing advanced sarcoma. Following review of preclinical combination studies, we initiated a Phase 1 dose escalation study of palifosfamide in combination with doxorubicin, primarily in patients with soft tissue sarcoma. We reported favorable results and safety profile from this study at ASCO's 2009 annual meeting. In light of reported favorable Phase 2 single agent clinical activity data and with the combination being well tolerated in the Phase 1 trial, we initiated a Phase 2 randomized controlled trial ("PICASSO") in the second half of 2008 to compare doxorubicin plus palifosfamide to doxorubicin alone in patients with front- and second-line metastatic or unresectable soft tissue sarcoma. The study generated positive top-line interim data in 2009. Upon successfully reaching a pre-specified efficacy milestone and following safety and efficacy data review by the Data Committee, sarcoma experts, and our Medical Advisory Board, we elected to suspend enrollment in the trial in October 2009. We subsequently presented further positive interim data from the trial at the 15th Annual Connective Tissue Oncology Society meeting held in November 2009 and again at the 2010 ASCO annual meeting in June 2010, where the presentation was also selected for "Best of ASCO." In July 2010, we announced the initiation of a worldwide registration trial on a protocol design developed through a FDA End of Phase 2 meeting and the Special Protocol Assessment (SPA) process. Although we did engage in the SPA process, we, with guidance from the FDA, elected to initiate the trial without having obtained SPA agreement from the FDA. The Phase 3 trial is in front-line metastatic soft tissue sarcoma, entitled PICASSO 3, and is an international, randomized, double-blinded, placebo-controlled trial with a targeted enrollment of 424 patients. The study is designed to evaluate the safety and efficacy of palifosfamide administered with doxorubicin compared with doxorubicin administered with placebo, with no cross-over between the arms. Progression-free survival is the primary endpoint for accelerated approval, with overall survival as the primary endpoint for full approval. Orphan Drug Designation for palifosfamide has been obtained in both the United States and the European Union for the treatment of soft tissue sarcomas.

We have also initiated a Phase 1 trial with palifosfamide in combination with etoposide and carboplatin to determine appropriate safety for initiating a subsequent potentially pivotal, adaptive trial in front-line small-cell lung cancer ("SCLC"). An oral form of palifosfamide has been the subject of preclinical studies necessary for an Investigational New Drug ("IND") application to support commencing Phase 1 study. Based on an initial review, FDA has requested that we repeat an animal study, now underway, in order to support the planned Phase 1 protocol.

ZIO-301, Indibulin, ZybulinTM

Indibulin is a novel orally administered tubulin binding agent. Phase 1 study as a single agent in patients with advanced solid tumors has been completed. We have reported clinical activity at well-tolerated doses using a continuous dosing scheme without the development of clinically relevant peripheral neuropathy. Following encouraging preclinical results obtained with indibulin in combination with other chemotherapies, two Phase 1 combination studies were initiated with TarcevaTM and XelodaTM, respectively. Favorable activity and safety profile of oral indibulin with oral XelodaTM were reported at ASCO's annual meeting in May 2009. In all studies, a maximum tolerated dose ("MTD") was not established. Preclinical work with our consultant, Dr. Larry Norton, established a dosing schedule to enhance activity and reduce toxicity, which is presently five days on drug and nine days off in a Phase 1 study in late-stage metastatic breast cancer. In light of the lack of establishing an MTD and the need to administer many capsules several times a day, we have recently modified the dosage form to administer once a day dosing in the Phase 1 trial.

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ZIN-CTI-001 (or DC-RTS-IL-12 + AL) and ZIN-ATI-001 (or Ad-RTS-IL-12 + AL)

ZIOPHARM is also pursuing the development of novel DNA-based therapeutics in the field of cancer pursuant to an exclusive channel partnership with Intrexon Corporation. The partnership includes two existing clinical-stage product candidates. ZIN-CTI-001 is in a Phase 1b trial in the U.S. and employs intratumoral injection of modified dendritic cells from each patient and oral dosing of an activator ligand to turn on in vivo expression of interleukin-12 ("IL-12"). ZIN-CTI-001 uses a RheoSwitch Therapeutic System® (RTS) to control the timing and level of transgene expression for gene and cell therapy. The RTS® technology functions as a "gene switch" for the regulated expression of human IL-12 in the patients' dendritic cells, which are transduced with a replication-deficient adenoviral vector carrying the IL-12 gene under the control of the RTS® and in this study injected intratumorally for the treatment of patients with stage III or IV melanoma. The binding of the small molecule activator to the fusion proteins of RTS® is intended to regulate the timing and level of IL-12 expression. In the absence of the activator ligand ("AL"), the level of IL-12 is below detectable levels.

