

ZIOPHARM ONCOLOGY INC  
Form 424B3  
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File No. 333-129680

**ZIOPHARM Oncology, Inc.**

**7,140,702 Shares**

**Common Stock**

The selling stockholders identified on pages 15-20 of this prospectus are offering on a resale basis a total of 7,140,702 shares of our common stock, of which 482,407 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 quoted on the Over-the-Counter Bulletin Board under the symbol "ZIOP." On June 26, 2006, the last sale price for our common stock as reported on the OTC Bulletin Board was \$5.20.

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

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**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 July 6, 2006.

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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 management and advisors are focused on licensing and developing proprietary drug candidate families that are related to cancer therapeutics on the market and where the application of new biology and our drug development expertise will facilitate clinical development, risk management and expedited regulatory approval. 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 one or more other companies with the requisite financial resources. Currently, we are in Phase I and Phase I/II studies for two product candidates known as ZIO-101 and ZIO-201. We currently intend to continue with clinical development of ZIO-101 for advanced myeloma and ZIO-201 for advanced sarcoma. 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.

· ZIO-101 is an organic arsenic compound covered by issued U.S. patents and applications internationally. A form of commercially available inorganic arsenic (arsenic trioxide (Trisenox®) or ATO) has been approved for the treatment of acute promyelocytic leukemia (APL), a precancerous condition, 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. Nevertheless, ATO has been shown to be toxic to the heart, liver and brain, limiting its use as an anti-cancer agent. Inorganic arsenic has also been shown to cause cancer of the skin and lung in humans. The toxicity of arsenic generally is correlated to its accumulation in organs and tissues. Our preclinical and Phase I studies to date have demonstrated that ZIO-101 (and organic arsenic in general) is considerably less toxic than inorganic arsenic, particularly with regard to heart toxicity. In vitro testing of ZIO-101 using the National Cancer Institute's human cancer cell panel detected activity against lung, colon, brain, melanoma, ovarian and kidney cancer. Moderate activity was detected against breast and prostate cancer. In addition to solid tumors, in vitro testing in both the National Cancer Institute's cancer cell panel and in vivo testing in a leukemia animal model demonstrated substantial activity against hematological cancers (cancers of the blood and blood-forming tissues) such as leukemia, lymphoma, myelodysplastic syndromes and multiple myeloma.

Phase I testing of ZIO-101 is ongoing with two safety and dose finding studies at the University of Texas M. D. Anderson Cancer Center. The Company has seen encouraging signs of clinical activity in both of these studies including impact on blood and bone marrow blast cells in patients with acute myelogenous leukemia (AML) and including one patient with metastatic renal cell carcinoma where metastases to the brain resolved. The Company recently initiated a phase I/II advanced multiple myeloma (SGL2001) study to be conducted in the U.S., Canada and Europe designed to determine maximum tolerated dose and to assess clinical activity in this specific indication. The Company expects to pursue registration in the U.S. for the treatment of advanced multiple myeloma with a potentially pivotal trial to begin in 2007.

· ZIO-201, or isophosphoramidate mustard (IPM), is a proprietary stabilized metabolite of ifosfamide that is also related to cyclophosphamide. A patent application for pharmaceutical composition has been filed.

Cyclophosphamide and ifosfamide are alkylating agents. The Company believes cyclophosphamide is the most widely used alkylating agent in cancer therapy and is used to treat breast cancer and non-Hodgkin's lymphoma. Ifosfamide has been shown to be effective in high dose by itself, or in combination in treating sarcoma and lymphoma. 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, IPM 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. Ifosfamide is metabolized to IPM. In addition to IPM, another metabolite of ifosfamide is acrolein, which is toxic to the kidneys and bladder. The presence of acrolein can mandate the administration of a protective agent called mesna, which is inconvenient and expensive. Chloroacetaldehyde is another metabolite of ifosfamide and 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 may avoid many of the toxicities of ifosfamide and cyclophosphamide without compromising efficacy. In addition to anticipated lower toxicity, ZIO-201 (and without the coadministration of mesna) may have other advantages over ifosfamide. In preclinical studies, ZIO-201 likely cross-links DNA differently than ifosfamide or cyclophosphamide metabolites, resulting in a different activity profile. Moreover, in some instances ZIO-201 appears to show activity in ifosfamide- and/or cyclophosphamide-resistant cancer cells.

Phase I testing of ZIO-201 is ongoing at two sites in the U.S. (Karmanos Cancer Center at Wayne State University in Detroit and Premiere Oncology in Los Angeles). IPM has been administered without the “uroprotectant” mesna and the toxicities associated with acrolein and chloroacetaldehyde have not been observed. Kidney toxicity seen with ifosfamide has occurred in the higher dose cohorts. One patient with advanced mesothelioma had stable disease following 18 cycles of therapy with ZIO-201 as a single agent. The Company recently initiated a phase I/II trial in advanced sarcoma at the University of Texas M. D. Anderson Cancer Center (the “MDACC”). Additional studies in patients with advanced sarcoma will begin shortly in the U.S. and plans for a phase I/II study in pediatric sarcoma are well advanced. The Company expects to pursue registration in the U.S. for the treatment of advanced sarcoma with a potentially pivotal trial to begin in 2007.

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 executive offices are located at 1180 Avenue of the Americas, 19th Floor, New York, NY 10036, and our telephone number is (646) 214-0700. Our internet site is [www.ziopharm.com](http://www.ziopharm.com). None of the information on our internet site is part of this prospectus.

### Risk Factors

As with most pharmaceutical product candidates, the development of ZIO-101 and ZOI-201 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 shares offered by this prospectus were previously covered by our prospectus dated April 14, 2006, as supplemented to date, which originally covered the resale of an aggregate of 7,462,095 shares of our common stock by the selling stockholders identified in such prospectus, of which 482,407 shares are issuable upon the exercise of outstanding warrants. The selling stockholders identified on pages 15-20 of this prospectus are offering an aggregate of 7,140,702 shares of our common stock, including 482,407 shares issuable upon the exercise of outstanding warrants. The shares offered by such selling stockholders reflect those shares of our common stock remaining unsold by the selling stockholders identified in our April 14, 2006 prospectus.

Common stock offered	7,140,702 shares
	15,264,248
Common stock outstanding before the offering <sup>(1)</sup>	shares
	15,746,655
Common stock outstanding after the offering <sup>(1)(2)</sup>	shares
Common Stock OTC Bulletin Board symbol	ZIOP

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(1) Based on the number of shares outstanding as of June 26, 2006, not including shares issuable upon exercise of various warrants and options to purchase common stock.

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

## **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:*

***We currently have no product revenues and will need to raise additional capital to operate our business.***

To date, we have generated no product revenues. 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. Currently, our only product candidates are ZIO-101 (organic arsenic) and ZIO-201 (isophosphoramidate mustard), and they are not approved by the FDA for sale.

***We will need to seek additional sources of financing which may not be available on favorable terms, if at all.***

As of March 31, 2006, we had incurred approximately \$18.6 million of cumulative net losses and had approximately \$5.6 million of cash, cash equivalents and short-term investments. Our consolidated financial statements as of December 31, 2005 were prepared under the assumption that we will continue as a going concern for the year ending December 31, 2006. The Company's independent registered public accounting firm, Vitale, Caturano & Company, Ltd., issued a report dated March 9, 2006 that included an explanatory paragraph referring to our significant operating losses and expressing substantial doubt in its ability to continue as a going concern (See Note (1) in the Notes to Consolidated Financial Statements) without additional capital becoming available. As of May 3, 2006, and after receiving the proceeds from our May 3, 2006 offering of common stock and warrants, we had approximately \$39.2 million of cash, cash equivalents and short-term investments. Although we expect that the proceeds from this offering will provide us with sufficient cash to fund our operations into the first quarter of 2008, our ability to continue as a going concern beyond that time is dependent upon our ability to obtain additional equity or debt financing, attain further operating efficiencies and, ultimately, to generate revenue. Our financial statements do not include any adjustments that might result from the outcome of this uncertainty. Although we expect our cash on-hand to fund our operations into the first 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. 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. Any additional sources of financing will likely involve the issuance of our equity securities, which will have a dilutive effect on our existing stockholders.

***We are not currently profitable and may never become profitable.***

We have a history of losses and expect to incur substantial losses and negative operating cash flow for the foreseeable future, and we may never achieve or maintain profitability. Even if we succeed in developing and commercializing one or more product candidates, we expect to incur substantial losses for the foreseeable future and may never become profitable. We expect also 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;
- Seek regulatory approvals for product candidates;
- Implement additional internal systems and infrastructure; and
- Hire additional personnel and expand office space.

We also expect to experience negative cash flow for the foreseeable future as we fund our operating losses and capital expenditures. This may result in a negative impact on the value of our common stock.

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



Prior to the Merger, ZIOPHARM, Inc. was 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 and ZIO-201, and manufacturing ZIO-101 and ZIO- 201. 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 may not obtain the necessary U.S. or worldwide regulatory approvals to commercialize any product candidate.***

We may not be able to obtain the approvals necessary to commercialize our product candidates, ZIO-101 and ZIO-201, 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 preclinical studies, as well as human tests, which are referred to as clinical trials. Satisfaction of the FDA's regulatory requirements typically takes many years, depending upon the type, complexity and novelty of the product candidate, and will require substantial resources for research, development and testing. We cannot predict whether our research, development, and clinical approaches will result in drugs that the FDA 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 and ZIO-201. 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, and we cannot be certain when we will be able to file an NDA with the FDA.***

Our product candidates, ZIO-101 and ZIO-201, 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.

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***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;
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Availability of reimbursement for our products from government or other healthcare payers; and

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- 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.

***Our drug development program materially depends upon third-party researchers who are outside 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.

***We rely exclusively on third parties to formulate and manufacture our product candidates.***

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 commercial scale 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.

- 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.

***We do not have experience selling, marketing or distributing products and we have no internal capability to do so.***

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 affect 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 such efforts will be successful. In addition, there can also be no assurance that we will be able to market and sell our products in the United States or overseas.

***If we 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 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.

***If we infringe the rights of third parties we could be prevented from selling products, forced to pay damages, and defend against litigation.***

If our products, methods, processes or other technologies infringe the proprietary rights of other parties, we could incur substantial costs and we may have to:

- Obtain licenses, which may not be available on commercially reasonable terms, if at all;
- Abandon an infringing drug candidate;
- Redesign our products or processes to avoid infringement;
- Stop using the subject matter claimed in the patents held by others;
- Pay damages; or
- Defend litigation or administrative proceedings which may be costly whether we win or lose, and which could result in a substantial diversion of our valuable management resources.

***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.

Significant uncertainty exists as to the reimbursement status of newly approved healthcare products. Healthcare payers, including Medicare, are challenging the prices charged for medical products and services. Government and other healthcare payers increasingly attempt to contain healthcare costs by limiting both coverage and the level of reimbursement for drugs. Even if our product candidates are approved by the FDA, insurance coverage may not be available, and reimbursement levels may be inadequate, to cover our drugs. If government and other healthcare payers do not provide adequate coverage and reimbursement levels for our products, once approved, market acceptance of such products could be reduced.

***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 our principal scientific, regulatory and medical advisors. We do not have “key person” life insurance policies on any of our officers. 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.

***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 testing, clinical research and testing, government regulation, formulation and manufacturing, as well as 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. 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.

***There are certain interlocking relationships among us and certain affiliates of a significant stockholder of ours, which may present potential conflicts of interest.***

Lindsay A. Rosenwald, M.D., who may be deemed to beneficially own approximately 9.9% of our common stock as of June 26, 2006, is Chairman and Chief Executive Officer of Paramount BioCapital, Inc., an investment banking firm that served as a co-placement agent in connection with our May 2006 financing. Paramount BioCapital also served as placement agent in connection with a private placement of ZIOPHARM, Inc.’s Series A Convertible Preferred Stock that was completed in May 2005 and served as a finder in connection with our option and research agreements with Southern Research Institute. We paid fees and issued securities to Paramount BioCapital or its designees in connection with these transactions and Paramount BioCapital currently has a right of first refusal to act as the placement agent for

the private sale of our securities until May 31, 2008. Dr. Michael Weiser and Timothy McInerney, each of whom is a member of our board of directors, are also full-time employees of Paramount BioCapital.

Paramount BioCapital, Dr. Rosenwald, Dr. Weiser, and Mr. McInerney are not obligated pursuant to any agreement or understanding with us to make any additional products or technologies available to us, nor can there be any assurance that any biomedical or pharmaceutical products or technologies identified in the future by such parties will be made available to us. In addition, certain of our current officers and directors, as well as officers or directors that may be hereafter appointed, may from time to time serve as officers or directors of other biopharmaceutical or biotechnology companies. There can be no assurance that such other companies will not have interests in conflict with our own.

***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.

***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 lack of segregation of duties. Furthermore, management is aware that many of our currently existing internal controls are undocumented. Our management will be working to document such internal controls over the coming year. 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.

***Our common stock trades only in an illiquid trading market.***

Trading of our common stock is conducted on the Over-The-Counter Bulletin Board (“OTCBB”). This has an adverse effect on the liquidity of our common stock, not only in terms of the number of shares that can be bought and sold at a given price, but also through delays in the timing of transactions and reduction in security analysts’ and the media’s coverage of our Company and its common stock. This may result in lower prices for our common stock than might otherwise be obtained and could also result in a larger spread between the bid and asked prices for our common stock.

***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 the Company’s 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 it is a “penny stock,” you may have difficulty selling shares of our common stock.***

Our common stock is a “penny stock” and is therefore subject to the requirements of Rule 15c-9 under the Securities and Exchange Act of 1934. Under this rule, broker-dealers who sell penny stocks must provide purchasers of these

stocks with a standardized risk-disclosure document prepared by the Securities and Exchange Commission. Under applicable regulations, our common stock will generally remain a “penny stock” until and for such time as it meets certain per share price requirements (as determined in accordance with SEC regulations), or until we meet certain net asset or revenue thresholds.

The penny stock rules severely limit the liquidity of securities in the secondary market, and many brokers choose not to participate in penny stock transactions. As a result, there is generally less trading in penny stocks. If you become a holder of our common stock, 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.

*We have never paid dividends and do not intend to do so for the foreseeable future.*

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 7,140,702 shares of our common stock, including shares issuable upon the exercise of warrants. This offering includes 6,517,124 shares of our common stock issued to the former stockholders of ZIOPHARM, Inc. in connection with our September 2005 merger with that company, 482,407 shares of our common stock issuable upon the exercise of warrants held by such former ZIOPHARM, Inc. stockholders at the time of the merger, 83,348 shares of our common stock issued to a previous EasyWeb Inc. stockholder upon the exercise of a stock option, and 57,723 shares of EasyWeb, Inc. which were outstanding prior to the merger.

The following table sets forth the number of shares of the common stock owned by the selling stockholders as of June 14, 2006, and after giving effect to this offering.

<b>Selling Stockholder</b>	<b>Shares Beneficially Owned Before Offering (1)</b>	<b>Number of Outstanding Shares Offered by Selling Stockholder</b>	<b>Number of Shares Offered by Selling Stockholder upon Exercise of Certain Warrants</b>	<b>Percentage Beneficial Ownership After Offering (2)</b>
335 MAD LLC (f/k/a/ Beck Technologies LLC)	3,757	3,757	0	--
Aaron Rollins	3,036	3,036	0	-
Aaron Speisman	1,566	1,566	0	--
Al Hoff	100	100	0	--
Alan Clingman	1,252	1,252	0	--
Alan H. Auerbach	5,798	5,798	0	--
Alan J. Young	4,000	4,000	0	--
Albert J. Zirkelbach	50	50	0	--
Alfred Abraham	4,639	4,639	0	--
Allen R Goldstone	25	25	0	--
Allison Robbins	1,518	1,518	0	-
Anderson J Henshaw C. Eugene Gronning	100	100	0	--
Andrew H. Sabreen and Carol Sabreen JTWROS	11,596	11,596	0	--
Andrew W. Albstein and Carolyn Albstein JTWROS	37,232	23,193	0	--
Andrew W. Schonzeit	13,472	5,049	0	--
Anil Chenthitta	3,036	3,036	0	-
Anthony G. Polak "S"	5,798	5,798	0	--
Anthony J. Gerace	11,597	11,597	0	--
Anthony J. Ottavio	20,947	12,524	0	--
Associate Capital Consulting Inc.	50	50	0	--
Atlas Equity I, Ltd.	695,796	695,796	0	--
B Kathleen Goldstone	25	25	0	--
Balanced Investment, LLC	46,386	46,386	0	--
Barbara Petrinsky	442	442	0	--
Barry Lind Revocable Trust	38,386	38,386	0	--
Barry P. McIntosh	5,798	5,798	0	--

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Baruch Z. Halberstam	5,798	5,798	0	--
Basil Christakos	8,678	6,072	0	--
Benito Bucay	11,596	11,596	0	--
Benjamin Feinswog Trust	3,757	3,757	0	--
Bernard Gross	10,285	1,518	8,767	--
Bernard Wachsman	5,798	5,798	0	--
Black Marlen Inc	100	100	0	--

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Brad Henshaw C. Eugene Gronning	100	100	0	--
Brad Rhodes	200	200	0	--
Brent Henshaw	7,959	7,959	0	--
Brino Investment Ltd.	5,798	5,798	0	--
Bryant Kligerman	100	100	0	--
Carl S. Sorenson	11,597	11,597	0	--
Carlene Smith	25	25	0	--
Carolyn N. Taylor	3,506	3,506	0	--
Carolyn P. Dietrich	6,006	6,006	0	--
Carucci Family Partners	73,828	34,789	0	*
Charles Earl Cartmill	11,596	11,596	0	--
Charles Schwab & Co. Inc.	50	50	0	--
Chase Financing, Inc.	83,348	83,348	0	-
Claudia Donat	3,036	3,036	0	-
Concordia Partners L.P.	175,341	175,341	0	--
Cooper A. McIntosh, MD	22,827	11,596	0	*
Coqui Capital Partners	57,983	57,983	0	--
Craig M Blake	50	50	0	--
Curtis M McQueen	50	50	0	--
Daniel J. Kevles and Betty Ann Kevles JTWROS	8,117	8,117	0	--
Daniel Krieger	5,798	5,798	0	--
Danielle Flatly	1,518	1,518	0	-
Darrell J Brunken	25	25	0	--
David Butera	60,723	60,723	0	-
David C. Olson	4,586	4,586	0	--
David G. Pudelsky and Nancy H. Pudelsky JTWROS	10,019	10,019	0	--
David J. Bershad	3,131	3,131	0	--
David Nussbaum	3,036	3,036	0	-
David P. Luci	2,319	2,319	0	--
David Tanen	12,144	12,144	0	-
Dean Glasser	3,757	3,757	0	--
Delaware Charter Guarantee & Trust Co. FBO Howard M. Tanning MD IRA	25,048	25,048	0	--
Delaware Charter Guarantee Trust FBO Mark Berg IRA	57,612	57,612	0	--
Delaware Charter Guarantee Trust FBO Richard S. Simms II Keogh Plan	3,478	3,478	0	--
Delores Ferraro	1,518	1,518	0	-
Demitrios Marras	1,518	1,518	0	-
Denise Mormile-Liglino	1,252	0	1,252	--
Dennis F. Steadman	5,798	5,798	0	--
Derek J. Zappa	100	100	0	--
Domaco Venture Capital Fund	5,798	5,798	0	--
Don F. Sims	50	50	0	--
Donna Kash & Peter Kash JT TEN	5,010	5,010	0	--
Donna Lozito	6,072	6,072	0	-
Douglas A Wilkerson & Leola A Wilkerson JTEN	25	25	0	--
Doyle S Elliott	25	25	0	--



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Edmund A. Debler	17,033	17,033	0	--
Edward W Bellarose	100	100	0	--
Edwin A. Buckham and Wendy F. Buckham, JTWROS	11,596	11,596	0	--
Elbert Chu	1,822	1,822	0	-
Elena Ridloff	5,465	5,465	0	-
Eli Jaconson	23,194	23,194	0	--
Elizabeth Maas	5,798	5,798	0	--
Elizabeth Marrero	1,518	1,518	0	-
Elizabeth R. Moore	5,798	5,798	0	--
Ennio DePianto	6,011	6,011	0	--
Eric Lee	3,036	3,036	0	-
Eric Reed	5,009	5,009	0	--
Everest Capital (f/k/a Four Brothers Investment Holding)	12,524	12,524	0	--
Fabio Migliaccio	2,504	0	2,504	--
Fae Moore	5,798	5,798	0	--
Far Ventures	10,019	10,019	0	--
Fiserv Securities, Inc. A/C/F Anthony G. Polak Std. IRA	5,798	5,798	0	--
Fiserv Securities, Inc. A/C/F Jack Polar IRA	5,798	5,798	0	--
Fiserv Securities, Inc. A/C/F Ronald M. Lazar, STD IRA	5,798	5,798	0	--
Frank Calcutta	12,524	12,524	0	--
Future Global Holding, Inc.	626	626	0	--
Gabriel Pilalao	1,518	1,518	0	--
Gary J. Strauss	23,193	23,194	0	--
Gary Mendenhall	25	25	0	--
Gavin Kent	5,798	5,798	0	--
Gitel Family Partnership, LP	23,193	23,193	0	--
Gregory J. Dovolis	10,019	10,019	0	--
Harris Lydon	58,931	0	22,349	*
Harry Newton and Susan Newton JTWROS	38,591	17,534	0	*
Harvey Levin	25	25	0	--
Harvey Lustig and Ronnie Lustig JTWROS	5,009	5,009	0	--
Henry and Monica Millin	1,252	1,252	0	--
Hill Blalock, Jr.	23,195	23,195	0	--
Howard Sorkin	23,193	23,193	0	--
Isaac R. Dweck	23,193	23,193	0	--
Issac M. Dabah	10,019	10,019	0	--
Ivy Scheinholz Revocable Trust U/A Dated 1/26/05	5,009	5,009	0	--
Jack B. Petersen	5,798	5,798	0	--
James C. Shepler and Diana B. Shepler JTWROS	6,957	6,957	0	--
James H Swalwell & Judith A Swalwell JTEN	50	50	0	--
James J Trainor	125	125	0	--
Jamie Cabibihan	1,768	1,768	0	-
Janis H. Camp	5,798	5,798	0	--
Jason Stein	83,445	83,445	0	-
Jay Lobell	94,252	59,156	0	*

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Jeana Sommers	1,808	1,518	290	--
Jeff Rodriguez	25	25	0	--
Jeffrey Kraws & Patricia Kraws	5,798	5,798	0	--
Jeffrey Myers	1,692	1,692	0	--
Jeffrey Serbin	91,035	91,035	0	-
Jennifer McNealy	5,465	5,465	0	-
Jerrold Abrahams	6,957	6,957	0	--
Jill Meleski	19,674	3,036	16,638	--

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Jillian Hoffman	7,590	7,590	0	-
Joe L. