ZIOPHARM ONCOLOGY INC
Form 8-K
February 03, 2011

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

FORM 8-K

CURRENT REPORT
PURSUANT TO SECTION 13 OR 15(d) OF THE
SECURITIES EXCHANGE ACT OF 1934

Date of report (Date of earliest event reported): February 2, 2011

ZIOPHARM Oncology, Inc.
(Exact Name of Registrant as Specified in Charter)

Delaware	001-33038	84-1475672
(State or Other Jurisdiction of Incorporation)	(Commission File Number)	(IRS Employer Identification No.)

1180 Avenue of the Americas 19th Floor New York, NY	10036
(Address of Principal Executive Offices)	(Zip Code)

(646) 214-0700
(Registrant's telephone number, including area code)

Not applicable
(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

o Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425).

o Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12).

o Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b)).

o Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c)).

Item 2.02. Results of Operations and Financial Condition.

On February 2, 2011, we filed with the Securities and Exchange Commission, or SEC, a prospectus supplement to our Registration Statement on Form S-3 (File No. 333-166444), which included the following preliminary financial information as of December 31, 2010 and for the three and twelve month periods then ended:

The following table sets forth the Company's forecast of selected financial data at December 31, 2010 and for the three and twelve month periods then ended, as well as selected financial data of the Company at December 31, 2009 and for the twelve month period then ended. The selected financial data at December 31, 2009 and for the twelve month period then ended are derived from our audited financial statements included in our annual report on Form 10-K for the fiscal year ended December 31, 2009, which is filed with the SEC and incorporated by reference into this Current Report on Form 8-K. You should read such selected financial data in conjunction with the corresponding audited financial statements and the related notes and with "Management's Discussion and Analysis of Financial Condition and Results of Operations" included in such annual report on Form 10-K and generally in the periodic reports that we file with the SEC. Our forecast of selected financial data at December 31, 2010 and for the three and twelve month periods then ended is preliminary in nature, has not been audited and is subject to change upon completion of our ongoing audit. Therefore, our actual financial condition and results of operations at December 31, 2010 and for the three and twelve month periods then ended may differ materially from the forecasts reflected above and we assume no obligation to update the disclosures in this Current Report on Form 8-K based upon our actual financial results. Moreover, this data does not reflect the proceeds from the sale of shares of our common stock to Intrexon Corporation on January 12, 2011 in a private placement transaction for a purchase price of approximately $11.6 million. Additional information and disclosures would be required for a more complete understanding of our financial position as of December 31, 2010 and our results of operations for the period then ended.

Balance Sheet Data
(in thousands)

	December 31, 2010 (unaudited)	December 31, 2009
Cash and cash equivalents	$ 60,392	$ 48,839
Working capital	$ 57,208	$ 46,098
Total assets	$ 61,543	$ 49,736
Current liabilities	$ 3,631	$ 3,095
Warrant liabilities	$ 27,311	$ 18,471
Total liabilities	$ 30,986	$ 21,632
Total stockholders' equity	$ 30,557	$ 28,104

ZIOPHARM Oncology, Inc.
Condensed Statements of Operations
(in thousands except share and per share data)

	For the Three Months Ended December 31, (unaudited)		For the Year Ended December 31,	
	2010	2009	2010 (unaudited)	2009
Research contract revenue	$ -	$ -	$ -	$ -
Operating expenses:				
Research and development, including costs of research contracts	3,054	1,216	12,927	4,556
General and administrative	3,302	2,813	11,615	7,567
Total operating expenses	6,356	4,029	24,542	12,123
Loss from operations	(6,356)	(4,029)	(24,542)	(12,123)
Other income, net	735	12	765	13
Change in fair value of warrants	(6,226)	4,981	(8,889)	4,461
Net loss	$ (11,847)	$ 964	$ (32,666)	$ (7,649)
Basic and diluted net loss per share	$ (0.25)	$ 0.03	$ (0.71)	$ (0.33)
Weighted average common shares outstanding used to compute basic and diluted net loss per share	48,039,345	28,002,429	46,003,679	23,108,039

Additional information and disclosures would be required for a more complete understanding of our financial position and results of operations as of December 31, 2010.

Item 8.01 Other Events

Public Offering Announcement

On February 2, 2011, the Company issued a press release announcing that it is offering to sell 9,600,000 shares of its common stock pursuant to an effective shelf registration statement in an underwritten public offering. Barclays Capital Inc. is acting as sole book-running manager in this offering and ZIOPHARM has granted the underwriter a 30 day option to purchase up to 1,440,000 additional shares. A copy of the press release is furnished herewith as Exhibit 99.1 to this Current Report.

The offering is expected to close on or about February 7, 2011, subject to customary closing conditions. A registration statement relating to the shares described above was filed with, and deemed effective by, the Securities and Exchange Commission on May 10, 2010. A prospectus supplement relating to the offering will be filed with the Securities and Exchange Commission.

Updated Business Description and Risk Factors

We are filing the following information with the Securities and Exchange Commission for the purpose of updating certain aspects of the publicly disclosed descriptions of our business, risk factors and related matters. All references below to “ZIOPHARM Oncology,” “ZIOPHARM,” the “Company,” “we,” “us,” “our,” or similar references refer to ZIOPHA Oncology, Inc., except where the context otherwise requires or as otherwise indicated.

Description of the Business

Company Overview

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 and/or oral dosing. On January 6, 2011, we entered into a Exclusive Channel Partner Agreement with Intrexon Corporation pursuant to which we will supplement our small molecule drug development efforts by pursuing the development and commercialization of novel DNA-based therapeutics in the field of cancer treatment using Intrexon's Rheoswitch® and UltraVector® synthetic biology technologies. See "Recent Developments—Exclusive Channel Partnership with Intrexon Corporation." This partnering arrangement contemplates our using Intrexon's advanced transgene engineering platform for the controlled and precise cellular production of anti-cancer effectors. Under the arrangement, we obtained rights to Intrexon's entire in vivo effector platform for use in the field of oncology, which includes two existing clinical-stage product candidates. The first lead product, INXN 3001/1001, is currently in a Phase Ib study and the second, INXN 2001/1001, is the basis of an Investigational New Drug ("IND") application that we expect to submit during the first half of 2011. We plan to leverage Intrexon's synthetic biology platform for 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.

We believe that our strategy will result in expedited drug development programs with product candidates having a low cost of manufacturing that address changing reimbursement requirements around the world. We are currently in Phase I, II and/or III studies for four product candidates identified as palifosfamide (Zymafos TM , ZIO-201), darinaparsin (Zinapar TM , ZIO-101), indibulin (Zybulin TM , ZIO-301), and INXN-3001/1001, with a particular emphasis on completing the recently initiated palifosfamide pivotal Phase III trial to support registration in combination with doxorubicin in the front-line setting of soft tissue sarcoma.

- ZIO-201 or palifosfamide (Zymafos TM) comprises 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 and in the U.S. we recently received a patent covering pharmaceutical composition. 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. We believe 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 Oncology in the U.S. and Europe to treat certain hematological malignancies. Ifosfamide has been shown to be effective in the treatment of sarcoma and lymphoma, either by itself or in combination with other anticancer agents. Ifosfamide is approved by the 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 approved 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.