The activator ligand has been the subject of a number of preclinical, safety and pharmacology studies under FDA and ICH guidelines. Preclinical studies in the B16 mouse melanoma model consistently induced regression of established melanoma lesions, both in those directly injected and those elsewhere in the body. Preclinical studies have shown DC-RTS-IL-12, in combination with an activator ligand, to have strong activity against a broad array of cancers, including brain, colon, renal, and pancreatic cancers and melanoma.

A Phase 1a clinical study of the activator ligand was conducted in 65 healthy volunteers, with the two most common side effects being dysgeusia (impairment of taste) and throat irritation. A subsequent Phase 1b trial, which is ongoing in patients with advanced melanoma, has been amended to study efficacy and immunological and biological effects in addition to safety with cohort-based dose escalation of the activator ligand during repeated treatment cycles. Initial positive clinical results from the Phase 1b trial were presented at the June 2011 ASCO annual meeting. The trial enrolled ten patients (median age 61) with unresectable Stage III or IV melanoma. Among eight evaluable patients, partial or complete regression of injected and some uninjected lesions was observed by CT in three patients, with one patient having a RECIST PR of >11 months and three patients demonstrating stable disease by RECIST, for an overall disease control rate of 50%. Treatment was generally well tolerated, and maximum tolerated dose has not yet been reached. Adverse events were mild to moderate, with one to two patients each experiencing nausea, vomiting, anorexia, arthralgia, fever or chills. One severe adverse event was reported 18 hours after treatment onset with 60 mg AL + ZIN-CTI-001, and included diarrhea, followed by hypotension and reversible acute renal failure, which completely resolved.

The U.S. Food & Drug Administration (FDA) has recently accepted our investigational new drug (IND) application to begin clinical study of ZIN-ATI-001 in oncology. When initiated, the Phase 1 study will evaluate safety in addition to immunological and biological effects of the therapeutic candidate in patients with melanoma. We expect ZIN-ATI-001 to enter Phase 1 study during the first half of this year.

We intend to evaluate both ZIN-CTI-001 and ZIN-ATI-001 with the intent either to further develop both candidates or to select one of the two candidates for further study. ZIN-ATI-001 is identical to ZIN- CTI-001 except that the autologous dendritic cell component is omitted. Both product candidates are targeted for further development in different indications.

Development Plans

We are currently pursuing several clinical programs which include:

- palifosfamide (ZymafosTM or ZIO-201) – completing our Phase 3 pivotal trial in front-line metastatic soft tissue sarcoma, entitled PICASSO 3, and completing our recently initiated Phase 1 trial with palifosfamide in combination with etoposide and carboplatin to determine appropriate safety for initiating a subsequent randomized trial in front-line small-cell lung cancer.

- darinaparsin (ZinaparTM or ZIO-101) – completing an ongoing Phase 1 study with the oral form and determining future pivotal study with the IV and/or oral form.

- indibulin (ZybulinTM or ZIO-301) – entering the Phase 2 portion of the Phase 1/2 trial having established the MTD in Phase 1 with once daily dosing.

- ZIN-CTI-001 - completing a Phase 1b trial in patients with advanced melanoma that is on-going in the U.S.

- ZIN-ATI-001 – completing the Phase 1 trial targeting treatment of patients with late-stage malignant melanoma that is the subject of an IND application recently accepted by FDA.

We are also in late preclinical evaluation with respect to several additional potential product candidates under our channel partnership with Intrexon and we anticipate continuing evaluation to select product candidates for clinical study, which could commence as early as 2012. We also anticipate continuing discovery efforts aimed at identifying additional potential product candidates under the Intrexon channel partnership for study thereafter.

Our current plans involve using internal financial resources to develop palifosfamide and pursue the clinical work outlined above, with the intention of ultimately partnering or otherwise raising additional resources to support further development activities for all of our product candidates. 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 product candidates in any market and, therefore, have not generated any revenues from our product candidates.

Exclusive Channel Partnership and Private Placement with Intrexon Corporation

On January 6, 2011, we entered into an Exclusive Channel Partner Agreement (the “Channel Agreement”) with Intrexon Corporation (“Intrexon”) that governs a “channel partnering” arrangement in which we will use Intrexon’s technology directed towards in vivo expression of effectors in connection with the development of two existing clinical-stage product candidates and generally to research, develop and commercialize products, in each case in which DNA is administered to humans for expression of anti-cancer effectors for the purpose of treatment or prophylaxis of cancer.

In connection with the Channel Agreement, we entered into a Stock Purchase Agreement and Registration Rights Agreement with Intrexon. On January 12, 2011, and pursuant to the Stock Purchase Agreement, Intrexon purchased 2,426,235 shares of our common stock (the “Purchase Shares”) in a private placement for a total purchase price of $11,645,928, or $4.80 per share. We simultaneously issued to Intrexon for no additional consideration an additional 3,636,926 shares of our common stock (the “First Tranche Shares”). Under the terms of the Stock Purchase Agreement, we have agreed to issue to Intrexon an additional 3,636,926 shares of our common stock for no additional consideration (the “Second Tranche Shares”), under certain conditions upon dosing of the first patient in a ZIOPHARM-conducted U.S. Phase II clinical trial of a product candidate created, produced or developed by us using Intrexon technology. Pursuant to the Registration Rights Agreement, we have agreed to file registration statements with the Securities and Exchange Commission registering the resale of the Purchase Shares, First Tranche Shares and Second Tranche Shares. The shares being offered hereby consist of the Purchase Shares and the First Tranche Shares.

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 SEC 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

An investment in our common stock involves a number of risks. Before deciding to invest in our common stock, you should carefully consider the risk factors and all of the other information included under the section entitled "Risk Factors" beginning on page 6 of this prospectus, including the information incorporated by reference to the reports that we file with the Securities and Exchange Commission.

The Offering

This prospectus covers a total of 6,063,161 shares of our common stock.

Common stock covered hereby	6,063,161 shares
Common stock outstanding before the offering (1)	68,312,227 shares
Common stock outstanding after the offering	68,312,227 shares
Common Stock Nasdaq Capital Market symbol	ZIOP

(1) Based on the number of shares outstanding as of June 29, 2011, not including 18,038,198 shares issuable upon exercise of various warrants and options to purchase common stock.

RISK FACTORS

An investment in our common stock involves a number of risks. Before deciding to invest in our common stock, you should carefully consider the risks related to our Company and an investment in our common stock, including risks associated with delays in or discontinuance of development of our pharmaceutical product candidates, our inability to obtain necessary regulatory approvals to market products, unforeseen safety issues relating to the products, dependence on third-party collaborators and our ability to obtain financing sufficient to maintain our operations. 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. These and other risks could materially harm our business, financial condition or future results. If any such risks materialize, the value of our common stock could decline, and you could lose all or part of your investment. For a more detailed discussion of the risks you should consider before purchasing shares of our common stock, you are urged to carefully review and consider the information detailed in Item 1A of our Annual Report on Form 10-K for the year ended December 31, 2010, our Quarterly Report of Form 10-Q for the quarter ended March 31, 2011 and in the other reports that we file from time to time with the Securities and Exchange Commission, which are incorporated by reference into this prospectus and any applicable prospectus supplement.

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus, including the documents that we incorporate by reference, contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933 (the "Securities Act") and Section 21E of the Securities Exchange Act of 1934 (the "Exchange Act"). Any statements about our expectations, beliefs, plans, objectives, assumptions or future events or performance are not historical facts and may be forward-looking. These statements are often, but not always, made through the use of words or phrases such as anticipate, estimate, plan, project, continuing, ongoing, expect, management believes, we believe, we intend and similar words or phrases. Accordingly, these statements involve estimates, assumptions and uncertainties that could cause actual results to differ materially from those expressed. Any forward-looking statements are qualified in their entirety by reference to the factors discussed in this prospectus or incorporated by reference.

Because the factors discussed in this prospectus or incorporated herein by reference could cause actual results or outcomes to differ materially from those expressed in any forward-looking statements made by us or on our behalf, you should not place undue reliance on any such forward-looking statements. These statements are subject to risks and uncertainties—both known and unknown—which could cause actual results and developments to differ materially from those expressed or implied in such statements. Such risks and uncertainties relate to, among other factors: the development of our drug candidates; the regulatory approval of our drug candidates; our use of clinical research centers and other contractors; our ability to find collaborative partners for research, development and commercialization of potential products; acceptance of our products by doctors, patients or payors; our ability to market any of our products; our history of operating losses; our ability to compete against other companies and research institutions; our ability to secure adequate protection for our intellectual property; our ability to attract and retain key personnel; availability of reimbursement for our product candidates; the effect of potential strategic transactions on our business; our ability to obtain adequate financing; and the volatility of our stock price. These and other risks are detailed in Item 1A of our Annual Report on Form 10-K for the year ended December 31, 2010 and in the other reports that we file from time to time under the Securities Act or the Exchange Act, which are incorporated by reference into this prospectus and any applicable prospectus supplement. You are encouraged to read these filings as they are made.

Finally, 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 will not receive any proceeds from the disposition by the selling stockholder of any of the shares covered by this prospectus.

SELLING STOCKHOLDER

This prospectus covers the disposition by the selling stockholder identified below, or its transferee(s), of a total of 6,063,161 shares of our common stock. All of these shares were issued in connection with our January 2011 private placement described on page 4 above under the caption "Prospectus Summary — Exclusive Channel Partnership and Private Placement with Intrexon Corporation".

The following table sets forth the number of shares of the common stock owned by the selling stockholder as of June 29, 2011 and after giving effect to this offering assuming all of the shares covered hereby are sold by the selling stockholder. The percentage of beneficial ownership is based on 68,312,227 shares of our common stock outstanding as of June 29, 2011.

