ZIOPHARM ONCOLOGY INC
Form 10KSB
February 13, 2007

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, 2006

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, 19 th 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 12, 2007, the aggregate market value of common stock held by non-affiliates of the registrant approximated $78,349,972 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 12, 2007, there were 15,272,899 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 2007 annual meeting of stockholders, which is to be filed within 120 days after the end of the fiscal year ended December 31, 2006, 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

ZIOPHARM Oncology, Inc.
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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 - Recent 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 candidate families that are related to cancer therapeutics that are already on the market or in development. We believe this strategy will result in lower risk and expedited drug development programs. We expect to commercialize our products on our own in North America but recognize that promising clinical trial results in cancers with a high incidence and prevalence might also be addressed in a commercial 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 ZIO-101, ZIO-201, and ZIO-301. We intend to continue with clinical development to register ZIO-101 for the treatment of advanced myeloma, ZIO-201 to treat advanced sarcoma and ZIO-301 for an as yet undetermined solid tumor indication. We will continue with preclinical study of our products and back-up candidates, dosing forms and schedules, while evaluating additional later stage clinical candidates.

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 Charlestown, 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. Sarcomas begin in tissue that connects, supports or surrounds other tissues and organs. Lymphomas are cancers of the lymph system, the 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, or 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.

In 2007, the American Cancer Society estimates that 559,650 Americans are expected to die from cancer, more than 1,500 every day. The cost of cancer to the healthcare system 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. There are many different drugs that are used to treat cancer, including cytotoxics or antineoplastics, hormones, and biologics. There are also many experimental treatments under investigation including radiation sensitizers, vaccines, gene therapy and immunotoxins. We believe cancer treatment represents a significant unmet medical need.

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 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, repair or activity which affects the production or function of DNA, RNA or protein. Although there are many cytotoxic agents, there is a considerable amount of 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 the 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, one of the most common side effects of chemotherapy is nausea and vomiting. Several drugs have been developed to help prevent and control chemotherapy-induced nausea and vomiting, including 5HT3 receptor antagonists, like ondansetron, which is a selective blocking agent of the hormone serotonin.

Product Candidates

ZIO-101

General. ZIO-101 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®) or ATO) has been approved for the treatment of acute promyelocytic leukemia (APL) and is on the compendia listing for the therapy of multiple myeloma as well as having been studied for the treatment of various other cancers. ATO has been shown to be toxic to the heart, nerves and liver, limiting its use as a broad anti-cancer agent. Our preclinical studies demonstrated that ZIO-101 is considerably less toxic than ATO, particularly with regard to heart toxicity. In phase I testing, significantly higher doses of ZIO-101 have been safely administered than the approved dose of Trisenox®, confirming preclinical findings.

In vitro testing of ZIO-101 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, ZIO-101 has potent anti-angiogenic activity as demonstrated in *in vitro* as well as *in vivo* studies.

In a murine leukemia model, ZIO-101 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.

Clinical Lead Indication: Multiple Myeloma. We expect that advanced myeloma, a hematologic cancer, will be the target indication for our first regulatory approval for ZIO-101. Myeloma is a group of plasma cell cancers associated with the overproduction of monoclonal immunoglobulin (M-protein). Each year approximately 17,000 patients are diagnosed with multiple myeloma in the United States, while 65,000 patients are living with the disease. Primary treatment for myeloma is chemotherapy. Approximately 15-20% of patients with myeloma are resistant to aggressive primary treatment. Patients that initially respond to treatment usually develop resistance to primary therapy after several years. The average survival of patients with progressive or resistant disease is three to four years.

The standard of care for progressive or resistant multiple myeloma is in transition. Velcade® and Revlimid® are approved to treat patients with myeloma that have had at least one prior therapy. Recent clinical trials offer evidence supporting the use of these therapies either alone or in combination with other agents. However, neither treatment is universally effective. The ongoing need for new and non-cross resistant therapies for the treatment of myeloma suggests that as new therapeutic options come to market, the market will continue to grow. Penetration into the market for new agents is to a large extent independent of the number of therapies available, as most patients generally will fail all available agents at some point. A more rapid market penetration can be expected for new therapies with a wide therapeutic window and where efficacy is equal to or greater than currently available agents.

Clinical Development Plan for ZIO-101. ZIO-101 safety, pharmacokinetics, and drug activity continue to be evaluated in phase I studies. These trials have involved different patient populations, namely solid tumors, multiple myeloma, and hematalogic malignancies. One study is completed (multiple myeloma) while two studies are nearing completion. In summary, ZIO-101 has shown single agent activity in hematologic cancers (including multiple myeloma), and solid tumors. Phase II clinical trials in each of these populations have been initiated. In addition, a number of additional studies are planned, including a phase I trial utilizing an oral formulation of ZIO-101.

Upon the completion of the phase II multiple myeloma program in 2007, the Company anticipates having an end of phase II meeting with the FDA to discuss a Fast Track development program for advanced myeloma under Special Protocol Assessment (SPA) .

ZIO-201

General. ZIO-201, 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 (the "FDA").

Our preclinical studies have shown that, in animal and laboratory models, ZIO-201 evidences activity against leukemia and solid tumors. These studies also indicate that ZIO-201 has a better pharmacokinetic and safety profile than ifosfamide or cyclophosphamide, offering the possibility of safer and more efficacious therapy with ZIO-201.

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 ZIO-201 is independently active—without acrolein or chloroacetaldehyde metabolites—the Company believes that the administration of ZIO-201 (without the administration of mesna) may avoid many of the toxicities of ifosfamide without compromising efficacy.

In addition to anticipated lower toxicity, ZIO-201 may have other advantages over ifosfamide and cyclophosphamide. ZIO-201 cross-links DNA differently than the active metabolite of cyclophosphamide, resulting in a different activity profile. Moreover, in some preclinical studies, ZIO-201 shows activity in cisplatin-, ifosfamide- and/or cyclophosphamide-resistant cancer cells. In xenografts of human breast cancer and in a mouse leukemia model, ZIO-201 has anti-tumor activity when administered orally, a potential additional advantage over ifosfamide and cyclophosphamide.

Potential Lead Indications for ZIO-201. Sarcomas. 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 age greater than 60 years, tumors larger than five centimeters, and high-grade histology. While small, low-grade tumors are usually curable by surgery alone; higher-grade or larger sarcomas are associated with higher local treatment failure rates and increased metastatic potential.

ZIO-201 may be a useful agent that, either alone or in combination with other agents, can 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 and some types of non-Hodgkin's lymphomas and other solid tumors. The Company believes that ZIO-201 may be able to replace ifosfamide in any or all of these combination protocols.

Clinical Development Plan for ZIO-201. ZIO-201 has now been evaluated in two phase I studies, one in advanced cancers and one in advanced sarcoma. In both phase I trials, ZIO-201 was given without mesna. There was no hemorrhagic cystitis or CNS-toxicity. Bone marrow toxicity was modest. One subject with mesothelioma had stable disease >13 months and two patients with sarcoma had a response of at least stable disease.

A phase II trial in advanced sarcoma has been initiated while the phase I study in advanced cancers continues. A number of additional studies are planned for 2007 including a phase II study in lymphoma, a phase I/II study in pediatric malignancies, and a possible phase I study with an oral formulation. Other routes of administration where alkylating agents are active are being evaluated i.e., intrathecal and intraperitoneal.

The Company anticipates evaluating the phase II sarcoma study in the second half of 2007, followed by an end of phase II meeting with the FDA to discuss a Fast Track development program for advanced sarcoma under an SPA.

ZIO-301

General. ZIO-301 (indibulin) is a novel small molecular weight tubulin polymerization inhibitor that has been acquired from Baxter Healthcare. The microtubule component, tubulin, is one of the best established anti-tumor targets in the treatment of cancer today. A number of other tubulin targeting drugs are currently on the market, including paclitaxel (Taxol®) and the vinca alkaloids (vincristine, vinorelbine). The use of these drugs is associated with important toxicities, notably peripheral neuropathy. In contrast, no peripheral neurotoxicity has been observed with ZIO-301 either in preclinical testing or in phase I testing to date. In addition, its activity as an oral formulation could offer significant patient convenience, since to date no oral formulations of paclitaxel or related compounds have been developed.

ZIO-301 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 (MDR-1, MRP-1) and taxane resistant tumors. ZIO-301 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 ZIO-301 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 of different organ origin. *In vivo*, ZIO-301 is active in a number of xenograft and rodent tumor models. Its unique pharmacodynamic properties in preclinical studies and its excellent safety profile observed so far in the ongoing phase I study warrants further evaluation in the clinic.

Potential Lead Indications for ZIO-301. Bladder, head & neck, prostate, colorectal, renal. At the current time, the Company anticipates pursuing a Fast Track development program in a niche indication following the completion of phase II testing that would initiate this year. Registration in one of these indications would then be followed by label expansion trials that will have been already initiated in anticipation of registration. In addition, the development of an IV formulation could further expand the market opportunity.

Clinical Development Plan for ZIO-301. A phase I study is currently underway in the Netherlands with ZIO-301 to evaluate safety, pharmacokinetics (PK), maximum tolerated dose (MTD) and dose limiting toxicity (DLT) in patients with advanced solid tumors. MTD has not yet been reached in the phase I study. Drug activity has been observed in patients with several histologic subtypes. The clinical regulatory strategy is to include a phase II study of ZIO-301 in the United States in 2007.

Competition

The development and commercialization for new products to treat cancer is highly competitive, and there will be considerable competition from major pharmaceutical, biotechnology, and specialty cancer companies. Many of our competitors have substantially more resources than the Company, including both financial and technical. In addition, many of these companies have more experience than the Company 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.

There are a number of companies developing chemotherapies for cancer and in particular for multiple myeloma and sarcoma. Millennium Pharmaceuticals, Inc. and Celgene Corporation have marketed products to treat multiple myeloma, and many other product candidates are in clinical trials and preclinical research. There is a more limited number of competitors developing new approaches to treat sarcoma, Ariad Pharmaceuticals principal among them.

In addition to competitive companies, 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, to preserve our trade secrets, and to operate without infringing 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 includes ZIO-101.

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-(simethylarsino) glutathione as treatments for cancer." The patent was granted on June 28, 2005 as U.S. Patent No. 6,911,471. The patent application claims both therapeutic uses and pharmaceutical compositions containing a novel class of organic arsenicals, including ZIO-101, for the treatment of cancer. In February 2006, we announced that a second organic arsenic case has been issued under U.S. Patent No. 6,995,188. This patent provides further coverage of cancer treatment using organic arsenic, including ZIO-101, in combination with other agents or therapies. In addition, there were seven (7) patents related to ZIO-101 that issued in various foreign countries in 2006.

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 approximately $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. The option will vest and become exercisable with respect to another 50% of its shares upon completion of the dosing of the last patient for both the blood and solid tumor phase I trials for ZIO-101 and 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 ZIO-101). 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 ZIO-101 in May 2005 and $250,000 upon the dosing of the first patient in the Registrant-sponsored phase II clinical trial for ZIO-101 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. We have the exclusive right to all intellectual property rights resulting from such research pursuant to the terms of the agreements. One of these agreements has now been extended to a third year by mutual agreement.

The agreement also contains other provisions customary and common in 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, ZIO-201.

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 the 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, which option vested with respect to 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 ZIO-201. DEKK-Tec is entitled to receive royalty payments on the sales of ZIO-201 should it be approved for commercial sale. The license agreement also contains other provisions customary and common in similar agreements within the industry.

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 license maintenance fee, and $100,000 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. The purchase price includes the entire indibulin intellectual property portfolio as well as existing drug substance and capsule inventories.

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 must be exercised within 60 days of December 22, 2006.

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, or the

"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
-