### **OFFERING PROSPECTUS**



### **ZIOPHARM Oncology, Inc.**

7,269,366 Shares

**Common Stock** 

The selling stockholders identified on pages 17-19 of this prospectus are offering on a resale basis a total of 7,269,366 shares of our common stock, of which 1,359,317 shares are issuable upon the exercise of outstanding warrants. We will not receive any proceeds from the sale of these shares by the selling stockholders.

Our common stock is listed on the NASDAQ Capital Market under the symbol "ZIOP." On March 23, 2007, the last sale price for our common stock as reported on the NASDAQ Stock Market, Inc. was \$5.65.

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

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

The date of this Prospectus is March 26, 2007.

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#### **PROSPECTUS SUMMARY**

This summary provides a brief overview of the key aspects of this offering. Because it is only a summary, it does not contain all of the detailed information contained elsewhere in this prospectus or in the documents incorporated by reference into this prospectus or included as exhibits to the registration statement that contains this prospectus. Accordingly, you are urged to carefully review this prospectus (including all documents incorporated by reference into this prospectus) in its entirety.

### **Our Company**

We are 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.

None of our product candidates have been approved by the United States Food and Drug Administration (the "FDA") or any other regulatory body. Further, we have not received any commercial revenues to date, and until we receive the necessary approvals from the FDA or a similar foreign regulatory authority, we will not have any commercial revenues.

#### **Our 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 <sup>®</sup>) 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 <sup>®</sup>, 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 <sup>®</sup> and Revlimid <sup>®</sup> 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 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.

*Clinical Lead Indications: 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.

#### **Our History**

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

### **Our Corporate and Business Offices**

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. Our internet site is www.ziopharm.com. None of the information on our internet site is part of this prospectus.

#### **Recent Developments**

#### February 2007 Financing

On February 23, 2007, we issued and sold in a private placement transaction an aggregate of 5,910,049 shares of our common stock at a price of \$5.225 per share. In addition to the shares of common stock, we also issued to each investor a five-year warrant to purchase, at an exercise price of \$5.75 per share, an additional number of shares of our common stock equal to 20 percent of the shares purchased by such investor in the offering. In the aggregate, these warrants entitle investors to purchase an additional 1,182,015 shares of our common stock. The total gross proceeds resulting from the sale of these shares and warrants was approximately \$30.9 million, before deducting selling commissions and expenses.

We engaged Oppenheimer & Co. Inc., Paramount BioCapital, Inc. and Griffin Securities, Inc. as co-placement agents in connection with the offering. In consideration with the offering, we paid aggregate cash commissions and fees of approximately \$1.9 million and issued five-year placement agent warrants to purchase an aggregate of 177,302 shares (three percent of the shares sold in the private placement) at an exercise price of \$5.75 per share.

The shares being offered hereby are comprised of the 5,910,049 shares of common stock and the 1,182,015 shares issuable upon exercise of the warrants issued to the investors in the private placement, as well as the 177,302 shares issuable upon exercise of the placement agent warrants.

#### **Risk Factors**

As with most pharmaceutical product candidates, the development of ZIO-101, ZOI-201 and ZIO-301 is subject to numerous risks, including the risk of delays in or discontinuation of development from lack of financing, inability to obtain necessary regulatory approvals to market the products, unforeseen safety issues relating to the products and dependence on third party collaborators to conduct research and development of the products. Because we are a development stage company with a limited history of operations, we are also subject to many risks associated with early-stage companies. For a more detailed discussion of the risks you should consider before purchasing shares of our common stock, you are urged to carefully review and consider the section entitled "Risk Factors" beginning on page 6 of this prospectus.

### The Offering

The selling stockholders identified on pages 17-18 of this prospectus are offering on a resale basis a total of 7,269,366 shares of our common stock, of which 1,359,317 shares are issuable upon the exercise of outstanding warrants.

Common stock offered	7,269,366 shares
Common stock outstanding before the offering <sup>(1)</sup>	21,182,948 shares
Common stock outstanding after the offering <sup>(2)</sup>	22,542,265 shares
Common Stock NASDAQ Capital Market symbol	ZIOP

<sup>(1)</sup> Based on the number of shares outstanding as of February 26, 2007, not including 7,038,628 shares issuable upon exercise of various warrants and options to purchase common stock.

<sup>(2)</sup> Assumes the issuance of all shares offered hereby that are issuable upon exercise of outstanding warrants.

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### **RISK FACTORS**

An investment in our common stock is very risky. You may lose the entire amount of your investment. Prior to making an investment decision, you should carefully review this entire prospectus and consider the following risk factors:

### **Risks Related to our Business**

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

We have never generated revenue and have incurred significant net losses in each year since our inception. For the year ended December 31, 2006, we had a net loss of \$17.9 million and we had incurred approximately \$33.2 million of cumulative net losses since our inception in 2003. We expect to continue to incur significant operating and capital expenditures and anticipate that our expenses will increase substantially in the foreseeable future as we:

- · Continue to undertake preclinical development and clinical trials for product candidates;
- · Scale up the formulation and manufacturing of our product candidates;
- · Scale up the formulation and manufacturing of our product candidates;
- · Seek regulatory approvals for product candidates;
- · Implement additional internal systems and infrastructure; and
- Hire additional personnel.

Because we expect to incur losses for the foreseeable future, we will need to generate significant revenues in order to achieve and maintain profitability. Even if we succeed in developing and commercializing one or more of our product candidates, which success is not assured, we may not be able to generate significant revenues. If we do generate significant revenues, we may never achieve or maintain profitability. Our failure to achieve or maintain profitability could negatively impact the trading price of our common stock.

# If we are not able to successfully develop and commercialize our product candidates, we may not generate sufficient revenues to continue our business operations.

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 drug candidates is long, complex and costly. Until and unless we receive approval from the FDA and/or other regulatory authorities for our product candidates, we cannot sell our drugs 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 earn sufficient revenues to continue our business without raising significant additional capital, which may not be available.

### We may need to raise additional capital to fund our operations. If we are unable to raise additional capital when needed, we may have to discontinue our product development programs. The manner in which we raise any additional funds may affect the value of your investment in our common stock.

As of December 31, 2006, we had incurred approximately \$33.2 million of cumulative net losses and had approximately \$28.4 million of cash, cash equivalents, and short-term investments. In February 2007, we completed an offering of common stock and warrants in which we received proceeds of approximately \$29.0 million after paying cash commissions, fees and offering expenses. Currently, we expect that we will have sufficient cash to fund our operations late into the fourth quarter of 2008. Although we expect our cash on-hand to fund our operations late into the fourth quarter of 2008, changes may occur that would consume our existing capital prior to that time, including the progress of our research and development efforts, changes in governmental regulation and acquisitions of additional product candidates.

Currently, we have no committed sources of additional capital. We do not know whether additional financing will be available on terms favorable to us when needed, if at all. If we fail to advance 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 obtaining additional financing. To the extent that we raise additional capital by issuing equity securities, our stockholders may experience dilution. We may grant future investors rights superior to those of our common 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.

If we do not succeed in raising additional funds on acceptable terms, we may be unable to complete planned preclinical and clinical trials or obtain approval of any product candidates from the FDA and other regulatory authorities. In addition, we could be forced to discontinue product development, reduce or forego sales and marketing efforts or forego attractive business opportunities, or discontinue our operations altogether.

### 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, undertaking preclinical trials and clinical trials of our product candidates ZIO-101, ZIO-201 and ZIO-301, and manufacturing ZIO-101 and ZIO- 201 and, in the near future, ZIO-301. 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.

# We intend to acquire rights to develop and commercialize additional product candidates. 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. The success of our strategy depends upon our ability to identify, select and acquire pharmaceutical 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 us and have significantly more financial resources than we do. Our competitors may have stronger relationships with certain third parties with whom we are interested in partnering, such as academic research institutions, and may, therefore, have 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 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 manufactured or produced economically or commercialized successfully. If we are unable to successfully manage our growth, our business may be harmed.

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 these capabilities. Any future growth will place a significant strain on our management and on our administrative, operational and financial resources. 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. 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.

Our success will depend upon the expansion of our operations and the effective management of our growth, which will place a significant strain on our management and on our administrative, operational and financial resources. 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, Richard E. Bagley, our 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 2008 and July 2007, 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 any of our 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.

### 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.

#### 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 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;
- · Conducting sales and marketing activities;
- · Costs of related litigation;
- · Substantial monetary awards to patients;
- · Product recalls;
- · Loss of revenue; and
- · The inability to commercialize our product candidates.

Our inability to obtain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the commercialization of pharmaceutical products we develop, alone or with collaborators. We currently carry clinical trial insurance and product liability insurance.

### 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, ZIO-101, ZIO-201 and ZIO-301, 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 (NDA), 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 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 clinical approaches will result in drugs that the FDA considers 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. We cannot be sure that we will ever obtain regulatory clearance for our product candidates, ZIO-101, ZIO-201 and ZIO-301. Failure to obtain FDA approval of 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.

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



Our product candidates, ZIO-101, ZIO-201, and ZIO-301 are in early 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.

### 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 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;
- · Inability to monitor patients adequately during or after treatment; and
- · Inability or unwillingness of medical investigators to follow our clinical protocols.

We are hopeful that we may be able to obtain "Fast Track" and or "Orphan Drug" status from the FDA for one or more of 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 and affords certain financial and market protection benefits to successful applicants. However, there is no guarantee that any of our product candidates will be granted Fast Track or Orphan Drug 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. Therefore, we cannot predict with any certainty the schedule for future clinical trials.

### 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. Success in preclinical testing and early clinical trials does not ensure that later clinical trials will be successful, and we cannot be sure 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 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 filing of our NDAs 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 small sample size, the results of these clinical trials may not be indicative of future results.

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, regarding the safety and effectiveness of our drugs;
- · Cost-effectiveness of our products relative to competing products;
- · Availability of reimbursement for our products from government or other healthcare payers; and
- · Effectiveness of marketing and distribution efforts by us and our licensees and distributors, if any.

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.

# Because we are dependent on 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 drugs, 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 and do not intend to establish our own manufacturing facilities. 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 to manufacture our drugs. 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 drugs 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 (the "DEA"), 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; and
- 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 to 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, 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 our products, there can be no assurance that we will be able to establish or maintain our own sales operations or effect collaborative arrangements, or that if we are able to do so, our collaborators will have effective sales forces. 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 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 which may not be successful and which will be only partially in our control. Our product revenues would likely be lower than if we marketed and sold our products directly.

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

# 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 drugs;
- 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.

# Our ability to generate product revenues will be diminished if our drugs 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 policies and proposals in recent years to change the healthcare system in ways that could impact our ability to sell our products profitably. On December 8, 2003, President Bush signed into law the Medicare Prescription Drug, Improvement and Modernization Act of 2003, or the MMA, which contains, among other changes to the law, a wide variety of changes that have and will impact Medicare reimbursement of pharmaceuticals to physicians and hospitals.

There also likely will continue to be legislative and regulatory proposals that could bring about significant changes in the healthcare industry. We cannot predict what form those changes might take or 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. We anticipate filing additional patent applications both in the U.S. and in other countries, as appropriate. However, we cannot predict:

- 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 issue;



- 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 which may be costly whether we win or lose.

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 policy generally to require our employees, consultants, advisors and contractors to enter into agreements which 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 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 opposed by third parties in foreign jurisdictions having opposition proceedings. The defense and prosecution, if necessary, of intellectual property actions are costly and divert technical and management personnel 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 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.

As a company with limited capital and human resources, our management has identified that there is a lack of segregation of duties due to the limited number of employees within our company's financial and administrative functions. Management believes that, based on the employees involved and the control procedures in place, risks associated with such lack of segregation are not significant and that the potential benefits of adding employees to segregate duties more clearly do not justify the associated added expense. However, management continues to evaluate this segregation of duties. Our management is working to continuously monitor the segregation of duties as well as reviewing internal controls. We have engaged the services of a Sarbanes-Oxley consultant to tighten our internal controls and ensure adherence to the regulations once finalized. In the event we identify significant deficiencies or material weaknesses 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.

#### There is not now, and there may not ever be an active market for shares of our common stock.

In general, there has been limited trading activity in shares of our common stock. The small trading volume may make it more difficult for our stockholders to sell their shares as and when they choose. Furthermore, small trading volumes generally depress market prices. As a result, you may not always be able to resell shares of our common stock publicly at the time and prices that you feel are fair or appropriate.

### Because we became public by means of a reverse merger, we may not be able to attract the attention of major brokerage firms.

Additional risks may exist as a result of our becoming a public reporting company through a "reverse merger." Security analysts of major brokerage firms may not provide coverage of the Company. Because we became public through a reverse merger, there is no incentive to brokerage firms to recommend the purchase of our common stock. No assurance can be given that brokerage firms will want to provide analyst coverage of our Company in the future.

### 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, Section 203 of the Delaware General Corporation Law, which prohibits business combinations between us and one or more significant stockholders unless specified conditions are met, may discourage, delay or prevent a third party from acquiring us.

### 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 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.

### NOTE REGARDING FORWARD-LOOKING STATEMENTS

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

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

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

### **USE OF PROCEEDS**

We will not receive any proceeds from the resale of any of the shares offered by this prospectus by the selling stockholders.

### SELLING STOCKHOLDERS

This prospectus covers the resale by the selling stockholders identified below of 7,269,366 shares of our common stock, including shares issuable upon the exercise of warrants. This offering includes the 5,910,049 common shares and 1,359,317 common shares issuable upon the exercise of the warrants issued in our February 2007 private placement, of which 177,302 common shares are issuable upon the exercise of warrants issued to placement agents and other consultants that provided services to us in the private placement. The warrants received by the investors and by the placement agents and consultants in the private placement are exercise price of \$5.75 per share.

The following table sets forth the number of shares of the common stock owned by the selling stockholders as of February 26, 2007, and after giving effect to this offering.

Solling Stockholdor	Shares Beneficially Owned Before Offering (1)	Number of Outstanding Shares Offered by Selling Stockholder	Number of Shares Offered by Selling Stockholder Upon Exercise of Certain Warrants	Percentage Beneficial Ownership After Offering (2)
Selling Stockholder	Offering (1)	Stockholder		Offering (2)
Harewood Nominees Ltd				
A/C 468 9000 (3)	33,072(4)	27,560	5,512	0%
Diamondback Master Fund, Ltd. (5)	344,498(6)	287,081	57,417	0%
Essex Woodlands Health Ventures				
Fund VI, LP (7)	2,296,652(8)	1,913,876	382,776	0%
Henderson Global Multi-Strategy	02 226(0)	70.000	15 200	00/
Equity Fund (3) Henderson North American	92,326(9)	76,938	15,388	0%
Multi-Strategy Equity Fund (3)	23,885(10)	19,904	3,981	0%
JP Morgan Securities Inc. (11)	45,934(12)	38,278	7,656	0%
LB I Group Inc. (13)	1,467,607(14)	287,081	57,417	5.22%
Man Mac Todi 17B Limited (15)	191,113(16)	149,282	29,857	*
Millennium Partners, L.P. (17)	1,283,074(18)	382,775	76,555	3.85%
Oppenheim Pramerica Asset Management S.a.r.l. on behalf of FCP OP MEDICAL BioHe@lth-	1,200,07 1(10)	562,775	, 0,000	0.0070
Trends (19)	454,288(20)	191,388	38,278	1.05%
PHARMA/wHEALTH Management Company				
S.A.				
on behalf of PHARMAw/HEALTH (21)	130,516(22)	47,847	9,570	*
ProQuest Investments III, L.P. (23)	2,092,885(24)	574,164	114,833	6.49%
PTV Sciences II, L.P. (25)	1,837,320(26)	1,531,100	306,220	0%
Special Situations Life Sciences Fund, L.P. (27)	459,330(28)	382,775	76,555	0%
Oppenheimer & Co. Inc. (29)	47,910(30)	0	47,910	0%
Adrian Stycek (31)	149,589(32)	0	10,612	*
ThinkEquity Partners LLC (33)	21,244(34)	0	21,244	0%
	230,477	0	35,739	*
Timothy McInerney (35)				*
Scott Katzmann	70,155	0	4,395	*
Harris Lydon	59,747	0	816	*
Michael Rosenman	66,366	0	1,569	*
Basil Christakos	11,678	0	3,000	*
John Knox (36)	28,970	0	9,500	*
Lindsay A. Rosenwald, M.D. (37)	1,590,058(38)	0	42,517	7.11%
Total		5,910,049	1,359,317	

Less than 1%.

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

- (2) Assumes sales of all shares by the selling stockholder.
- (3) C. Castronero, as Fund Manager, has voting and investment control over the shares held by the selling stockholder.
- (4) Includes 5,512 shares issuable upon the exercise of warrants.
- (5) Timothy M. Higgins has voting and investment control over the shares held by the selling stockholder.
- (6) Includes 57,417 shares issuable upon the exercise of warrants.
- (7) Mark Pacala, as Managing Director of Essex Woodlands Health Ventures Fund VI, LP, has voting and investment control over the shares held by the selling stockholder.
- (8) Includes 382,776 shares issuable upon the exercise of warrants.
- (9) Includes 15,388 shares issuable upon the exercise of warrants.
- (10) Includes 3,981 shares issuable upon the exercise of warrants.
- (11) Avik S. A. Roy has voting and investment control over the shares held by the selling stockholder. JP Morgan Securities Inc. is a proprietary trading group and is an affiliate of a broker-dealer. The selling stockholder has represented to us that it acquired the securities being offered hereby in the ordinary course of its business and that, at the time it acquired such securities, it did not have any agreements or understandings, directly or indirectly, with any person to distribute such securities.
- (12) Includes 7,656 shares issuable upon the exercise of warrants.
- (13) Jeffrey Ferrell has voting and investment control over the shares held by the selling stockholder. LB I Group Inc. is an affiliate of Lehman Brothers Holdings Inc., a registered broker-dealer. The selling stockholder has represented to us that it acquired the securities being offered hereby in the ordinary course of its business and that, at the time it acquired such securities, it did not have any agreements or understandings, directly or indirectly, with any person to distribute such securities.
- (14) Includes 316,596 shares issuable upon the exercise of warrants.
- (15) Edmund Debler has voting and investment control over the shares held by the selling stockholder.
- (16) Includes 29,857 shares issuable upon the exercise of warrants.
- (17) Millennium Management, L.L.C., a Delaware limited liability company, is the managing partner of Millennium Partners, L.P., a Cayman Islands exempted limited partnership, and, consequently, may be deemed to have voting control and investment discretion over securities owned by Millennium Partner, L.P. Israel A. Englander is the managing member of Millennium Management, L.L.C. As a result, Mr. Englander may be considered the beneficial owner of any shares deemed to be beneficially owned by Millennium Management, L.L.C. The foregoing should not be construed in and of itself as an admission by either of Millennium Management, L.L.C. or Mr. Englander as to the beneficial ownership of the shares held by Millennium Partners, L.P.Millennium Partners L.P. is an affiliate of Millenco L.L.C., a registered broker dealer, and two additional broker dealers. The selling stockholder has represented to us that it acquired the securities being offered hereby in the ordinary course of its business and that, at the time it acquired such securities, it did not have any agreements or understandings, directly or indirectly, with any person to distribute such securities.
- (18) Includes 40,133 shares held by Millenco, L.P., an affiliate of the selling stockholder, and 206,145 shares issuable upon the exercise of warrants.
- (19) FCP OP MEDICAL BioHe@lth-Trends is a sub-fund of FCP OP MEDICAL, a Luxembourg investment fund. FCP OP MEDICAL BioHe@lth-Trends is managed by Oppenheim Pramerica Asset Management S.a.r.l. Detlef Bierbaum, Dr. Rupert Hengster, Ferdinand-Alexander Leisten, Stephen Pelletier, Susan M. Scheader, John P. Smalling, Andreas Jockel, Harry Rosenbaum, Anita Zuleger, Ute Becker, Alexander Schulligen, Max van Frantzius, Peter Balle, Thomas Becker, Julia Brauckman, Otmar Gorges, Detlef Vallender, Johann Will, Adreas Becker, Katja Kirchen, Ralf Klein, Ulrike Sauer and Ronny Wagner share voting and investment control over the shares held by the selling stockholder. The selling stockholder is an affiliate of a broker-dealer and has represented to us that it acquired the securities being offered hereby in the ordinary course of its business and that, at the time it acquired such securities, it did not have any agreements or understandings, directly or indirectly, with any person to distribute such securities.
- (20) Includes 90,114 shares issuable upon the exercise of warrants.
- (21) PHARMA/wHEALTH is a Luxembourg investment fund that is managed by PHARMAw/HEALTH Management Company S.A. PHARMAw/HEALTH Management Company S.A has delegated the management of a portion of the assets of PHARMAw/HEALTH to Medical Strategy. Dr. Michael Fischer Andreas Jockel and Alexander Schulligen share voting and investment control over the shares held by the selling stockholder.
- (22) Includes 9,570 shares issuable upon the exercise of warrants.

- (23) ProQuest Associates III LLC is the general partner of the selling stockholder. Jay Moorin and Alain Schreiber are managing members of ProQuest Investments III, L.P. and share voting and investment control over the shares held by the selling stockholder.
- (24) Includes 438,807 shares issuable upon the exercise of warrants.
- (25) Evan S. Melrose, M.D., as Managing Director of PTV Sciences II, L.P., has voting and investment control over the shares held by the selling stockholder.
- (26) Includes 306,220 shares issuable upon the exercise of warrants.
- (27) Austin Marxe, as Managing Director of Special Situations Life Science Fund, L.P., has voting and investment control over the shares held by the selling stockholder.

- (28) Includes 76,555 shares issuable upon the exercise of warrants.
- (29) Albert G. Lowenthal has voting and investment control over the shares held by the selling stockholder. Oppenheimer & Co. Inc. is a registered brokerdealer and has represented to us that it acquired the securities being offered hereby in the ordinary course of business and that, at the time it acquired such securities, it did not have any agreements or understandings, directly or indirectly, with any person to distribute such securities.
- (30) Includes 47,910 shares issuable upon the exercise of warrants.
- (31) Mr. Stecyk is affiliated with Griffin Securities, Inc., a registered broker-dealer, serving as its President and Chief Executive Officer. Mr. Stecyk has represented to us that he acquired the securities being offered hereby in the ordinary course of business and that, at the time he acquired such securities, he did not have any agreements or understandings, directly or indirectly, with any person to distribute such securities.
- (32) Includes 10,612 shares issuable upon the exercise of warrants.
- (33) Michael Moe has voting and investment control over the shares held by the selling stockholder. ThinkEquity Partners LLC is a registered broker-dealer and has represented to us that it acquired the securities being offered hereby in the ordinary course of business and that, at the time it acquired such securities, it did not have any agreements or understandings, directly or indirectly, with any person to distribute such securities.
- (34) Includes 21,244 shares issuable upon the exercise of warrants. ThinkEquity Partners LLC is a registered broker-dealer and has represented to us that it acquired the securities being offered hereby in the ordinary course of businesses and that, at the time it acquired such securities, it did not have any agreements or understandings, directly or indirectly, with any person to distribute such securities.
- (35) Mr. McInerney is a member of the Company's Board of Directors.
- (36) Mr. Knox previously served as Treasurer of Ziopharm, Inc., the Company's predecessor, from September 2003 until March 2005. Mr. Knox is affiliated with Paramount BioCapital, Inc., a registered broker-dealer, serving as its Chief Financial Officer. Mr. Knox has represented to us that he acquired the securities being offered hereby in the ordinary course of business and that, at the time he acquired the securities he did not have, any agreements, plans or understandings, directly or indirectly, with any person to distribute the securities being offered hereby.
- (37) Dr. Rosenwald is affiliated with Paramount BioCapital, Inc., a registered broker-dealer. Dr. Rosenwald has represented to us that he acquired the securities being offered hereby in the ordinary course of business and that, at the time he acquired the securities he did not have, any agreements, plans or understandings, directly or indirectly, with any person to distribute the securities being offered hereby.
- (38) Excludes any shares which may be held by certain trusts for the benefit of Dr. Rosenwald and his family for which Dr. Rosenwald disclaims beneficial ownership. Includes 513,464 shares issuable upon the exercise of warrants granted to Dr. Rosenwald and 62,621 shares issuable upon the exercise of warrants granted to Paramount BioCapital Investments, LLC, of which Dr. Rosenwald is the managing member, both such warrants are currently exercisable or will become exercisable within the next 60 days. Also includes 563,296 shares that Dr. Rosenwald has the right to acquire from existing stockholders under certain circumstances pursuant to the terms of pledge agreements between Dr. Rosenwald and such stockholders.

### PLAN OF DISTRIBUTION

We are registering the shares of Common Stock issued to the selling stockholders and issuable upon exercise of the warrants to permit the resale of these shares of Common Stock by the holders of the shares of Common Stock and warrants from time to time after the date of this prospectus. We will not receive any of the proceeds from the sale by the selling stockholders of the shares of Common Stock. We will bear all fees and expenses incident to our obligation to register the shares of Common Stock.

The selling stockholders, which as used herein includes donees, pledgees, transferees or other successors-in-interest selling shares of Common Stock or interests in shares of Common Stock received after the date of this prospectus from a selling stockholder as a gift, pledge, partnership distribution or other transfer, may sell all or a portion of the shares of Common Stock beneficially owned by them and offered hereby from time to time directly or through one or more underwriters, broker-dealers or agents. If the shares of Common Stock are sold through underwriters or broker-dealers, the selling stockholders will be responsible for underwriting discounts or commissions or agent's commissions. The shares of Common Stock may be sold in one or more transactions at fixed prices, at prevailing market prices at the time of the sale, at varying prices determined at the time of sale, or at negotiated prices. These sales may be effected in transactions, which may involve crosses or block transactions. To the extent any of the selling stockholders gift, pledge or otherwise transfer the shares offered hereby, such transferees may offer and sell the shares from time to time under this prospectus, provided that this prospectus has been amended under Rule 424(b)(3) or other applicable provision of the Securities Act to include the name of such transferee in the list of selling stockholders under this prospectus. The selling stockholders may use any one or more of the following methods when selling shares:

- on any national securities exchange or quotation service on which the securities may be listed or quoted at the time of sale;
- in the over-the-counter market;
- in transactions otherwise than on these exchanges or systems or in the over-the-counter market;
- · through the writing of options, whether such options are listed on an options exchange or otherwise;
- · ordinary brokerage transactions and transactions in which the broker-dealer solicits purchasers;
- block trades in which the broker-dealer will attempt to sell the shares as agent but may position and resell a portion of the block as principal to facilitate the transaction;
- · purchases by a broker-dealer as principal and resale by the broker-dealer for its account;
- · an exchange distribution in accordance with the rules of the applicable exchange;
- privately negotiated transactions;
- settlement of short sales entered into after the effective date of the registration statement of which this prospectus is a part;
- · broker-dealers may agree with the selling securityholders to sell a specified number of such shares at a stipulated price per share;
- · a combination of any such methods of sale; and
- · any other method permitted pursuant to applicable law.

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



Broker-dealers engaged by the selling stockholders may arrange for other brokers-dealers to participate in sales. If the selling stockholders effect such transactions by selling shares of Common Stock to or through underwriters, broker-dealers or agents, such underwriters, broker-dealers or agents may receive commissions in the form of discounts, concessions or commissions from the selling stockholders or commissions from purchasers of the shares of Common Stock for whom they may act as agent or to whom they may sell as principal. Such commissions will be in amounts to be negotiated, but, except as set forth in a supplement to this Prospectus, in the case of an agency transaction will not be in excess of a customary brokerage commission in compliance with NASD Rule 2440; and in the case of a principal transaction a markup or markdown in compliance with NASD IM-2440.

In connection with sales of the shares of Common Stock or otherwise, the selling stockholders may enter into hedging transactions with broker-dealers or other financial institutions, which may in turn engage in short sales of the shares of Common Stock in the course of hedging in positions they assume. The selling stockholders may also sell shares of Common Stock short and if such short sale shall take place after the date that this Registration Statement is declared effective by the Commission, the selling stockholders may deliver shares of Common Stock covered by this prospectus to close out short positions and to return borrowed shares in connection with such short sales. The selling stockholders may also loan or pledge shares of Common Stock to broker-dealers that in turn may sell such shares. The selling stockholders may also enter into option or other transactions with broker-dealers or other financial institutions or the creation of one or more derivative securities which require the delivery to such broker-dealer or other financial institution of shares offered by this prospectus, which shares such broker-dealer or other financial institution may resell pursuant to this prospectus (as supplemented or amended to reflect such transaction).

The selling stockholders may pledge or grant a security interest in some or all of the warrants or shares of Common Stock owned by them and, if they default in the performance of their secured obligations, the pledgees or secured parties may offer and sell the shares of Common Stock from time to time pursuant to this prospectus or any amendment to this prospectus under Rule 424(b)(3) or other applicable provision of the Securities Act of 1933, as amended, amending, if necessary, the list of selling stockholders to include the pledgee, transferee or other successors in interest as selling stockholders under this prospectus. The selling stockholders also may transfer and donate the shares of Common Stock in other circumstances in which case the transferees, donees, pledgees or other successors in interest will be the selling beneficial owners for purposes of this prospectus.

The selling stockholders participating in the distribution of the shares of Common Stock may, and any broker-dealers participating in the distribution of the shares of Common Stock will, be deemed to be "underwriters" within the meaning of the Securities Act, and any commission paid, or any discounts or concessions allowed to, any such broker-dealer may be deemed to be underwriting commissions or discounts under the Securities Act. At the time a particular offering of the shares of Common Stock is made, a prospectus supplement, if required, will be distributed which will set forth (i) the name of each such selling stockholder and of the participating broker-dealer(s), (ii) the number of shares involved, (iii) the price at which such the shares of Common Stock were sold, (iv) the commissions paid or discounts or concessions allowed to such broker-dealer(s), where applicable, (v) that such broker-dealer(s) did not conduct any investigation to verify the information set out or incorporated by reference in this prospectus, and (vi) other facts material to the transaction. In no event shall any broker-dealer receive fees, commission and markups which, in the aggregate, would exceed eight percent (8%). In addition, upon the Company being notified in writing by a Selling Stockholder that a donee or pledgee intends to sell more than 500 shares of Common Stock, a supplement to this prospectus will be filed if then required in accordance with applicable securities law.

Under the securities laws of some states, the shares of Common Stock may be sold in such states only through registered or licensed brokers or dealers. In addition, in some states the shares of Common Stock may not be sold unless such shares have been registered or qualified for sale in such state or an exemption from registration or qualification is available and is complied with.

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

We have advised each selling stockholder that it may not use shares registered on the registration statement of which this prospectus is a part to cover short sales of common stock made prior to the date on which the registration statement shall have been declared effective by the SEC. If a selling stockholder uses this prospectus for any sale of shares of our common stock, it will be subject to the prospectus delivery requirements of the Securities Act. The selling stockholders and any other person participating in such distribution will be subject to applicable provisions of the Securities Exchange Act of 1934, as amended, and the rules and regulations thereunder, including, without limitation, Regulation M of the Exchange Act, which may limit the timing of purchases and sales of any of the shares of Common Stock by the selling stockholders and any other participating person. Regulation M may also restrict the ability of any person engaged in the distribution of the shares of Common Stock to engage in market-making activities with respect to the shares of Common Stock. All of the foregoing may affect the marketability of the shares of Common Stock and the ability of any person or entity to engage in market-making activities with respect to the shares of Common Stock.

We will pay all expenses of the registration of the shares of Common Stock pursuant to the registration rights agreement, including, without limitation, Securities and Exchange Commission filing fees and expenses of compliance with state securities or "blue sky" laws; *provided, however*, that a selling stockholder will pay all underwriting discounts and selling commissions, if any and any related legal expenses incurred by it. We will indemnify the selling stockholders against liabilities, including some liabilities under the Securities Act, in accordance with the registration rights agreements, or the selling stockholders will be entitled to contribution. We may be indemnified by the selling stockholder specifically for use in this prospectus, in accordance with the related registration rights agreements, or we may be entitled to contribution.

### **Shares Eligible For Future Sale**

Upon completion of this offering and assuming the issuance of all of the shares covered by this prospectus that are issuable upon the exercise of outstanding warrants, there will be 22,542,265 shares of our common stock issued and outstanding. The shares purchased in this offering will be freely tradable without registration or other restriction under the Securities Act, except for any shares purchased by an "affiliate" of our Company (as defined under the Securities Act).

Our currently outstanding shares that were issued in reliance upon the "private placement" exemptions provided by the Securities Act include the 6,967,941 outstanding shares issued in connection with our September 2005 merger transaction with ZIOPHARM, Inc., the 7,991,392 shares issued in our May 3, 2006 private placement (the "2006 Offering") and the 5,910,049 shares issued in our February 23, 2007 private placement (the "2007 Offering"). These shares are deemed "restricted securities" within the meaning of Rule 144. Restricted securities may not be sold unless they are registered under the Securities Act or are sold pursuant to an applicable exemption from registration, including an exemption under Rule 144. In general, under Rule 144, any person (or persons whose shares are aggregated) including persons deemed to be affiliates, whose restricted securities have been fully paid for and held for at least one year from the later of the date of issuance by us or acquisition from an affiliate, may sell such securities in broker's transactions or directly to market makers, provided that the number of shares sold in any three-month period may not exceed the greater of one percent of the then-outstanding shares of our common stock or the average weekly trading volume of our shares of common stock in the over-the-counter market during the four calendar weeks preceding the sale. Sales under Rule 144 are also subject to certain notice requirements and the availability of current public information about our Company. After two years have elapsed from the later of the issuance of restricted securities by us or their acquisition from an affiliate, persons who are not affiliates under the rule may sell such securities without any limitation. Assuming that all of the other requirements of Rule 144 are then satisfied: (i) the 6,967,941 restricted shares of our common stock that were issued in connection with the Merger will first be eligible for resale without registration in September 2007; (ii) the 7,991,392 restricted shares of our common stock that were issued in the 2006 Offering will first be eligible for resale without registration in May 2008; and (iii) 5,910,049 restricted shares of our common stock that were issued in the 2007 Offering will first be eligible for resale without registration in February 2009.

Following the date of this prospectus, we cannot predict the effect, if any, that sales of our common stock or the availability of our common stock for sale will have on the market price prevailing from time to time. Nevertheless, sales by existing stockholders of substantial amounts of our common stock could adversely affect prevailing market prices for our stock.

# DISCLOSURE OF COMMISSION POSITION ON INDEMNIFICATION FOR SECURITIES ACT LIABILITIES

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

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

### ABOUT THIS PROSPECTUS

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

### WHERE YOU CAN FIND MORE INFORMATION

Before you decide whether to invest in our common stock, you should read this prospectus and the information we otherwise file with the Securities and Exchange Commission, or the SEC. We are a reporting company and file annual, quarterly and current reports, proxy statements and other information with the SEC. You may read and copy these reports, proxy statements and other information at the SEC's public reference room at 100 F. Street, N.E., Washington, D.C. 20549 or at the SEC's other public reference facilities. Please call the SEC at 1-800-SEC-0330 for more information about the operation of the public reference rooms. You can request copies of these documents by writing to the SEC and paying a fee for the copying costs. In addition, the SEC maintains an Internet site at <a href="http://www.sec.gov">http://www.sec.gov</a> that contains reports, proxy and information statements and other information regarding issuers that file electronically with the SEC. Our SEC filings are available on the SEC's an Internet site.

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

We incorporate by reference the documents listed below and any future filings we will make with the SEC under Section 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934, as amended, or the Exchange Act (other than any Current on Reports on Form 8-K filed under Item 12):

- Annual Report on Form 10-KSB for the fiscal year ended December 31, 2006, filed on February 13, 2007;
- Items 9 through 12 of the Annual Report on Form 10-KSB for the fiscal year ended December 31, 2005, filed on March 20, 2006 (including the information incorporated therein by reference to the definitive proxy statement filed March 20, 2006);

- · Current Reports on Form 8-K filed on February 16, 2007 and February 26, 2007, respectively; and
- Registration Statement on Form SB-2 filed November 14, 2005, as amended by Post-effective Amendment No. 1 to Form SB-2 filed April 3, 2006, containing the description of capital stock as set forth in the section entitled "Description of Capital Stock," as such description is amended in the section entitled "Description of Capital Stock," in Prospectus Supplement No. 1 filed April 26, 2006 pursuant to Rule 424(b) promulgated under the Securities Act of 1933, as amended.

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

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

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

#### VALIDITY OF COMMON STOCK

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

### EXPERTS

The financial statements of ZIOPHARM Oncology, Inc. as of December 31, 2006 and 2005, and for each of the years in the three year period then ended and the period from inception (September 9, 2003) through December 31, 2006 included in this prospectus, have been included herein in reliance on the report, dated February 6, 2007, of Vitale Caturano & Company, Ltd., independent registered public accounting firm, given on the authority of that firm as experts in auditing and accounting. 7,269,366 Shares

**Common Stock** 



ZIOPHARM Oncology, Inc.

PROSPECTUS

March 26, 2007