Selling Stockholder	Shares Beneficially Owned Before Offering (1)	Total Shares Offered By Selling Stockholder	Shares Beneficially Owned After Offering (1) (2)	Percentage of Beneficial Ownership After Offering (1) (2)
Intrexon Corporation (3)	7,973,161	6,063,161	1,910,000	2.8%

(1) Beneficial ownership is determined in accordance with SEC rules, beneficial ownership includes any shares as to which the security or stockholder has sole or shared voting power or investment power, and also any shares which the security or stockholder has the right to acquire within 60 days of the date hereof, whether through the exercise or conversion of any stock option, convertible security, warrant or other right. The indication herein that shares are beneficially owned is not an admission on the part of the security or stockholder that he, she or it is a direct or indirect beneficial owner of those shares.

(2) Assumes the sale of all shares offered under this prospectus by the selling stockholder.

(3) Randal J. Kirk, the Chief Executive Officer of the selling stockholder, Intrexon Corporation, and a member of the Company's board of directors, directly and through certain affiliates, has voting and dispositive power over a majority of the outstanding capital stock of Intrexon Corporation. Mr. Kirk may therefore be deemed to have voting and dispositive power over the shares of the issuer owned by Intrexon Corporation. Mr. Kirk disclaims beneficial ownership of such shares, except to the extent of any pecuniary interest therein.

PLAN OF DISTRIBUTION

The selling stockholder and any of its pledgees, donees, transferees, assignees or other successors-in-interest may, from time to time, sell, transfer or otherwise dispose of any or all of their shares of common stock or interests in shares of common stock on any stock exchange, market or trading facility on which the shares are traded or in private transactions. These dispositions may be at fixed prices, at prevailing market prices at the time of sale, at prices related to the prevailing market price, at varying prices determined at the time of sale, or at negotiated prices. The selling stockholder may use one or more of the following methods when disposing of the shares or interests therein:

- ordinary brokerage transactions and transactions in which the broker-dealer solicits purchasers;
- block trades in which the broker-dealer will attempt to sell the shares as agent but may position and resell a portion of the block as principal to facilitate the transaction;
- purchases by a broker-dealer as principal and resale by the broker-dealer for its account;
- an exchange distribution in accordance with the rules of the applicable exchange;
- privately negotiated transactions;
- through the writing or settlement of options, swaps, derivatives or other hedging transactions, whether through an options exchange or otherwise;
- broker-dealers may agree with the selling stockholder to sell a specified number of such shares at a stipulated price per share;
- in the over the counter market;
- a combination of any such methods of disposition; and
- any other method permitted pursuant to applicable law.

The selling stockholder may also sell shares under Rule 144 under the Securities Act, if available, rather than under this prospectus.

Broker-dealers engaged by the selling stockholder may arrange for other broker-dealers to participate in sales. Broker-dealers may receive commissions or discounts from the selling stockholder (or, if any broker-dealer acts as agent for the purchaser of shares, from the purchaser) in amounts to be negotiated, but, except as set forth in a supplement to this prospectus, in the case of an agency transaction will not be in excess of a customary brokerage commission in compliance with FINRA Rule 2440; and in the case of a principal transaction a markup or markdown in compliance with FINRA IM-2440 or the successor to such FINRA rules.

The selling stockholder may from time to time pledge or grant a security interest in some or all of the shares owned by it and, if they default in the performance of their secured obligations, the pledgees or secured parties may offer and sell shares of common stock from time to time under the prospectus, or under an amendment to the prospectus under Rule 424(b) or other applicable provision of the Securities Act, amending the list of selling stockholders to include the pledgee, transferee or other successors in interest as selling stockholders under the prospectus. The selling stockholder does not expect these commissions and discounts to exceed what is customary in the types of transactions involved.

There can be no assurance that the selling stockholder will sell any or all of the shares of common stock pursuant to the registration statement, of which this prospectus forms a part.

The selling stockholder may enter into option or other transactions with broker-dealers or other financial institutions or the creation of one or more derivative securities which require the delivery to such broker-dealer or other financial institution of shares offered by the prospectus, which shares such broker-dealer or other financial institution may resell pursuant to the prospectus (as supplemented or amended to reflect such transaction).

The selling stockholder and any broker-dealer or agents that are involved in selling the shares of common stock may be deemed to be "underwriters" within the meaning of the Securities Act in connection with such sales. In such event, any commissions received by such broker-dealers or agents and any profit on the resale of common stock purchased by them may be deemed to be underwriting commissions or discounts under the Securities Act. In no event shall any broker-dealer receive fees, commission and markups which, in the aggregate, would exceed eight percent (8%). The selling stockholder has informed the Company that it does not have any written or oral agreement or understanding, directly or indirectly, with any person to distribute the common stock.

