ZIOPHARM ONCOLOGY INC
Form 10KSB
February 21, 2008

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, DC 20549

FORM 10-KSB

x ANNUAL REPORT UNDER SECTION 13 OR 15(d)
OF THE SECURITIES EXCHANGE ACT OF 1934

For the fiscal year ended December 31, 2007

OR

o TRANSITION REPORT UNDER SECTION 13 OR 15(d)
OF THE SECURITIES EXCHANGE ACT OF 1934

For the transition period from _____ to _____

Commission File Number 0-32353

ZIOPHARM Oncology, Inc.
(Exact Name of Small Business Issuer as Specified in Its Charter)

Delaware	**84-1475642**
(State or Other Jurisdiction of Incorporation or Organization)	(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
(Issuer's Telephone Number, Including Area Code)

(Former Name, Former Address and Former Fiscal Year, if Changed Since Last Report)

Securities registered pursuant to Section 12(g) of the Act:
Common Stock (par value $0.001 per share)

Check whether the issuer is not required to file reports pursuant to Section 13 or 15(d) of the Exchange Act. o

Check whether the issuer (1) has filed all reports required to be filed by Section 13 or 15(d) of the Exchange Act during the past 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes x No o

Check if there is no disclosure of delinquent files pursuant to Item 405 of Regulation S-B is not contained in this form, and no disclosure will be contained, to the best of registrant's knowledge, in definitive proxy or information statements

incorporated by reference in Part III of this Form 10-KSB or any amendment to this form 10-KSB. o

Indicate by check mark whether the registration is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes o No x

The registrant had no revenue for the most recent fiscal year.

As of February 19, 2008, the aggregate market value of common stock held by non-affiliates of the registrant approximated $69,221,633 based upon the closing price of the common stock on the NASDAQ Capital Market as of the close of business on that date. Shares of common stock held by each executive officer and director and by each entity that owns 10% or more of the outstanding common stock have been excluded in that such persons may be deemed to be affiliates. This determination of affiliate status is not necessarily a conclusive determination for other purposes.

As of February 19, 2008, there were 21,298,964 shares of the issuer’s common stock, $.001 par value per share, outstanding.

DOCUMENTS INCORPORATED BY REFERENCE:

Portions of the definitive proxy statement for our 2008 annual meeting of stockholders, which is to be filed within 120 days after the end of the fiscal year ended December 31, 2007, are incorporated by reference into Part III of this Form 10-KSB, to the extent described in Part III.

Traditional Small Business Disclosure Format (check one): Yes x No o

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Additional Information

Descriptions in this report are qualified by reference to the contents of any contract, agreement or other documents and are not necessarily complete. Reference is made to each such contract or document filed as an exhibit to this report, or previously filed by the Company pursuant to regulations of the Securities and Exchange Commission (the "SEC") (see "Item 13. Exhibits").

References in this document to "us", "we", "our", "the Company", or "the Registrant" refer to ZIOPHARM Oncology, Inc. On September 13, 2005, our wholly-owned subsidiary, ZIO Acquisition Corp., merged with and into ZIOPHARM, Inc. with ZIOPHARM, Inc. remaining as the surviving corporation and our wholly-owned subsidiary. This transaction is referred to throughout this report as the "Merger." On September 14, 2005, ZIOPHARM, Inc. merged with and into us, leaving us as the surviving corporation. In connection with this parent-subsidiary merger, we relinquished our prior corporate name, EasyWeb, Inc., and assumed in its place the name "ZIOPHARM Oncology, Inc." The parent-subsidiary merger and name change became effective on September 14, 2005. Unless provided otherwise, references in this document to "us", "we", "our", "the Company", or "the Registrant" for periods prior to these transactions refer to ZIOPHARM Inc. See "Description of Business - Corporate Developments - Acquisition of ZIOPHARM, Inc."

Special Note Regarding Forward Looking Statements

This Annual Report on Form 10-KSB contains statements that are not historical, but are forward-looking in nature, including statements regarding the expectations, beliefs, intentions or strategies regarding the future. In particular, the discussion contained in this report under the heading "Management's Discussion and Analysis or Plan of Operation" includes forward-looking statements that reflect our current views with respect to future events and financial performance. We use words such as we "expect," "anticipate," "believe," and "intend" and similar expressions to identify forward-looking statements. A number of important factors could, individually or in the aggregate, cause actual results to differ materially from those expressed or implied in any forward-looking statements. Such factors include, but are not limited to, our ability to develop successfully our product candidates, to obtain regulatory approval for such product candidates or to successfully commercialize them, our ability to obtain additional financing, our ability to develop and maintain vendor relationships, regulatory developments relating to and the general success of our products, and our ability to protect our proprietary technology. Other risks that may impact forward-looking statements contained in this Annual Report on 10-KSB are described under the heading "Risk Factors."

PART I

Item 1. Description of Business

General

ZIOPHARM Oncology, Inc. is a biopharmaceutical company that is seeking to develop and commercialize a diverse, risk-sensitive portfolio of in-licensed cancer drugs that address unmet medical needs. Our principal focus is on the licensing and development of proprietary drug candidates that are related to cancer therapeutics already on the market or in development and that can be developed in intravenous ("IV") and/or oral forms of administration. We believe this strategy will result in lower risk and expedited drug development programs. While we expect to commercialize our products on our own in North America, we also recognize that promising clinical trial results might also be addressed in partnership with another company with the requisite financial resources. Currently, we are in phase I and/or II studies for three product candidates identified as darinaparsin ("ZIO-101"), palifosfamide ("ZIO-201"), and indibulin ("ZIO-301"). We intend to continue the clinical development of IV darinaparsin for the treatment of certain lymphomas and other hematological malignancies or liver cancer. We also continue to explore the clinical utility of the oral form of darinaparsin in solid tumors. Currently underway are clinical trials to evaluate IV palifosfamide to treat advanced sarcoma. We are also seeking clearance from the U.S. Food and Drug Administration ("FDA") in the form of an

investigational new drug (“IND”) application to explore the clinical utility of oral administration of palifosfamide. Clinical studies with oral indibulin either alone or in combination for the treatment of an as-yet undetermined solid tumor indication(s) are initiated. We will continue with preclinical studies of our product candidates, and analogs thereof, while evaluating additional candidates for licensing.

Our corporate office is located at 1180 Avenue of the Americas, 19th Floor, New York, NY 10036, and our telephone number is (646) 214-0700. Our business and development operations are located in Boston, Massachusetts.

Cancer Overview

Cancer is a group of diseases characterized by either the runaway growth of cells or the failure of cells to die normally. Often, cancer cells spread to distant parts of the body, where they can form new tumors. Cancer can arise in any organ of the body and, according to the American Cancer Society, strikes one of every two American men and one of every three American women at some point in their lives.

It is reported that there are more than 100 different varieties of cancer divided into six major categories. Carcinomas, the most common type of cancer, originate in tissues that cover a surface or line a cavity of the body. Sarcoma begins in tissue that connects, supports or surrounds other tissues and organs. Lymphomas are cancers of the lymph system, which is a circulatory system that bathes and cleanses the body's cells. Leukemias involve blood-forming tissues and blood cells. As their name indicates, brain tumors are cancers that begin in the brain, and skin cancers, including melanomas, originate in the skin. Cancers are considered metastatic if they spread via the blood or lymphatic system to other parts of the body to form secondary tumors.

Cancer is caused by a series of mutations (alterations) in genes that control cells' ability to grow and divide. Some mutations are inherited; others arise from environmental factors such as smoking or exposure to chemicals, radiation, or viruses that damage cells' DNA. The mutations cause cells to divide relentlessly or lose their normal ability to die.