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Following completion of Phase I study, we completed Phase II testing of the intravenous form of palifosfamide as a single agent to treat advanced sarcoma. 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. We reported clinical activity of palifosfamide when used alone in the Phase II study addressing advanced sarcoma. Following review of preclinical combination studies, clinical data, and discussion with sarcoma experts, we initiated a Phase I 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 II clinical activity data and with the combination being well tolerated in the Phase I trial, we initiated a Phase II randomized controlled trial 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 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 II meeting and the Special Protocol Assessment (SPA) process. Although the Company did engage in the SPA process, the Company, with guidance from the FDA, elected to initiate the trial without having obtained SPA agreement from the FDA. The Phase III 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. As an orphan designated indication, the patient population available for participation in the PICASSO 3 trial is generally limited. To date, the company has experienced slower than anticipated enrollment in the PICASSO 3 trial and has recently taken steps to accelerate patient enrollment and address shortages of doxorubicin, a drug that is necessary for conduct of the trial.

We have also initiated a Phase I 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 ("SCLC"). An oral form of palifosfamide is expected to enter Phase I study in the first quarter of this year.

- ZIO-101 or darinaparsin (Zinapar TM) 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 ®] or "ATO") has been approved in the United States, the European Union and Japan for the treatment of acute promyelocytic leukemia, 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 ATO, 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, provided support for the development of an oral 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 was completed and we reported clinical activity and, importantly, a safety profile from these studies as predicted by preclinical results. We subsequently completed Phase II studies in advanced myeloma, primary liver cancer and in certain other hematological cancers. In addition, we have re-opened Phase I study with an oral form which is ongoing. At the May 2009 annual meeting of the American Society of Clinical Oncology, we reported favorable results from the trial with IV-administered darinaparsin in lymphoma, particularly peripheral T-cell lymphoma. We have initiated a Phase I study of darinaparsin with the combination treatment regimen called "CHOP", which is standard of care for front-line peripheral T-cell lymphoma ("PTCL"), as a basis to address the front-line setting of PTCL. We presently plan to initiate a two-stage potentially pivotal trial likely in certain relapsed patients. We have obtained Orphan Drug Designation in the United States for the treatment of PTCL, and a positive recommendation from the Committee for Orphan Medicinal Products (COMP) within the European Medicines Agency (EMA) for designation as an orphan medicinal product for the same indication. Upon completion of the on-going Phase I oral study, we anticipate conducting a Phase II study in solid tumors that would build upon recently reported preclinical work in which darinaparsin had a significant cytotoxic and radiosensitizing effect against different cancer cells under both normal and hypoxic conditions.

- ZIO-301 or indibulin (Zybulin TM) is a novel, orally available small molecular-weight inhibitor of tubulin polymerization that we acquired from Baxter Healthcare in 2006 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 new classes of tubulin inhibitors including the epothilones. 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 Phase I trials. Indibulin has also demonstrated synergy with approved anti-cancer agents in preclinical studies. The availability of an oral formulation of indibulin creates significant commercial opportunity because no oral capsule formulations of the taxane family are currently on the market in the United States.

Indibulin, as a single agent, has completed a Phase I study in patients with advanced solid tumors. We have 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 TM and Xeloda TM , respectively. Favorable activity and safety profile of oral indibulin with oral Xeloda TM were reported at ASCO's annual meeting in May 2009. Preclinical work with our consultant, Dr. Larry Norton, to explore dose scheduling for the clinical setting have been completed, with results supporting the recently initiated Phase I safety trial necessary for a Phase II breast cancer trial and using the mathematical dosing schedule established preclinically. We have recently modified the dosage form to be able to administer a smaller number of capsules and expect to substitute the new dosage form into our ongoing Phase I trial in the first quarter of this year.

- INXN 3001/1001 (or DC-RTS-IL-12) and INXN 2001/1001 (or Ad-RTS-IL-12) are the two lead clinical-stage projects currently in development under our partnering arrangement with Intrexon Corporation.

INXN 3001/1001 is in a Phase Ib trial in the U.S. and employs intratumoral injection of modified dendritic cells from each patient (INXN-3001) and oral dosing of an activator ligand (INXN-1001) to turn on in vivo expression of interleukin-12 ("IL-12"). INXN-3001/1001 uses the RheoSwitch Therapeutic System (RTS TM) to control the timing and level of transgene expression for gene and cell therapy. RTS TM 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 TM 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 TM is intended to regulate the timing and level of IL-12 expression. In the absence of the activator ligand, 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 INXN-1001, to have strong activity against a broad array of cancers, including brain, colon, renal, and pancreatic cancers and melanoma.

A Phase Ia 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. In the subsequent Phase Ib trial, which is now ongoing in patients with advanced melanoma, one patient reported a severe adverse event that constitutes a dose limiting toxicity (DLT). According to the protocol, additional patients are being evaluated to determine if the dose escalation will continue or the maximum tolerated dose has been reached. Among the first four patients treated, one patient demonstrated an overall partial response and a second demonstrated a response in some lesions. The Phase Ib trial 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.

INXN 2001/1001 is expected to enter the clinic in the first half of this year, also targeting treatment of patients with late-stage malignant melanoma. We intend to evaluate both product candidates with the intent either to further develop both candidates or to select one of the two candidates for further study. INXN 2001/1001 is identical to INXN 3001/1001 except that the autologous dendritic cell component (INXN-3001) is omitted.

Recent Developments

Exclusive Channel Partnership 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 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.

Intrexon Corporation Private Placement and Equity Commitment

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 that Stock Purchase Agreement, Intrexon purchased 2,426,235 shares of our common stock 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. 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 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 a registration statement with the SEC registering the resale of the shares that we have issued or may issue to Intrexon under the Stock Purchase Agreement.

Also under the Stock Purchase Agreement, Intrexon has agreed that, subject to certain conditions and restrictions and limitations, it will purchase our securities in conjunction with “qualified” securities offerings that we conduct while the Channel Agreement remains in effect. In conjunction with a particular qualified offering, Intrexon has committed to purchase up to 19.99% of the securities offering and sold therein (exclusive of Intrexon’s purchase) if requested to do so by us. However, Intrexon will not be obligated to purchase securities in a “qualified” securities offering unless we are then in substantial compliance with our obligations under the Channel Agreement and, with respect to a “qualified” securities offering that is completed following January 6, 2012, we confirm our intent that 40% of the offering’s net proceeds shall have been spent, or in the next year will be spent, by us under the Channel Agreement. In the case of a “qualified” securities offering that is completed after January 6, 2012, Intrexon’s purchase commitment will be further limited to an amount equal to one-half of the proceeds spent or to be spent by us under the Channel Agreement. Intrexon’s aggregate purchase commitment for all future qualified offerings is capped at $50.0 million. The Company and Intrexon subsequently amended the Stock Purchase Agreement to clarify that gross proceeds from the sale of Company securities to Intrexon in a qualified offering will apply against Intrexon’s $50.0 million purchase commitment regardless of whether Intrexon participates voluntarily or at the request of the Company.

Summary Development Plans

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.

On February 2, 2010, the Company announced that it is offering to sell 9,600,000 shares of its common stock pursuant to an effective shelf registration statement in an underwritten public offering. Barclays Capital Inc. is acting as sole book-running manager in this offering and ZIOPHARM has granted the underwriter a 30 day option to purchase up to 1,440,000 additional shares. Assuming completion of this offering and given our current plans to use internal financial resources to develop palifosfamide and pursue the clinical work discussed above, but with the intention of partnering or otherwise raising additional resources to support further development activities for all of our product candidates, we expect to incur the following expenses during the next twelve months: approximately $57.5 million on research and development expenses and approximately $10.4 million on general corporate and administrative expenses. With our current cash position, we believe that we currently have sufficient capital that will support our current operations until late 2012. Our forecast of the period of time through which our financial resources will be adequate to support our

operations, the costs to complete development of products and the cost to commercialize our future products are forward-looking statements and involve risks and uncertainties, and actual results could vary materially and negatively as a result of a number of factors, including the factors discussed in the “Risk Factors” section of this Report. We have based these estimates on assumptions that may prove to be wrong, and we could exhaust our available capital resources sooner than we currently expect. Specifically, we commenced a registration trial for IV palifosfamide early in the third quarter of 2010. We have estimated the sufficiency of our cash resources based in part on this trial design and our timing expectations for enrollment in the study.

In addition, we assumed responsibility for two product candidates under our exclusive channel partnership with Intrexon Corporation in early January 2011. We expect that the costs associated with these additional product candidates will increase the level of our overall research and development expenses significantly going forward. Although all human clinical trials are expensive and difficult to design and implement, we believe that costs associated with clinical trials for synthetic biology products are greater than the corresponding costs associated with clinical trials for small molecule candidates. In addition to increased research and development costs, we have added headcount in part to support our exclusive channel partnership endeavors and are opening a small office in the greater Washington D.C. area, which will add to our general and administrative expenses going forward. Although our forecasts for expenses and the sufficiency of our capital resources takes into account our plans to develop the Intrexon products, we have only recently assumed development responsibility for these products and the actual costs associated therewith may be significantly in excess of forecast amounts. In addition to the amount and timing of expenses related to the clinical trials, our actual cash requirements may vary materially from our current expectations for a number of other factors that may include, but are not limited to, changes in the focus and direction of our development programs, competitive and technical advances, costs associated with the development of our product candidates, our ability to secure partnering arrangements, and costs of filing, prosecuting, defending and enforcing our intellectual property rights. If we exhaust our capital reserves more quickly than anticipated, regardless of the reason, and we are unable to obtain additional financing on terms acceptable to us or at all, we will be unable to proceed with development of some or all of our product candidates on expected timelines and will be forced to prioritize among them.

Risk Factors

The following important factors could cause our actual business and financial results to differ materially from those contained in forward-looking statements made in this Current Report on Form 8-K, in the Company’s other filings with the Securities and Exchange Commission or elsewhere by management from time to time.

Risks Related to our Exclusive Channel Partnership with Intrexon Corporation

The technology on which our channel partnering arrangement with Intrexon Corporation is based is early stage biotechnology in the field of human oncologic therapeutics.

Our exclusive channel partnership with Intrexon Corporation contemplates our using Intrexon’s advanced transgene engineering platform for the controlled and precise cellular production of anti-cancer effectors. The in vivo effector platform in which we have acquired rights represents early-stage technology in the field of human oncologic therapeutics, with INXN 3001/1001 currently in a Phase Ib study and INXN 2001/1001 the basis of an IND application that we expect to submit during the first half of 2011. Although we plan to leverage Intrexon’s synthetic biology platform for additional products targeting key pathways used by cancers to grow and metastasize, we may not be successful in developing and commercializing these products for a variety of reasons. The risk factors set forth in this Report that apply to our small molecule drug candidates, which are various stages of development, also apply to product candidates that we seek to develop under our exclusive channel partnership with Intrexon Corporation.

We will incur additional expenses in connection with the exclusive Intrexon channel partnership.

The in vivo effector platform in which we have acquired rights from Intrexon Corporation includes two existing product candidates, with INXN 3001/1001 currently in a Phase Ib study and INXN 2001/1001 the basis of an IND application that we expect to submit during the first half of 2011. Upon entry into the exclusive channel partnership with Intrexon we assumed responsibility for the clinical development of these product candidates, which we expect will increase the level of our overall research and development expenses significantly going forward. Although all human clinical trials are expensive and difficult to design and implement, we believe that costs associated with clinical trials for synthetic biology products are greater than the corresponding costs associated with clinical trials for

small molecule candidates. In addition to increased research and development costs, we have added headcount in part to support our exclusive channel partnership endeavors and are opening a small office in the greater Washington D.C. area, which will add to our general and administrative expenses going forward.

Although our forecasts for expenses and the sufficiency of our capital resources set forth elsewhere in this Report takes into account our plans to develop the Intrexon products, we have only recently assumed development responsibility for these products and the actual costs associated therewith may be significantly in excess of forecast amounts. In addition to the amount and timing of expenses related to the clinical trials, our actual cash requirements may vary materially from our current expectations for a number of other factors that may include, but are not limited to, changes in the focus and direction of our development programs, competitive and technical advances, costs associated with the development of our product candidates and costs of filing, prosecuting, defending and enforcing our intellectual property rights. If we exhaust our capital reserves more quickly than anticipated, regardless of the reason, and we are unable to obtain additional financing on terms acceptable to us or at all, we will be unable to proceed with development of some or all of our product candidates on expected timelines and will be forced to prioritize among them.

We are required to register the resale of a substantial number of shares of our common stock that have been and will be issued to Intrexon Corporation and the sale of those shares could adversely affect our stock price.

In connection with our issuance and sale of 6,063,131 shares of common stock to Intrexon Corporation on January 12, 2011 in a private sale, we agreed to file a registration statement on Form S-3 registering the resale of such shares on or before May 11, 2011 and to use our reasonable best efforts to cause the Registration Statement to become effective. If the selling stockholder(s) named in such resale registration statement sell, or indicate an intention to sell, all or a substantial portion of such shares after the registration is declared effective by the SEC, the trading price of our common stock could be adversely affected.

Risks Related to our Business

We will require additional financial resources in order to continue on-going development of our product candidates; if we are unable to obtain these additional resources, we may be forced to delay or discontinue clinical testing of our product candidates.

We have never generated revenue and have incurred significant net losses in each year since our inception. For the nine months ended September 30, 2010, we had a net loss of $20.8 million and we had incurred approximately $112.0 million of cumulative net losses since our inception in 2003. We expect to continue to incur significant operating expenditures. Further development of our product candidates, including product candidates that we develop under our channel partnering arrangement with Intrexon Corporation, will likely require substantial increases in our expenses as we:

- Continue to undertake clinical trials for product candidates;
- Continue with the formulation, manufacturing and scale-up of our product candidates;
- Seek regulatory approvals for product candidates;

- Implement additional internal systems and infrastructure; and
- Hire additional personnel.

We continue to seek additional financial resources to fund the further development of our product candidate portfolio. If we are unable to obtain sufficient additional capital, one or more of these programs could be placed on hold. Because we are currently devoting a significant portion of our resources to the development of palifosfamide, further progress with the development and our other candidates may be significantly delayed and may depend on the success of our ongoing clinical trial involving palifosfamide.

Other than the Intrexon equity commitment (See “Recent Developments — Intrexon Corporation Private Placement and Equity Commitment.”), we have no current committed sources of additional capital. We do not know whether additional financing will be available on terms favorable or acceptable to us when needed, if at all. Our business is highly cash-intensive and our ability to continue operations after our current cash resources are exhausted depends on our ability to obtain additional financing and achieve profitable operations, as to which no assurances can be given. If adequate additional funds are not available when required, or if we are unsuccessful in entering into partnership agreements for the further development of our small molecule products, we will be required to delay, reduce or eliminate planned preclinical and clinical trials and may be forced to terminate the approval process for our product candidates from the FDA or other regulatory authorities. In addition, we could be forced to discontinue product development, forego attractive business opportunities or pursue merger or divestiture strategies. In the event we are unable to obtain additional financing, we may be forced to cease operations altogether.

We need to raise additional capital to fund our operations. The manner in which we raise any additional funds may affect the value of your investment in our common stock.

As of September 30, 2010, we had incurred approximately $112.0 million of cumulative net losses and had approximately $66.5 million of cash and cash equivalents. Assuming completion of this offering and given our current plans for development of our product candidates, we anticipate that our cash resources will be sufficient to fund our operations until late 2012. However, changes may occur that would consume our existing capital prior to that time, including the scope and progress of our research and development efforts and changes in governmental regulation. Actual costs may ultimately vary from our current expectations, which could materially impact our use of capital and our forecast of the period of time through which our financial resources will be adequate to support our operations. Specifically, we commenced the PICASSO 3 pivotal trial for IV palifosfamide early in the third quarter of 2010. We have estimated the sufficiency of our cash resources based in part on this trial design and our timing expectations for enrollment in the study. In addition, our forecast anticipates the initiation of a two-stage potentially pivotal trial for the study of darinaparsin in combination with “CHOP” for the treatment of PTCL, likely in certain relapsed patients. We also recently assumed responsibility for two product candidates under our exclusive channel partnership with Intrexon Corporation and we expect that the costs associated with these additional product candidates will increase the level of our overall research and development expenses significantly going forward. Although our forecasts for expenses and the sufficiency of our capital resources takes into account our plans to develop the Intrexon products, we have only recently assumed development responsibility for these products and the actual costs associated therewith may be significantly in excess of forecast amounts. In addition to these factors our actual cash requirements may vary materially from our current expectations for a number of other factors that may include, but are not limited to, changes in the focus and direction of our development programs, competitive and technical advances, costs associated with the development of our product candidates, our ability to secure partnering arrangements, and costs of filing, prosecuting, defending and enforcing our intellectual property rights. If we exhaust our capital reserves more quickly than anticipated, regardless of the reason, and we are unable to obtain additional financing on terms acceptable to us or at all, we will be unable to proceed with development of some or all of our product candidates on expected timelines and will be forced to prioritize among them.

Recently, capital markets have experienced a period of unprecedented instability that may severely hinder our ability to raise capital within the time periods needed or on terms we consider acceptable, if at all. Moreover, if we fail to advance one or more of our current product candidates to later-stage clinical trials, successfully commercialize one or more of our product candidates, or acquire new product candidates for development, we may have difficulty attracting investors that might otherwise be a source of additional financing.

In the current economic environment, our need for additional capital and limited capital resources may force us to accept financing terms that could be significantly more dilutive than if we were raising capital when the capital markets were more stable. To the extent that we raise additional capital by issuing equity securities, our stockholders may experience dilution. In addition, we may grant future investors rights superior to those of our existing stockholders. If we raise additional funds through collaborations and licensing arrangements, it may be necessary to relinquish some rights to our technologies, product candidates or products, or grant licenses on terms that are not favorable to us. If we raise additional funds by incurring debt, we could incur significant interest expense and become subject to covenants in the related transaction documentation that could affect the manner in which we conduct our business.

Clinical trials are very expensive, time-consuming, and difficult to design and implement.

Human clinical trials are very expensive and difficult to design and implement, in part because they are subject to rigorous regulatory requirements. The clinical trial process itself is also time-consuming. We estimate that clinical trials of our product candidates will take at least several years to complete. Furthermore, failure can occur at any stage of the trials, and we could encounter problems that cause us to abandon or repeat clinical trials. The commencement and completion of clinical trials may be delayed by several factors, including:

- Unforeseen safety issues;
- Determination of dosing issues;
- Lack of effectiveness during clinical trials;
- Slower than expected rates of patient recruitment and enrollment;
- Inability to monitor patients adequately during or after treatment;
- Inability or unwillingness of medical investigators to follow our clinical protocols; and
- Regulatory determinations to temporarily or permanently cease enrollment for other reasons not related to patient safety.

We commenced the PICASSO 3 pivotal trial for IV palifosfamide early in the third quarter of 2010. The 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. To date, the Company has experienced slower than anticipated enrollment in the trial due in part to the timing of regulatory approvals for opening trials sites and unanticipated contractual delays attributable to international healthcare budgetary constraints. The Company has taken steps to accelerate patient enrollment in order to meet its previous forecasted timeline for full enrollment by the end of 2011, including utilizing significantly more trial sites in the United States and elsewhere. However, the Company cannot assure that it will be able to enroll sufficient numbers of patients in the PICASSO trial to meet its previous forecast for full enrollment. As an orphan designated indication, the patient population available for participation in the PICASSO 3 trial is generally limited. Also affecting the enrollment and pace of the study is a recent limited supply of doxorubicin necessary for the trial. If the Company cannot accelerate enrollment in the PICASSO 3 study to meet its forecasted timeline, if limited supply of doxorubicin prevents treatment of patients in the trial, or the trial is delayed for other reasons, the delay will postpone our receipt of results from the trial and, consequently, our ability to submit a corresponding NDA with FDA for regulatory approval in accordance with our plans. See also “Risk Factors — Our product candidates are in various stages of clinical trials, which are very expensive and time-consuming. We cannot be certain when we will be able to file an NDA or BLA with the FDA and any failure or delay in completing clinical

trials for our product candidates could harm our business."

We have received "Orphan Drug" status for palifosfamide in both the United States and Europe, for darinaparsin in the United States and pending final notification in Europe and we are hopeful that we may be able to obtain "Fast Track" and/or additional Orphan Drug status from the FDA, Europe and certain other countries for our product candidates. Fast Track allows the FDA to facilitate development and expedite review of drugs that treat serious and life-threatening conditions so that an approved product can reach the market expeditiously. Fast Track status does not apply to a product alone, but applies to a combination of a product and the specific indications for which it is being studied. Therefore, it is a drug's development program for a specific indication that receives Fast Track designation. Orphan Drug status promotes the development of products that demonstrate the promise for the diagnosis and treatment of one disease or condition affecting fewer than 200,000 patients in the U.S. and affords certain financial and market protection benefits to successful applicants. There is no guarantee that any of our other product candidates will be granted Orphan Drug status or will be granted Fast Track status by the FDA or that, even if such product candidate is granted such status, the product candidate's clinical development and regulatory approval process will not be delayed or will be successful.

In addition, we or the FDA may suspend our clinical trials at any time if it appears that we are exposing participants to unacceptable health risks or if the FDA finds deficiencies in our IND submission or in the conduct of these trials. For example, the Phase 1a study of INXN 3001/1001 was previously placed on clinical hold for safety concerns relating to intra-patient dose escalation. Therefore, we cannot predict with any certainty the schedule for future clinical trials.

We may not be able to commercialize any products, generate significant revenues, or attain profitability.

To date, none of our product candidates have been approved for commercial sale in any country. The process to develop, obtain regulatory approval for, and commercialize potential product candidates is long, complex, and costly. Unless and until we receive approval from the FDA and/or other regulatory authorities for our product candidates, we cannot sell our products and will not have product revenues. Even if we obtain regulatory approval for one or more of our product candidates, if we are unable to successfully commercialize our products, we may not be able to generate sufficient revenues to achieve or maintain profitability, or to continue our business without raising significant additional capital, which may not be available. Our failure to achieve or maintain profitability could negatively impact the trading price of our common stock.

We have a limited operating history upon which to base an investment decision.

We are a development-stage company that was incorporated in September 2003. To date, we have not demonstrated an ability to perform the functions necessary for the successful commercialization of any product candidates. The successful commercialization of any product candidates will require us to perform a variety of functions, including:

- Continuing to undertake preclinical development and clinical trials;
- Participating in regulatory approval processes;
- Formulating and manufacturing products; and
- Conducting sales and marketing activities.

Our operations have been limited to organizing and staffing our Company, acquiring, developing, and securing our proprietary product candidates, and undertaking preclinical and clinical trials of our product candidates. These operations provide a limited basis for you to assess our ability to commercialize our product candidates and the advisability of investing in our securities.

Because we currently neither have nor intend to establish internal research capabilities, we are dependent upon pharmaceutical and biotechnology companies and academic and other researchers to sell or license us their product candidates.

Proposing, negotiating, and implementing an economically viable product acquisition or license is a lengthy and complex process. We compete for partnering arrangements and license agreements with pharmaceutical, biopharmaceutical, and biotechnology companies, many of which have significantly more experience than we do, and have significantly more financial resources. Our competitors may have stronger relationships with certain third parties including academic research institutions, with whom we are interested in collaborating and may have, therefore, a competitive advantage in entering into partnering arrangements with those third parties. We may not be able to acquire rights to additional product candidates on terms that we find acceptable, or at all.

We expect that any product candidate to which we acquire rights will require significant additional development and other efforts prior to commercial sale, including extensive clinical testing and approval by the FDA and applicable foreign regulatory authorities. All drug product candidates are subject to the risks of failure inherent in pharmaceutical product development, including the possibility that the product candidate will not be shown to be sufficiently safe or effective for approval by regulatory authorities. Even if our product candidates are approved, they may not be economically manufactured or produced, or be successfully commercialized.

We actively evaluate additional product candidates to acquire for development. Such additional product candidates, if any, could significantly increase our capital requirements and place further strain on the time of our existing personnel, which may delay or otherwise adversely affect the development of our existing product candidates. We must manage our development efforts and clinical trials effectively, and hire, train and integrate additional management, administrative, and sales and marketing personnel. We may not be able to accomplish these tasks, and our failure to accomplish any of them could prevent us from successfully growing our Company.

We may not be able to successfully manage our growth.

In the future, if we are able to advance our product candidates to the point of, and thereafter through, clinical trials, we will need to expand our development, regulatory, manufacturing, marketing and sales capabilities or contract with third parties to provide for these capabilities. Any future growth will place a significant strain on our management and on our administrative, operational, and financial resources. Therefore, our future financial performance and our ability to commercialize our product candidates and to compete effectively will depend, in part, on our ability to manage any future growth effectively. To manage this growth, we must expand our facilities, augment our operational, financial and management systems, and hire and train additional qualified personnel. If we are unable to manage our growth effectively, our business may be harmed.

Our business will subject us to the risk of liability claims associated with the use of hazardous materials and chemicals.

Our contract research and development activities may involve the controlled use of hazardous materials and chemicals. Although we believe that our safety procedures for using, storing, handling and disposing of these materials comply with federal, state and local laws and regulations, we cannot completely eliminate the risk of accidental injury or contamination from these materials. In the event of such an accident, we could be held liable for any resulting damages and any liability could have a materially adverse effect on our business, financial condition, and results of operations. In addition, the federal, state and local laws and regulations governing the use, manufacture, storage, handling and disposal of hazardous or radioactive materials and waste products may require our contractors to incur substantial compliance costs that could materially adversely affect our business, financial condition, and results of operations.

We rely on key executive officers and scientific and medical advisors, and their knowledge of our business and technical expertise would be difficult to replace.

We are highly dependent on Dr. Jonathan Lewis, our Chief Executive Officer and Chief Medical Officer, Richard Bagley, our President, Chief Operating Officer and Chief Financial Officer, and our principal scientific, regulatory, and medical advisors. Dr. Lewis' and Mr. Bagley's employment are governed by written employment agreements that provide for terms that expire in January 2013 and July 2011, respectively. Dr. Lewis and Mr. Bagley may terminate their employment with us at any time, subject, however, to certain non-compete and non-solicitation covenants. The loss of the technical knowledge and management and industry expertise of Dr. Lewis and Mr. Bagley, or any of our other key personnel, could result in delays in product development, loss of customers and sales, and diversion of management resources, which could adversely affect our operating results. We do not carry "key person" life insurance

policies on any of our officers or key employees.

If we are unable to hire additional qualified personnel, our ability to grow our business may be harmed.

We will need to hire additional qualified personnel with expertise in preclinical and clinical research and testing, government regulation, formulation and manufacturing, and eventually, sales and marketing. We compete for qualified individuals with numerous biopharmaceutical companies, universities, and other research institutions. Competition for such individuals is intense and we cannot be certain that our search for such personnel will be successful. Attracting and retaining qualified personnel will be critical to our success. If we are unable to hire additional qualified personnel, our ability to grow our business may be harmed.

We may incur substantial liabilities and may be required to limit commercialization of our products in response to product liability lawsuits.

The testing and marketing of medical products entail an inherent risk of product liability. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of our products, if approved. Even a successful defense would require significant financial and management resources. Regardless of the merit or eventual outcome, liability claims may result in:

- Decreased demand for our product candidates;
- Injury to our reputation;
- Withdrawal of clinical trial participants;
- Withdrawal of prior governmental approvals;
- Costs of related litigation;
- Substantial monetary awards to patients;
- Product recalls;
- Loss of revenue; and
- The inability to commercialize our product candidates.

We currently carry clinical trial insurance and product liability insurance. However, our inability to renew our policies or to obtain sufficient insurance at an acceptable cost could prevent or inhibit the commercialization of pharmaceutical products that we develop, alone or with collaborators.

Risks Related to the Clinical Testing, Regulatory Approval and Manufacturing of our Product Candidates

If we are unable to obtain the necessary U.S. or worldwide regulatory approvals to commercialize any product candidate, our business will suffer.

We may not be able to obtain the approvals necessary to commercialize our product candidates, or any product candidate that we may acquire or develop in the future for commercial sale. We will need FDA approval to commercialize our product candidates in the U.S. and approvals from regulatory authorities in foreign jurisdictions equivalent to the FDA to commercialize our product candidates in those jurisdictions. In order to obtain FDA approval of any product candidate, we must submit to the FDA a New Drug Application or Biologics License Application

("BLA"), demonstrating that the product candidate is safe for humans and effective for its intended use. This demonstration requires significant research and animal tests, which are referred to as preclinical studies, as well as human tests, which are referred to as clinical trials. Satisfaction of the FDA's regulatory requirements typically takes many years, depending upon the type, complexity, and novelty of the product candidate, and will require substantial resources for research, development, and testing. We cannot predict whether our research, development, and clinical approaches will result in drugs that the FDA will consider safe for humans and effective for their intended uses. The FDA has substantial discretion in the drug approval process and may require us to conduct additional preclinical and clinical testing or to perform post-marketing studies. The approval process may also be delayed by changes in government regulation, future legislation, or administrative action or changes in FDA policy that occur prior to or during our regulatory review. Delays in obtaining regulatory approvals may:

- Delay commercialization of, and our ability to derive product revenues from, our product candidates;
- Impose costly procedures on us; and
- Diminish any competitive advantages that we may otherwise enjoy.

Even if we comply with all FDA requests, the FDA may ultimately reject one or more of our NDAs or BLAs. We cannot be sure that we will ever obtain regulatory clearance for any of our product candidates. Although individuals within Ziopharm have experience working with biologic product candidates, to date we as a company have not had any interactions with FDA's Center for Biologics Evaluation and Research, and our submission of the IND for INXN 2001/1001 will be our first biologic IND. Failure to obtain FDA approval for our product candidates will severely undermine our business by leaving us without a saleable product, and therefore without any potential revenue source, until another product candidate can be developed. There is no guarantee that we will ever be able to develop or acquire another product candidate or that we will obtain FDA approval if we are able to do so.

In foreign jurisdictions, we similarly must receive approval from applicable regulatory authorities before we can commercialize any drugs. Foreign regulatory approval processes generally include all of the risks associated with the FDA approval procedures described above.

Our product candidates are in various stages of clinical trials, which are very expensive and time-consuming. We cannot be certain when we will be able to submit an NDA or BLA to the FDA and any failure or delay in completing clinical trials for our product candidates could harm our business.

Our product candidates are in various stages of development and require extensive clinical testing. Notwithstanding our current clinical trial plans for each of our existing product candidates, we may not be able to commence additional trials or see results from these trials within our anticipated timelines. As such, we cannot predict with any certainty if or when we might submit an NDA for regulatory approval of our product candidates or whether such an NDA will be accepted. Because we do not anticipate generating revenues unless and until we submit one or more NDAs and thereafter obtain requisite FDA approvals, the timing of our NDA submissions and FDA determinations regarding approval thereof, will directly affect if and when we are able to generate revenues.

The results of our clinical trials may not support our product candidate claims.

Even if our clinical trials are completed as planned, we cannot be certain that their results will support approval of our product candidates. FDA normally expects two randomized, well controlled Phase 3 pivotal studies in support of approval of an NDA or BLA. Our PICASSO 3 trial, even if successful, may not be sufficient to support approval and we may be required to conduct additional pivotal trials of palifosfamide in soft tissue sarcoma in order to obtain NDA approval. Success in preclinical testing and early clinical trials does not ensure that later clinical trials will be successful, and we cannot be certain that the results of later clinical trials will replicate the results of prior clinical trials and preclinical testing. The clinical trial process may fail to demonstrate that our product candidates are safe for humans and effective for the indicated uses. This failure would cause us to abandon a product candidate and may delay development of other product candidates. Any delay in, or termination of, our clinical trials will delay the submission of our NDAs or BLAs with the FDA and, ultimately, our ability to commercialize our product candidates and generate product revenues. In addition, our clinical trials involve small patient populations. Because of the small sample size, the results of these clinical trials may not be indicative of future results.

Because we are dependent upon clinical research institutions and other contractors for clinical testing and for research and development activities, the results of our clinical trials and such research activities are, to a certain extent, beyond our control.

We materially rely upon independent investigators and collaborators, such as universities and medical institutions, to conduct our preclinical and clinical trials under agreements with us. These collaborators are not our employees and we cannot control the amount or timing of resources that they devote to our programs. These investigators may not assign as great a priority to our programs or pursue them as diligently as we would if we were undertaking such programs ourselves. If outside collaborators fail to devote sufficient time and resources to our drug development programs, or if

their performance is substandard, the approval of our FDA applications, if any, and our introduction of new products, if any, will be delayed. These collaborators may also have relationships with other commercial entities, some of whom may compete with us. If our collaborators assist our competitors to our detriment, our competitive position would be harmed.

Our reliance on third parties to formulate and manufacture our product candidates exposes us to a number of risks that may delay the development, regulatory approval and commercialization of our products or result in higher product costs.

We do not have experience in drug formulation or manufacturing of drugs or biologics and do not intend to establish our own manufacturing facilities. Although we will work closely with and rely upon Intrexon on the manufacturing and scale-up of Intrexon product candidates, we lack the resources and expertise to formulate or manufacture our own product candidates. We currently are contracting for the manufacture of our product candidates. We intend to contract with one or more manufacturers to manufacture, supply, store, and distribute drug supplies for our clinical trials. If a product candidate we develop or acquire in the future receives FDA approval, we will rely on one or more third-party contractors or Intrexon to manufacture our products. Our anticipated future reliance on a limited number of third-party manufacturers exposes us to the following risks:

- We may be unable to identify manufacturers on acceptable terms or at all because the number of potential manufacturers is limited and the FDA must approve any replacement contractor. This approval would require new testing and compliance inspections. In addition, a new manufacturer would have to be educated in, or develop substantially equivalent processes for, production of our products after receipt of FDA approval, if any.

- Our third-party manufacturers might be unable to formulate and manufacture our products in the volume and of the quality required to meet our clinical needs and commercial needs, if any.

- Our future contract manufacturers may not perform as agreed or may not remain in the contract manufacturing business for the time required to supply our clinical trials or to successfully produce, store, and distribute our products.

- Drug manufacturers are subject to ongoing periodic unannounced inspection by the FDA, the Drug Enforcement Administration and corresponding state agencies to ensure strict compliance with good manufacturing practices and other government regulations and corresponding foreign standards. We do not have control over third-party manufacturers' compliance with these regulations and standards.

- If any third-party manufacturer makes improvements in the manufacturing process for our products, we may not own, or may have to share, the intellectual property rights to the innovation.

Each of these risks could delay our clinical trials, the approval, if any, of our product candidates by the FDA or the commercialization of our product candidates or result in higher costs or deprive us of potential product revenues.

Risks Related to our Ability Commercialize Our Product Candidates

If we are unable either to create sales, marketing and distribution capabilities or enter into agreements with third parties to perform these functions, we will be unable to commercialize our product candidates successfully.

We currently have no marketing, sales, or distribution capabilities. If and when we become reasonably certain that we will be able to commercialize our current or future products, we anticipate allocating resources to the marketing, sales and distribution of our proposed products in North America and in certain other countries; however, we cannot assure that we will be able to market, sell, and distribute our products successfully. Our future success also may depend, in part, on our ability to enter into and maintain collaborative relationships for such capabilities and to encourage the collaborator's strategic interest in the products under development, and such collaborator's ability to successfully market and sell any such products. Although we intend to pursue certain collaborative arrangements regarding the sale and marketing of certain of our products, there are no assurances that we will be able to establish or maintain

collaborative arrangements or, if we are able to do so, whether we would be able to conduct our own sales efforts. There can also be no assurance that we will be able to establish or maintain relationships with third-party collaborators or develop in-house sales and distribution capabilities. To the extent that we depend on third parties for marketing and distribution, any revenues we receive will depend upon the efforts of such third parties, and there can be no assurance that such efforts will be successful. In addition, there can also be no assurance that we will be able to market and sell our products in the United States or overseas.

If we are not able to partner with a third party and are not successful in recruiting sales and marketing personnel or in building a sales and marketing infrastructure, we will have difficulty commercializing our product candidates, which would harm our business. If we rely on pharmaceutical or biotechnology companies with established distribution systems to market our products, we will need to establish and maintain partnership arrangements, and we may not be able to enter into these arrangements on acceptable terms or at all. To the extent that we enter into co-promotion or other arrangements, any revenues we receive will depend upon the efforts of third parties that may not be successful and that will be only partially in our control.

If we cannot compete successfully for market share against other drug companies, we may not achieve sufficient product revenues and our business will suffer.

The market for our product candidates is characterized by intense competition and rapid technological advances. If a product candidate receives FDA approval, it will compete with a number of existing and future drugs and therapies developed, manufactured and marketed by others. Existing or future competing products may provide greater therapeutic convenience or clinical or other benefits for a specific indication than our products, or may offer comparable performance at a lower cost. If our products fail to capture and maintain market share, we may not achieve sufficient product revenues and our business will suffer.

We will compete against fully integrated pharmaceutical companies and smaller companies that are collaborating with larger pharmaceutical companies, academic institutions, government agencies and other public and private research organizations. Many of these competitors have products already approved or in development. In addition, many of these competitors, either alone or together with their collaborative partners, operate larger research and development programs or have substantially greater financial resources than we do, as well as significantly greater experience in:

- Developing drugs and biopharmaceuticals;
- Undertaking preclinical testing and human clinical trials;
- Obtaining FDA and other regulatory approvals of drugs and biopharmaceuticals;
- Formulating and manufacturing drugs and biopharmaceuticals; and
- Launching, marketing, and selling drugs and biopharmaceuticals.

If physicians and patients do not accept and use our product candidates, our ability to generate revenue from sales of our products will be materially impaired.

Even if the FDA approves our product candidates, physicians and patients may not accept and use them. Acceptance and use of our products will depend upon a number of factors including:

- Perceptions by members of the health care community, including physicians, about the safety and effectiveness of our products;
- Pharmacological benefit and cost-effectiveness of our products relative to competing products;
- Availability of reimbursement for our products from government or other healthcare payors;
- Effectiveness of marketing and distribution efforts by us and our licensees and distributors, if any; and

- The price at which we sell our products.

Because we expect sales of our current product candidates, if approved, to generate substantially all of our product revenues for the foreseeable future, the failure of a drug to find market acceptance would harm our business and could require us to seek additional financing in order to fund the development of future product candidates.

Our ability to generate product revenues will be diminished if our products sell for inadequate prices or patients are unable to obtain adequate levels of reimbursement.

Our ability to commercialize our drugs, alone or with collaborators, will depend in part on the extent to which reimbursement will be available from:

- Government and health administration authorities;
- Private health maintenance organizations and health insurers; and
- Other healthcare payers.

Government and other healthcare payers increasingly attempt to contain healthcare costs by limiting both coverage and the level of reimbursement for drugs. As a result, we cannot provide any assurances that third-party payors will provide adequate coverage of and reimbursement for any of our product candidates. If we are unable to obtain adequate coverage of and payment levels for our product candidates from third-party payors, physicians may limit how much or under what circumstances they will prescribe or administer them and patients may decline to purchase them. This in turn could affect our ability to successfully commercialize our products and impact our profitability and future success.

In both the United States and certain foreign jurisdictions, there have been a number of legislative and regulatory proposals and changes in recent years to change the healthcare system in ways that could impact our ability to sell our products profitably.

We cannot predict the impact on our business of any legislation or regulations that may be adopted in the future. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our products.

In addition, in many foreign countries, particularly the countries of the European Union, the pricing of prescription drugs is subject to government control. We may face competition for our product candidates from lower-priced products in foreign countries that have placed price controls on pharmaceutical products. In addition, there may be importation of foreign products that compete with our own products, which could negatively impact our profitability.

Risks Related to Our Intellectual Property

If we fail to adequately protect or enforce our intellectual property rights or secure rights to patents of others, the value of our intellectual property rights would diminish.

Our success, competitive position, and future revenues will depend in part on our ability and the abilities of our licensors to obtain and maintain patent protection for our products, methods, processes and other technologies, to preserve our trade secrets, to prevent third parties from infringing on our proprietary rights, and to operate without infringing the proprietary rights of third parties.

To date, we have exclusive rights to certain U.S. and foreign intellectual property with respect to our small molecule product candidates but are dependent on Intrexon’s filings with respect to the existing Intrexon product candidates. Per the Channel Partner agreement, Intrexon has the sole right to control the filings, prosecution and maintenance of the Channel Program patents and applications. Although Intrexon has agreed to consider our comments regarding Channel Program patents and patent applications, we cannot guarantee that our comments will be solicited or followed. Without direct control of the Channel Program patents and patent applications, we are dependent on

Intrexon to keep us advised of prosecution, particularly in foreign jurisdictions where prosecution information may not be publicly available. We anticipate that we and Intrexon will file additional patent applications both in the U.S. and in other countries. However, we cannot predict or guarantee:

- The degree and range of protection any patents will afford us against competitors, including whether third parties will find ways to invalidate or otherwise circumvent our patents;
- If and when patents will be issued;
- Whether or not others will obtain patents claiming aspects similar to those covered by our patents and patent applications; or
- Whether we will need to initiate litigation or administrative proceedings that may be costly whether we win or lose.

Certain technologies utilized in our research and development programs are already in the public domain. Moreover, a number of our competitors have developed technologies, filed patent applications or obtained patents on technologies, compositions and methods of use that are related to our business and may cover or conflict with our patent applications, technologies or product candidates. Such conflicts could limit the scope of the patents that we may be able to obtain or may result in the denial of our patent applications. In addition, our own earlier filed patents and applications or those of Intrexon may limit the scope of later patents we obtain or may result in the denial of our later filed patent applications. If third parties filed patent applications or obtained patents on technologies, compositions and methods of use that are related to our business and that cover or conflict with our patent applications, technologies or product candidates, we may be required to challenge such protection, terminate or modify our programs impacted by such protection or obtain licenses from such third parties, which might not be available on acceptable terms, or at all.

Our success also depends upon the skills, knowledge, and experience of our scientific and technical personnel, our consultants and advisors, as well as our licensors and contractors. To help protect our proprietary know-how and our inventions for which patents may be unobtainable or difficult to obtain, we rely on trade secret protection and confidentiality agreements. To this end, it is our general policy to require our employees, consultants, advisors, and contractors to enter into agreements that prohibit the disclosure of confidential information and, where applicable, require disclosure and assignment to us of the ideas, developments, discoveries, and inventions important to our business. These agreements may not provide adequate protection for our trade secrets, know-how or other proprietary information in the event of any unauthorized use or disclosure or the lawful development by others of such information. If any of our trade secrets, know-how or other proprietary information is disclosed, the value of our trade secrets, know-how and other proprietary rights would be significantly impaired and our business and competitive position would suffer.

Third-party claims of intellectual property infringement would require us to spend significant time and money and could prevent us from developing or commercializing our products.

In order to protect or enforce patent rights, we or Intrexon may initiate patent litigation against third parties. Similarly, we may be sued by others. We also may become subject to proceedings conducted in the U.S. Patent and Trademark Office, including interference proceedings to determine the priority of inventions, or reexamination proceedings. In addition, any foreign patents that are granted may become subject to opposition, nullity, or revocation proceedings in foreign jurisdictions having such proceedings. The defense and prosecution, if necessary, of intellectual property actions are costly and divert technical and management personnel away from their normal responsibilities.

No patent can protect its holder from a claim of infringement of another patent. Therefore, our patent position cannot and does not provide any assurance that the commercialization of our products would not infringe the patent rights of another. While we know of no actual or threatened claim of infringement that would be material to us, there can be no assurance that such a claim will not be asserted.

If such a claim is asserted, there can be no assurance that the resolution of the claim would permit us to continue marketing the relevant product on commercially reasonable terms, if at all. We may not have sufficient resources to bring these actions to a successful conclusion. If we do not successfully defend any infringement actions to which we become a party or are unable to have infringed patents declared invalid or unenforceable, we may have to pay substantial monetary damages, which can be tripled if the infringement is deemed willful, or be required to discontinue or significantly delay commercialization and development of the affected products.

Any legal action against us or our collaborators claiming damages and seeking to enjoin developmental or marketing activities relating to affected products could, in addition to subjecting us to potential liability for damages, require us or our collaborators to obtain licenses to continue to develop, manufacture, or market the affected products. Such a

license may not be available to us on commercially reasonable terms, if at all.

An adverse determination in a proceeding involving our owned or licensed intellectual property may allow entry of generic substitutes for our products.

Other Risks Related to Our Company

We are subject to Sarbanes-Oxley and the reporting requirements of federal securities laws, which can be expensive.

As a public reporting company, we are subject to the Sarbanes-Oxley Act of 2002, as well as to the information and reporting requirements of the Securities Exchange Act of 1934, as amended, and other federal securities laws. As a result, we incur significant legal, accounting, and other expenses that we did not incur as a private company, including costs associated with our public company reporting requirements and corporate governance requirements. As an example of public reporting company requirements, we evaluate the effectiveness of disclosure controls and procedures and of our internal control over financing reporting in order to allow management to report on such controls. Sarbanes-Oxley generally requires that a public reporting company's independent registered public accounting firm attest to the effectiveness of the company's internal control over financial reporting as of the end of each fiscal year in the company's Annual Report on Form 10-K. While our management has not currently identified any material weaknesses in our internal control over financial reporting, there can be no assurance that we will not identify identified any material weaknesses during the current year or that our systems will be deemed effective when our independent registered public accounting firm reviews the systems during 2010 and tests transactions. In addition, any updates to our finance and accounting systems, procedures and controls, which may be required as a result of our ongoing analysis of internal controls, or results of testing by our independent auditor, may require significant time and expense.

Management is working to continuously monitor and improve internal controls and has set in place controls to mitigate the potential segregation of duties risk. In the event significant deficiencies or material weaknesses are indentified in our internal control over financial reporting that we cannot remediate in a timely manner, investors and others may lose confidence in the reliability of our financial statements and the trading price of our common stock and ability to obtain any necessary equity or debt financing could suffer. In addition, in the event that our independent registered public accounting firm is unable to rely on our internal controls over financial reporting in connection with its audit of our financial statements, and in the further event that it is unable to devise alternative procedures in order to satisfy itself as to the material accuracy of our financial statements and related disclosures, we may be unable to file our periodic reports with the Securities and Exchange Commission. This would likely have an adverse affect on the trading price of our common stock and our ability to secure any necessary additional equity or debt financing, and could result in the delisting of our common stock from the NASDAQ Capital Market, which would severely limit the liquidity of our common stock.

Anti-takeover provisions in our charter documents and under Delaware law may make an acquisition of us, which may be beneficial to our stockholders, more difficult.

Provisions of our amended and restated certificate of incorporation and bylaws, as well as provisions of Delaware law, could make it more difficult for a third party to acquire us, even if doing so would benefit our stockholders. These provisions authorize the issuance of "blank check" preferred stock that could be issued by our board of directors to increase the number of outstanding shares and hinder a takeover attempt, and limit who may call a special meeting of stockholders. In addition, we are subject to Section 203 of the Delaware General Corporation Law. In general, this statute prohibits a publicly-held Delaware corporation from engaging in a business combination with a party that owns at least 15% of its common stock unless the business combination is approved by the company's board of directors before the person acquires the 15% ownership stake or later by its board of directors and two-thirds of its stockholders. In connection with our January 12, 2011 issuance of shares of common stock to Intrexon Corporation in a private placement transaction (see "Recent Developments — Intrexon Corporation Private Placement and Equity Commitment"), our board of directors waived the Section 203 prohibition with respect to a future business combination with Intrexon Corporation. However, the Stock Purchase Agreement governing such issuance contains a standstill provision that generally prohibits Intrexon from seeking, initiating, offering or proposing to effect such a

transaction with our inviting them to do so. Section 203 and this standstill provision could have the effect of delaying, deferring or preventing a change in control that our stockholders might consider to be in their best interests.

Because we do not expect to pay dividends, you will not realize any income from an investment in our common stock unless and until you sell your shares at a profit.

We have never paid dividends on our capital stock and we do not anticipate that we will pay any dividends for the foreseeable future. Accordingly, any return on an investment in our Company will be realized, if at all, only when you sell shares of our common stock.

Safe Harbor Statement

This Current Report on Form 8-K contains forward-looking statements, including statements related to the public offering of shares of common stock by ZIOPHARM and the completion of the public offering that involve risks and uncertainties. These forward-looking statements are based upon ZIOPHARM's current expectations. Actual results and the timing of events could differ materially from those anticipated in such forward-looking statements as a result of risks and uncertainties, which include, without limitation, risks and uncertainties associated with market conditions and the satisfaction of customary closing conditions related to the proposed offering and other risks detailed in ZIOPHARM's filings with the SEC. You are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date of this Current Report on Form 8-K. All forward-looking statements are qualified in their entirety by this cautionary statement, and ZIOPHARM undertakes no obligation to revise or update any forward-looking statements to reflect events or circumstances after the date of this Current Report on Form 8-K.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

Exhibit No.	Description
99.1	Press Release, dated February 2, 2011

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

ZIOPHARM Oncology, Inc.

	By:	/s/ Richard Bagley
Date: February 2, 2011		Name: Richard Bagley Title: President, Chief Operating Officer and Chief Financial Officer

INDEX OF EXHIBITS

Exhibit No.	Description
99.1	Press Release, dated February 2, 2011