We have advised the selling stockholder that it may not use shares registered on the registration statement of which this prospectus is a part to cover short sales of common stock made prior to the date on which the registration statement shall have been declared effective by the Securities and Exchange Commission. If the selling stockholder uses this prospectus for any sale of shares of our common stock, it will be subject to the prospectus delivery requirements of the Securities Act. The selling stockholder and any other person participating in such distribution will be subject to applicable provisions of the Exchange Act, and the rules and regulations promulgated thereunder, including, without limitation, Regulation M of the Exchange Act, which may limit the timing of purchases and sales of any of the shares of common stock by the selling stockholder and any other participating person. Regulation M may also restrict the ability of any person engaged in the distribution of the shares of common stock to engage in market-making activities with respect to the shares of common stock. All of the foregoing may affect the marketability of the shares of common stock and the ability of any person or entity to engage in market-making activities with respect to the shares of common stock.

We may indemnify the selling stockholder against certain liabilities, including some liabilities under the Securities Act, in accordance with an agreement between us and the selling stockholder. We may be indemnified by the selling stockholder against civil liabilities, including liabilities under the Securities Act, that may arise from any written information furnished to us by the selling stockholder specifically for use in this prospectus, in accordance with the related registration rights agreement, or we may be entitled to contribution.

DISCLOSURE OF COMMISSION POSITION ON INDEMNIFICATION FOR SECURITIES ACT LIABILITIES

Pursuant to our certificate of incorporation and bylaws, we may indemnify an officer or director who is made a party to any proceeding, because of his position as such, to the fullest extent authorized by Delaware General Corporation Law, as the same exists or may hereafter be amended. In certain cases, we may advance expenses incurred in defending any such proceeding.

To the extent that indemnification for liabilities arising under the Securities Act may be permitted to directors, officers or persons controlling our company pursuant to the foregoing provisions, or otherwise, we have been advised that, in the opinion of the SEC, such indemnification is against public policy as expressed in the Securities Act and is therefore unenforceable. If a claim for indemnification against such liabilities (other than the payment by us of expenses incurred or paid by a director, officer or controlling person of our company in the successful defense of any action, suit or proceeding) is asserted by any of our directors, officers or controlling persons in connection with the securities being registered, we will, unless in the opinion of our counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by us is against public policy as expressed in the Securities Act and will be governed by the final adjudication of that issue.

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ABOUT THIS PROSPECTUS

This prospectus is not an offer or solicitation in respect to these securities in any jurisdiction in which such offer or solicitation would be unlawful. This prospectus is part of a registration statement that we filed with the SEC. The registration statement that contains this prospectus (including the exhibits to the registration statement) contains additional information about our company and the securities offered under this prospectus. That registration statement can be read at the SEC web site or at the SEC's offices mentioned below under the heading "Where You Can Find More Information." We have not authorized anyone else to provide you with different information or additional information. You should not assume that the information in this prospectus, or any supplement or amendment to this prospectus, is accurate at any date other than the date indicated on the cover page of such documents.

WHERE YOU CAN FIND MORE INFORMATION

We have filed with the SEC a registration statement on Form S-3 (including exhibits to such registration statement) under the Securities Act, with respect to the shares of our common stock offered by this prospectus. This prospectus does not contain all the information set forth in the registration statement. For further information with respect to our Company and the shares of our common stock to be sold under this prospectus, we refer you to the registration statement (SEC File No. 333-174292). Statements contained in this prospectus as to the contents of any contract, agreement or other document to which we make reference are not necessarily complete. In each instance, we refer you to the copy of such contract, agreement or other document filed as an exhibit to the registration statement, each such statement being qualified in all respects by the more complete description of the matter involved.

We are currently subject to the reporting and information requirements of the Exchange Act and, as a result, we are required to file periodic and current reports, and other information with the SEC. You may read and copy this information at the Public Reference Room of the SEC located at 100 F Street, N.E., Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for further information on the operation of the Public Reference Room. Copies of all or any part of the registration statement may be obtained from the SEC's offices upon payment of fees prescribed by the SEC. The SEC maintains an internet site that contains periodic and current reports, proxy and information statements, and other information regarding issuers that file electronically with the SEC. The address of the SEC's website is http://www.sec.gov.

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 Exchange Act (other than information furnished in Current Reports on Form 8-K filed under Item 2.02 or 7.01 of such form), including filings made after the date of the initial registration statement of which this prospectus is a part and prior to the effective date of such registration statement:

- Annual Report on Form 10-K for the fiscal year ended December 31, 2010, filed on March 1, 2011, including the information incorporated by reference into such report by reference to our annual meeting proxy statement on Schedule 14A filed May 2, 2011;

- Quarterly Report on Form 10-Q for the quarter ended March 31, 2011, filed on May 5, 2011;

- Current Reports on Form 8-K filed on each of January 5, January 12, January 26, February 3, February 7, February 7, February 8, March 7, May 9, May 13, May 19, May 23, June 3, June 6, June 10 and June 22, 2011, respectively; 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 stockholder 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.

VALIDITY OF COMMON STOCK

Legal matters in connection with the validity of the shares offered by this prospectus will be passed upon by Maslon Edelman Borman & Brand, LLP, of Minneapolis, Minnesota.

EXPERTS

The financial statements as of and for the year ended December 31, 2010 and for the period from September 9, 2003 (date of inception) through December 31, 2010 incorporated by reference into this Prospectus and Registration Statement, and the effectiveness of internal control over financial reporting as of December 31, 2010, have been audited by McGladrey & Pullen, LLP, an independent registered public accounting firm, as stated in their reports incorporated by reference herein, and are included in reliance upon such reports and upon the authority of such firm as experts in accounting and auditing.

The balance sheet as of December 31, 2009 and the related statements of operations, changes in preferred stock and stockholders' equity (deficit) and cash flows for each of the years in the two-year period ended December 31, 2009, incorporated by reference into the registration statement of which this prospectus is a part, have been included herein in reliance on the report, dated March 17, 2010, of Caturano and Company, P.C. (whose name has since been changed to Caturano and Company, Inc.), independent registered public accounting firm, given on the authority of that firm as experts in auditing and accounting.

6,063,161 Shares

Common Stock

ZIOPHARM Oncology, Inc.

_____

PROSPECTUS

_____

, 2011

PART II
INFORMATION NOT REQUIRED IN PROSPECTUS

Item 14. Other Expenses of Issuance and Distribution.

The registrant estimates that expenses payable in connection with the offering described in this registration statement will be as follows:

SEC registration fee	$	4,524
Legal fees and expenses		10,000
Accounting fees and expenses		10,000
Printing and engraving expenses		3,000
Miscellaneous		2,000
	$	29,524

Item 15. Indemnification of Directors and Officers.

Under Article 6 of the Registrant's bylaws, each director and officer of the Registrant will be indemnified to the fullest extent permitted by applicable law as it presently exists or may hereafter be amended, who was or is made or is threatened to be made a party or is otherwise involved in any action, suit or proceeding, whether civil, criminal, administrative or investigative, by reason of the fact that he or she, or a person for whom he or she is the legal representative, is or was a director or officer of the Registrant or, while a director or officer of the Registrant, is or was serving at the request of the Registrant as a director, officer, employee or agent of another corporation or of a partnership, joint venture, trust, enterprise or nonprofit entity, including service with respect to employee benefit plans, against all liability and loss suffered and expenses (including attorneys' fees) reasonably incurred by such director or officer. However, the Registrant shall be required to indemnify a director or officer in connection with a proceeding commenced by such director or officer only if the commencement of such proceeding (or part thereof) by the director or officer was authorized by the Board. The Registrant's Amended and Restated Certificate of Incorporation also eliminates the liability of directors of the Registrant for monetary damages to the fullest extent permissible under Delaware law.

Section 145 of the Delaware General Corporation Law states, in part:

(a) A corporation shall have power to indemnify any person who was or is a party or is threatened to be made a party to any threatened, pending or completed action, suit or proceeding, whether civil, criminal, administrative or investigative (other than an action by or in the right of the corporation) by reason of the fact that the person is or was a director, officer, employee or agent of the corporation, or is or was serving at the request of the corporation as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise, against expenses (including attorneys' fees), judgments, fines and amounts paid in settlement actually and reasonably incurred by the person in connection with such action, suit or proceeding if the person acted in good faith and in a manner the person reasonably believed to be in or not opposed to the best interests of the corporation, and, with respect to any criminal action or proceeding, had no reasonable cause to believe the person's conduct was unlawful. The termination of any action, suit or proceeding by judgment, order, settlement, conviction, or upon a plea of nolo contendere or its equivalent, shall not, of itself, create a presumption that the person did not act in good faith and in a manner which the person reasonably believed to be in or not opposed to the best interests of the corporation, and, with respect to any criminal action or proceeding, had reasonable cause to believe that the person's conduct was unlawful.

(b) A corporation shall have power to indemnify any person who was or is a party or is threatened to be made a party to any threatened, pending or completed action or suit by or in the right of the corporation to procure a judgment

in its favor by reason of the fact that the person is or was a director, officer, employee or agent of the corporation, or is or was serving at the request of the corporation as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise against expenses (including attorneys' fees) actually and reasonably incurred by the person in connection with the defense or settlement of such action or suit if the person acted in good faith and in a manner the person reasonably believed to be in or not opposed to the best interests of the corporation and except that no indemnification shall be made in respect of any claim, issue or matter as to which such person shall have been adjudged to be liable to the corporation unless and only to the extent that the Court of Chancery or the court in which such action or suit was brought shall determine upon application that, despite the adjudication of liability but in view of all the circumstances of the case, such person is fairly and reasonably entitled to indemnity for such expenses which the Court of Chancery or such other court shall deem proper.

The Registrant maintains insurance on behalf of its officers and directors, insuring them against liabilities that they may incur in such capacities or arising out of this status.

The above discussion of the Registrant's Amended and Restated Certificate of Incorporation and Bylaws and of Section 145 of the Delaware General Corporation Law is not intended to be exhaustive and is respectively qualified in its entirety by such Amended and Restated Certificate of Incorporation, Bylaws and statute.

To the extent that our directors, officers and controlling persons are indemnified under the provisions contained in our amended and restated 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 of 1933, as amended, and is therefore unenforceable.

Item 16. Exhibits.

The following exhibits are filed as part of this Registration Statement:

Exhibit No.	Description
2.1	Agreement and Plan of Merger among the registrant (formerly "EasyWeb, Inc."), ZIO Acquisition Corp. and ZIOPHARM, Inc., dated August 3, 2005 (incorporated by reference to Exhibit 10.1 to the registrant's Form 8-K filed August 9, 2005).
4.1	Amended and Restated Certificate of Incorporation, as filed with the Delaware Secretary of State on April 26, 2006 (incorporated by reference to Exhibit 3.1 to the registrant's Current Report of Form 8-K filed April 26, 2006).
4.2	Certificate of Merger dated September 13, 2005, relating to the merger of ZIO Acquisition Corp. with and into ZIOPHARM, Inc. (incorporated by reference to Exhibit 3.1 to the registrant's Form 8-K filed September 19, 2005).
4.3	Certificate of Ownership of the registrant (formerly "EasyWeb, Inc.") dated as of September 14, 2005, relating the merger of ZIOPHARM, Inc. with and into the registrant, and changing the registrant's corporate name from EasyWeb, Inc. to ZIOPHARM Oncology, Inc. (incorporated by reference to Exhibit 3.2 to the registrant's Form 8-K filed September 19, 2005).
4.4	Bylaws, as amended to date (incorporated by reference to Exhibit 3.3 to the registrant's Form 8-K filed September 19, 2005).
4.5	Specimen common stock certificate (incorporated by reference to Exhibit 4.1 to the registrant's Registration Statement on Form SB-2 [SEC File No. 333-129020] filed October 14, 2005).

4.6	Exclusive Channel Partner Agreement between the registrant and Intrexon Corporation, dated January 6, 2011 (incorporated by reference to Exhibit 10.1 to the registrant's Current Report on Form 8-K filed January 10, 2011).**
4.7	Securities Purchase Agreement between the registrant and Intrexon Corporation, dated January 6, 2011 (incorporated by reference to Exhibit 10.2 to the registrant's Current Report on Form 8-K filed January 10, 2011).
4.8	Amendment Stock Purchase Agreement by and between the Registrant and Intrexon Corporation dated as of February 1, 2011 (incorporated by reference to Exhibit 10.1 to the registrant's Current Report on Form 8-K filed February 7, 2011).
4.9	Registration Rights Agreement, dated January 12, 2011, by and between ZIOPHARM Oncology, Inc. and Intrexon Corporation (incorporated by reference to Exhibit A to the Stock Purchase Agreement filed as Exhibit 10.2 to the registrant's Current Report on Form 8-K filed January 10, 2011).
5.1	Legal opinion of Maslon Edelman Borman & Brand, LLP (filed herewith).
23.1	Consent of Independent Registered Public Accounting Firm - McGladrey & Pullen, LLP (filed herewith).
23.2	Consent of Independent Registered Public Accounting Firm – Caturano and Company, Inc. (filed herewith).
23.3	Consent of Maslon Edelman Borman & Brand, LLP (included as part of Exhibit 5.1).
24.1	Power of Attorney (included on signature page to this Registration Statement).

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** Confidential treatment has been granted as to certain portions of this exhibit pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.

Item 17. Undertakings.

(a) The undersigned Registrant hereby undertakes:

(1) To file, during any period in which offers or sales are being made, a post-effective amendment to this registration statement:

(i) To include any prospectus required by Section 10(a)(3) of the Securities Act of 1933;

(ii) To reflect in the prospectus any facts or events arising after the effective date of the registration statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in the registration statement. Notwithstanding the foregoing, any increase or decrease in volume of securities offered (if the total dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of prospectus filed with the Commission pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than a 20 percent change in the maximum aggregate offering price set forth in the

“Calculation of Registration Fee” table in the effective registration statement; and

(iii) To include any material information with respect to the plan of distribution not previously disclosed in the registration statement or any material change to such information in the registration statement;

provided, however, that

(A) the undertakings set forth in paragraphs (1)(i), (1)(ii) and (1)(iii) above do not apply if the registration statement is on Form S-8, and the information required to be included in a post-effective amendment by those paragraphs is contained in reports field with or furnished to the Commission by the registrant pursuant to section 13 or section 15(d) of the Securities Exchange Act of 1934 that are incorporated by reference in the registration statement; and

(B) the undertakings set forth in paragraphs (1)(i), (1)(ii) and (1)(iii) above do not apply if the registration statement is on Form S-3 or Form F-3 and the information required to be included in a post-effective amendment by those paragraphs is contained in reports filed with or furnished to the Commission by the registrant pursuant to Section 13 or Section 15(d) of the Securities Exchange Act of 1934 that are incorporated by reference in the registration statement or is contained in a form of prospectus filed pursuant to Rule 424(b) that is a part of the registration statement.

(C) provided further, however, that paragraphs (1)(i), (1)(ii) and (1)(iii) above do not apply if the registration statement is for an offering of asset-backed securities on From S-1 or Form S-3, and the information required to be included in a post-effective amendment is proved pursuant to Item 1100(c) of Regulation AB.

(2) That, for the purpose of determining any liability under the Securities Act of 1933, each such post-effective amendment shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

(3) To remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of the offering.

(4) That, for the purpose of determining liability under the Securities Act of 1933 to any purchaser:

(i) Each prospectus filed by the registrant pursuant to Rule 424(b)(3) shall be deemed to be part of the registration statement as of the date the filed prospectus was deemed part of and included in the registration statement; and

(ii) Each prospectus required to be filed pursuant to Rule 424(b)(2), (b)(5), or (b)(7) as part of a registration statement in reliance on Rule 430B relating to an offering made pursuant to Rule 415(a)(1)(i), (vii), or (x) for the purpose of providing the information required by section 10(a) of the Securities Act of 1933 shall be deemed to be part of and included in the registration statement as of the earlier of the date such form of prospectus is first used after effectiveness or the date of the first contract of sale of securities in the offering described in the prospectus. As provided in Rule 430B, for liability purposes of the issuer and any person that is at that date an underwriter, such date shall be deemed to be a new effective date of the registration statement relating to the securities in the registration statement to which that prospectus relates, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof. Provided, however, that no statement made in a registration statement or prospectus that is part of the registration statement or made in a document incorporated or deemed incorporated by reference into the registration statement or prospectus that is part of the registration statement will, as to a purchaser with a time of contract of sale prior to such effective date, supersede or modify any statement that was made in the registration statement or prospectus that was part of the registration statement or made in any such document immediately prior to such effective date.

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(5) That, for the purpose of determining liability of the registrant under the Securities Act of 1933 to any purchaser in the initial distribution of the securities, the undersigned registrant undertakes that in a primary offering of securities of the undersigned registrant pursuant to this registration statement, regardless of the underwriting method used to sell the securities to the purchaser, if the securities are offered or sold to such purchaser by means of any of the following communications, the undersigned registrant will be a seller to the purchaser and will be considered to offer or sell such securities to such purchaser:

(i) Any preliminary prospectus or prospectus of the undersigned registrant relating to the offering required to be filed pursuant to Rule 424;

(ii) Any free writing prospectus relating to the offering prepared by or on behalf of the undersigned registrant or used or referred to by the undersigned registrant;

(iii) The portion of any other free writing prospectus relating to the offering containing material information about the undersigned registrant or its securities provided by or on behalf of the undersigned registrant; and

(iv) Any other communication that is an offer in the offering made by the undersigned registrant to the purchaser.

(b) That, for purposes of determining any liability under the Securities Act of 1933, each filing of the registrant's annual report pursuant to section 13(a) or section 15(d) of the Securities Exchange Act of 1934 (and, where applicable, each filing of an employee benefit plan's annual report pursuant to section 15(d) of the Securities Exchange Act of 1934) that is incorporated by reference in the registration statement shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, the registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-3 and has duly caused this registration statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Boston, Commonwealth of Massachusetts on July 1, 2011.

ZIOPHARM Oncology, Inc.

By: /s/ Jonathan Lewis
Jonathan Lewis, Chief Executive Officer

POWER OF ATTORNEY

Pursuant to the requirements of the Securities Act of 1933, this registration statement has been signed by the following persons in the capacities and on the dates indicated.

Name	Title	Date
* Jonathan Lewis	Director and Chief Executive Officer (Principal Executive Officer)	July 1, 2011
/s/ Richard E. Bagley Richard E. Bagley	Director, President, Treasurer and Chief Operating Officer (Principal Accounting and Financial Officer)	July 1, 2011
* Murray Brennan	Director	July 1, 2011
* James Cannon	Director	July 1, 2011
* Wyche Fowler, Jr.	Director	July 1, 2011
* Randal J. Kirk	Director	July 1, 2011
* Timothy McInerney	Director	July 1, 2011
* Michael Weiser	Director	July 1, 2011

By: /s/ Richard E. Bagley

Richard E. Bagley, Attorney-in-fact

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