According to Cancer Statistics 2007 (published in CA: Cancer Journal for Clinicians, vol. 57), it was estimated that 559,650 Americans would die from cancer in 2007—more than 1,500 each day. The cost of treating cancer is significant. The National Institute of Health estimates that the overall cost of cancer in 2006 was $206.3 billion. This cost includes an estimate of $78.2 billion in direct medical expenses, $17.9 billion in indirect morbidity costs, and $110.2 billion in indirect mortality costs.

Cancer Treatments

Major treatments for cancer include surgery, radiotherapy, and chemotherapy; the latter including newer approaches generally referred to as anti-angiogenic or targeted therapies. There are many different drugs that are used to treat cancer, including supportive care. While there are also hundreds of experimental treatments under investigation, we believe cancer treatment will remain a significant unmet medical need for the foreseeable future.

Radiotherapy. Also called radiation therapy, radiotherapy is the treatment of cancer and other diseases with ionizing radiation. Ionizing radiation deposits energy that injures or destroys cells in the area being treated (the target tissue) by damaging their genetic material, making it impossible for these cells to continue growing. Although radiation damages both cancer cells and normal cells, the latter are able to repair themselves and regain proper function. Radiotherapy may be used to treat localized solid tumors such as cancers of the skin, tongue, larynx, brain, breast, or uterine cervix. It can also be used to treat leukemia and lymphoma.

Scientists are also looking for ways to increase the effectiveness of radiation therapy. Two types of investigational drugs are being studied for their effect on cells exposed to radiation. Radiosensitizers increase the damage done to tumor cells by radiation; radioprotectors protect normal tissues from the effects of radiation.

Cytotoxics. Cytotoxics are anticancer drugs that destroy cancer cells by stopping them from multiplying. Healthy cells, especially those that divide quickly can also be harmed with the use of cytotoxics. Harm to healthy cells is what causes side effects. These cells usually repair themselves after chemotherapy and in many cases, newer and often targeted agents may offer a greater therapeutic window—the difference between a dose that is helpful and one that is toxic.

Cytotoxic agents act primarily by disrupting cellular pathways involved in maintaining cellular integrity including blood supply, repair, or activity that affects the production or function of DNA, RNA, or protein. Although there are many cytotoxic agents, there is a considerable overlap in their mechanisms of action. As such, the choice of a particular agent or group of agents is generally not a consequence of a prior prediction of antitumor activity by the drug, but instead the result of empirical clinical trials.

Supportive Care. The treatment of a cancer may include the use of chemotherapy, radiation therapy, biologic response modifiers, surgery, or some combination of all of these or other therapeutic options. All of these treatment options are

directed at killing or eradicating the cancer that exists in a patient's body. Unfortunately, the delivery of many cancer therapies adversely affects the body's normal organs. The undesired consequence of harming an organ not involved with cancer is referred to as a complication of treatment or a side effect.

In addition to anemia, fatigue, hair-loss, reduction in blood platelets and white and red blood cells, and bone pain, two of the most common side effects of chemotherapy are nausea and vomiting. Several drugs have been developed to help prevent and control chemotherapy-induced nausea and vomiting, including 5HT3 receptor antagonists such as ondansetron, which is a selective blocking agent of the hormone serotonin.

Product Candidates

Darinaparsin ("ZIO-101")

General. Darinaparsin is an organic arsenic compound covered by issued U.S. patents and U.S. and international applications. A commercially available inorganic arsenic (arsenic trioxide [Trisenox®]); "ATO") has been approved for the treatment of acute promyelocytic leukemia ("APL"). ATO is on the compendia listing for the therapy of multiple myeloma and has been studied for the treatment of various other cancers. ATO has been shown to be toxic to the heart, nerves and liver, which limits its use as a broad anti-cancer agent. Our preclinical studies demonstrate that darinaparsin is considerably less toxic than ATO, particularly with regard to cardiac toxicity. In phase I and phase II clinical studies, darinaparsin has been safely administered at doses significantly higher than are approved for Trisenox®, confirming preclinical findings.

In vitro testing of darinaparsin using the National Cancer Institute's human cancer cell panel detected activity against cell lines derived from multiple cancers including lung, colon, brain, melanoma, ovarian, and kidney cancer. Moderate activity was detected against breast and prostate cancer. In addition to cell lines derived from 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. In addition, darinaparsin has potent anti-angiogenic activity as demonstrated in *in vitro* as well as *in vivo* studies.

In a murine leukemia model, darinaparsin demonstrated oral activity comparable to that achieved with systemic administration. Subsequent pharmacokinetic studies in dogs established oral bioavailability comparable to IV administration. Oral administration of an effective cancer drug would allow prolonged and potentially more effective dosing regimens.

Potential Lead Indications: lymphoma, advanced myeloma, and liver cancer Three phase II studies evaluating hematological malignancies, i.e., APL and lymphomas, advanced myeloma, and liver cancer, are planned to have accrual completed by the second half of 2008. Preliminary data from the hematological malignancies and lymphomas and advanced myeloma studies have been reported, namely, a complete response noted in a heavily pretreated patient with peripheral T-cell lymphoma and prolonged disease stabilization in advanced myeloma.

Clinical Development Plan for darinaparsin: Intravenously administered darinaparsin safety, pharmacokinetics, and drug activity has been evaluated in phase I studies. These trials have involved different patient populations, namely solid tumors, multiple myeloma and hematologic malignancies. The data reported had noted that darinaparsin was well tolerated and showed preliminary signs of activity at the recommended phase II dose. Three phase II studies evaluating hematological malignancies and lymphomas, advanced myeloma and liver cancer have started and accrual is expected to be completed by the second quarter of 2008. Based on the efficacy data generated in these studies and commercial evaluation, a lead indication is expected to be selected for further development.

In addition, an oral darinaparsin phase I program is ongoing and continues to accrue patients. Depending upon the number of cohorts required to achieve the maximum tolerated dose ("MTD"), a recommended phase II dose for the oral program is expected to be determined in the second half of 2008.

Palifosfamide ("ZIO-201")

General. Palifosfamide, or isophosphoramide mustard ("IPM"), is a proprietary active metabolite of the pro-drug ifosfamide. A number of patent applications have been filed in the U.S. and internationally. Ifosfamide, as well as the related drug cyclophosphamide, are alkylating agents. Cyclophosphamide is believed to be the most widely used alkylating agent in cancer therapy. Ifosfamide has been shown to be effective at high doses by itself, or in combination with other agents, in treating sarcoma and lymphoma and it is approved in the U.S. for the treatment of testicular cancer. Although ifosfamide-based treatment generally represents the standard of care for sarcoma, it is not licensed for this indication by the U.S. Food and Drug Administration.

Our preclinical studies have shown that, in animal and laboratory models, palifosfamide evidences activity against leukemia and solid tumors. These studies also indicate that palifosfamide has a better pharmacokinetic and safety profile than ifosfamide or cyclophosphamide, offering the possibility of safer and more efficacious therapy.

In addition to IPM, other metabolites of ifosfamide are produced including acrolein, which is toxic to the kidneys and bladder. The presence of acrolein mandates the administration of a protective agent called mesna, which is inconvenient to use and expensive. Chloroacetaldehyde, another metabolite of ifosfamide, 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. Because palifosfamide is the active metabolite—without acrolein or chloroacetaldehyde metabolites—the Company believes that the administration of palifosfamide (without the administration of mesna) may avoid many of the toxicities of ifosfamide without compromising efficacy.

In addition to anticipated lower toxicity, palifosfamide may have other advantages over ifosfamide and cyclophosphamide. Palifosfamide cross-links DNA differently than the active metabolite of cyclophosphamide, resulting in a different activity profile. Moreover, in some preclinical studies, palifosfamide shows activity in cisplatin-, ifosfamide- and/or cyclophosphamide-resistant cancer cells. In xenografts of human breast cancer and in a mouse leukemia model, palifosfamide has anti-tumor activity when administered orally, which is a potential additional advantage over ifosfamide and cyclophosphamide.

Potential Lead Indication for palifosfamide: Sarcoma. Sarcomas are cancers of the bone, cartilage, fat, muscle, blood vessels, or other connective or supportive tissue. There are more than 50 histological or tissue types of soft tissue sarcomas. The prognosis for patients with soft tissue sarcomas depends on several factors, including the patient's age, size of the primary tumor, histological grade, and stage of the tumor. Factors associated with a poorer prognosis include being older than 60 years of age, having tumors larger than five centimeters, and having tumors of high-grade histology. While small, low-grade tumors are usually curable by surgery alone, the higher-grade or larger sarcomas are associated with higher local treatment failure rates and increased metastatic potential.

Palifosfamide may be a useful agent that, either alone or in combination with other agents, may deliver therapeutic activity with fewer side effects of the type that have been associated with ifosfamide. In the United States, ifosfamide is regularly included in combination regimens for the treatment of sarcomas, testicular cancers, head and neck cancer, certain types of non-Hodgkin's lymphomas, and other solid tumors. The Company believes that palifosfamide may be able to replace ifosfamide in any or all of these combination protocols.

Clinical Development Plan for palifosfamide. The phase I studies of palifosfamide (solid tumors and advanced sarcoma) have been completed. In both of these trials, palifosfamide was given without mesna and no treatment-related hemorrhagic cystitis or CNS-toxicity was reported. Bone marrow toxicity was modest and the dose-limiting toxicity was renal toxicity. One subject with mesothelioma had stable disease for more than 13 months and two patients with sarcoma had a response of stable disease or better.

The phase II portion of the advanced sarcoma trial has completed accrual. Interim data from the study were reported in the fourth quarter of 2007. The trial indicated that palifosfamide was well tolerated, with renal toxicity being the most clinically relevant adverse event. Preliminary efficacy has been reported in a subject with liposarcoma that lasted 35 weeks. In addition, stable disease ("SD") was observed in 44% of the evaluable subjects.

The Company has initiated a study in which palifosfamide is administered in combination with doxorubicin, which is the most commonly used agent for treating advanced sarcoma. Should no additional safety concerns emerge during the phase I portion of this study, the Company anticipates planning a pivotal sarcoma study at the end of 2008. This is planned to be preceded by an End of Phase II meeting with the FDA to discuss a Fast Track development program for advanced sarcoma, under a special protocol assessment ("SPA").

In addition, an oral palifosfamide phase I program is planned for the near future under an IND submitted to the U.S. FDA. Depending upon the number of cohorts required to determine the maximum tolerated dose ("MTD"), a recommended phase II dose for the oral program could be achieved in mid-to-late 2008.

Indibulin ("ZIO-301")

General. Indibulin is a novel small molecular-weight tubulin polymerization inhibitor that was acquired from Baxter Healthcare. The microtubule component, tubulin, is currently one of the best established anti-tumor targets available as a the treatment of cancer. A number of other tubulin-targeting drugs are currently on the market, including paclitaxel (Taxol®) and vinca alkaloids (vincristine, vinorelbine). The use of these drugs is associated with important toxicities, notably peripheral neuropathy. By contrast, no peripheral neurotoxicity has been observed to date with indibulin administration, either in preclinical testing or in phase I clinical testing. In addition, its activity as an oral formulation could offer significant convenience to patients, since no oral formulations of paclitaxel or related compounds have been developed thus far.

Indibulin has a different pharmacological profile from other tubulin inhibitors currently on the market (paclitaxel, docetaxel, vinorelbine, vincristine, and vinblastin). It binds to a unique site on tubulin and is active in multi-drug-resistant (MDR-1, MRP-1) and taxane-resistant tumors. Indibulin binding causes destabilization of microtubules *in vitro*, an effect similar to that of the vinca alkaloid family or colchicine, but opposite to that of paclitaxel and related drugs.

Testing of indibulin for *in vitro* growth inhibitory activity against a panel of human and rodent tumor-derived cell lines revealed that the drug candidate is active in a broad spectrum of cell lines derived from different organs. *In vivo*, indibulin is active in a number of xenograft and rodent tumor models. Its unique pharmacodynamic properties demonstrated in preclinical studies, as well as an excellent safety profile observed thus far in ongoing phase I studies warrant further evaluation in the clinic.

Potential Lead Indications for Indibulin: NSCLC, head and neck, prostate, colorectal, breast. At the current time, the Company anticipates pursuing a Fast Track development program following the completion of phase I/II testing that it plans to initiate this year. Registration in one of these indications would then be followed by label expansion trials. In addition, the development of an IV formulation could further expand the market opportunity.

Clinical Development Plan for Indibulin. The phase I program with indibulin will evaluate safety, pharmacokinetics ("PK"), pharmacodynamics, biomarkers, MTD, and dose limiting toxicity ("DLT") in patients with advanced solid tumors; these trials are expected to complete in the first half of 2008. MTD has not yet been reached in phase I studies. Indibulin is well tolerated and clinical activity has been observed in patients with several histologic subtypes. This data will be used to select a phase II dose. Preclinical combination studies demonstrated synergy with erlotinib, docetaxel, and capecitabine. Two combination studies with erlotinib and capecitabine are planned to start in the first half of 2008; the phase I portion of the erlotinib combination trial has been initiated. Depending upon the number of cohorts needed to determine a recommended dose; these studies will be expanded in a phase II portion that will evaluate the efficacy of these combinations. Following a detailed review of data, additional studies will be proposed.

Competition

The development and commercialization for new products to treat cancer is highly competitive, and considerable competition from major pharmaceutical, biotechnology, and specialty cancer companies is anticipated. Many of our competitors have access to substantially more resources than does the Company, including both financial and technical. In addition, many of these companies have more experience in preclinical and clinical development, manufacturing, regulatory, and global commercialization. The Company is also competing with academic institutions, governmental agencies, and private organizations that are conducting research in the field of cancer. Competition for highly qualified employees is intense.

In addition to third-party competition, treatments for cancer that compete with our product candidates are summarized under the caption “Cancer Treatments.”

License Agreements and Intellectual Property

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

Patent and Technology License Agreement—University of Texas M. D. Anderson Cancer Center and the Texas A&M University System. On August 24, 2004, the Company entered into a Patent and Technology License Agreement with The Board of Regents of the University of Texas System, acting on behalf of The University of Texas M. D. Anderson Cancer Center and the Texas A&M University System (collectively, the “Licensors”). Under this agreement, the Company was granted an exclusive, worldwide license to rights (including rights to U.S. and foreign patent and patent applications and related improvements and know-how) for the manufacture and commercialization of two classes of organic arsenicals for human and animal use. One of these classes include darinaparsin.

In October 2004, we received a notice of allowance for U.S. Patent Application No. 10/337969, entitled “S-dimethylarsino-thiosuccinic acid S-dimethylarsino-2-thiobenzoic acid S-(dimethylarsino) glutathione as treatments for cancer.” The patent was granted on June 28, 2005 as U.S. Patent No. 6,911,471. The patent claims both therapeutic uses and pharmaceutical compositions containing a novel class of organic arsenicals, including darinaparsin, for the treatment of cancer. In February 2006, we announced a second organic arsenic patent that was issued under U.S. Patent No. 6,995,188 . This patent provides further coverage of cancer treatment using organic arsenic, including darinaparsin, in combination with other agents or therapies. Currently there are corresponding foreign applications relating to darinaparsin in various foreign countries.

As partial consideration for the license rights obtained by us, we paid the Licensors an upfront, nonrefundable $125,000 fee and issued 250,487 shares of our common stock to The University of Texas M. D. Anderson Cancer Center, and granted it an option to purchase an additional 50,222 shares of our common stock for $0.002 per share. The option vested and became exercisable with respect to 25% of its shares upon the Company’s filing of an Investigational New Drug (“IND”) in the fiscal year ended December 31, 2005. During the year ended December 31, 2007, an additional 50% of the option vested and became exercisable upon completion of the dosing of the last patient for both the blood and solid tumor phase I trials for darinaparsin. We recorded a $120,492 stock compensation expense in connection with vesting of 25,111 of the options granted outside of the 2003 Stock Option Plan. The remainder of the option will vest and become exercisable with respect to 25% of the shares upon enrollment of the first patient in a multi-center pivotal clinical trial (i.e., a human clinical trial intended to provide the substantial evidence of efficacy necessary to support the filing of an approvable New Drug Application (“NDA”) for darinaparsin). As additional consideration for the license, the Licensors are entitled to receive up to an aggregate of $4.85 million in cash payments, payable in varying amounts, upon the achievement of certain milestones, including $100,000 that we paid upon the commencement of the phase I clinical trial for darinaparsin in May 2005 and $250,000 upon the dosing of the first patient in the Registrant-sponsored phase II clinical trial for darinaparsin in November 2006. The Licensors are entitled to receive royalty payments from sales of a licensed product (should such a product be approved for commercial sale), as well and a portion of any fees that we may receive from a sublicensee under certain circumstances. Finally, the license agreement provided that we enter into two separate sponsored research agreements with the Licensors, each of which required that we make annual payments of $100,000 for no less than two years following the contract’s execution. We have the exclusive right to all intellectual property rights resulting from such research pursuant to the terms of the agreements. These sponsored research agreements and any related extensions will expire in February 2008.

The agreement also contains other provisions that are customary and common to similar agreements within the industry, such as our right to sublicense our rights under the agreement. Nevertheless, if we sublicense our rights prior to the commencement of a pivotal clinical trial (i.e., a human clinical trial intended to provide the substantial evidence of efficacy necessary to support the filing of an approvable NDA), the Licensors will generally be entitled to receive a share of the payments we receive in exchange for the sublicense (subject to certain exceptions).

License Agreement with DEKK-Tec, Inc. On October 15, 2004, we entered into a license agreement with DEKK-Tec, Inc., pursuant to which we were granted an exclusive, worldwide license to the second of our lead product candidates, palifosfamide. The licensed patent estate includes two pending United States patent applications and numerous foreign counterparts.

As partial consideration for the license rights obtained by us, we paid DEKK-Tec an upfront, non-refundable $50,000 fee. In addition, DEKK-Tec is entitled to receive cash payments in an aggregate amount of up to $3.9 million, which are payable in varying amounts upon the occurrence of certain milestone events. The majority of these milestone payments will be creditable against future royalty payments, as referenced below. During the year ended December 31, 2006, the Company recorded a charge of $100,000 for achieving phase II milestones. We also issued DEKK-Tec an option to purchase up to 27,616 shares of our common stock for approximately $0.02 per share, of which 6,904 shares vested upon the execution of the license agreement. DEKK-Tec has since exercised the vested portion of the option in its entirety. The option will vest with respect to the remaining shares upon certain milestone events, culminating with final FDA approval of the first NDA submitted by us (or by our sublicensee) for palifosfamide. DEKK-Tec is entitled to receive royalty payments on the sales of palifosfamide should it be approved for commercial sale. The license agreement also contains other provisions customary and common in similar agreements within the industry.

Option and Research Agreements with Southern Research Institute ("SRI"). On December 22, 2004, we entered into an Option Agreement with SRI, pursuant to which we were granted an exclusive option to obtain an exclusive license to SRI's interest in certain intellectual property, including exclusive rights related to certain isophosphoramide mustard analogs. Also on December 22, 2004, we entered into a Research Agreement with SRI pursuant to which we agreed to spend a sum not to exceed $200,000 between the execution of the agreement and December 21, 2006, including a $25,000 payment that we made simultaneously with the execution of the agreement, to fund research and development work by SRI in the field of isophosphoramide mustard analogs. The option agreement was exercised on February 13, 2007 and the exclusively licensed patent estate includes one U.S. patent (U.S. Patent No. 6,197,760) and two foreign patents as well as corresponding patent applications in Japan and Canada. An annual payment of $25,000 was made in 2007 for maintenance of this option agreement.

Asset Purchase of Indibulin from Baxter Healthcare Corporation. On November 3, 2006, the Company signed a definitive Asset Purchase Agreement and License Agreement to acquire indibulin (and license rights to nanosuspension technology) from affiliates of Baxter Healthcare Corporation. The terms of the agreement include an upfront cash payment of approximately $1.125 million, which has been expensed as purchased research and development. In the year ended December 31, 2006, $15,000 was paid for annual patent and license maintenance fee, and $100,000 was paid for existing inventory. In addition to the upfront payments, there will be follow-on milestone cash payments that could amount to approximately $8 million in the aggregate and royalties on net sales typical of a product at this stage of development. During the year ended December 31, 2007, we paid $625,000 in milestone payments for the successful U.S. Investigational New Drug ("IND") application for indibulin and also paid an additional $15,000 for the annual patent and license maintenance fee. The purchase price includes the entire indibulin intellectual property portfolio as well as existing drug substance and capsule inventories.

The patent estate related to indibulin currently includes one U.S. patent (U.S. Patent No. 6,008,231) and eighteen (18) foreign patents that cover the indibulin molecule, as well as numerous corresponding pending foreign applications. In addition, there are two U.S. Patents (U.S. Patent Nos. 6,232,327 and 6,693,119) and thirty-one (31) foreign patents covering methods of using indibulin as a cancer therapeutic, as well as four pending U.S. and numerous corresponding pending foreign applications.

Other Intellectual Property Rights and Protection. We depend upon the skills, knowledge, and experience of our scientific and technical personnel, as well as those of our advisors, consultants, and other contractors, none of which is patentable. To help protect proprietary know-how, which is not patentable, and for inventions for which patents may

be difficult to enforce, we currently rely, and in the future will continue to rely, on trade secret protection and confidentiality agreements to protect our interests. To this end, we generally require employees, consultants, advisors and other contractors to enter into confidentiality agreements that prohibit the disclosure of confidential information and, where applicable, require disclosure and assignment to us of the ideas, developments, discoveries and inventions important to our business.

Governmental Regulation

The research, development, testing, manufacture, labeling, promotion, advertising, distribution, and marketing, among other things, of our products are extensively regulated by governmental authorities in the United States and other countries. In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act ("FDCA") and its implementing regulations. Failure to comply with the applicable U.S. requirements may subject us to administrative or judicial sanctions, such as FDA refusal to approve pending New Drug Applications ("NDAs"), warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, and/or criminal prosecution.

Drug Approval Process. None of our drugs may be marketed in the U.S. until the drug has received FDA approval. The steps required before a drug may be marketed in the U.S. include:

- Preclinical laboratory tests, animal studies, and formulation studies;
- Submission to the FDA of an IND for human clinical testing, which must become effective before human clinical trials may begin;
- Adequate and well-controlled human clinical trials to establish the safety and efficacy of the drug for each indication;
- Submission to the FDA of an NDA;
- Satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the drug is produced to assess compliance with current good manufacturing practices, or “cGMPs”; and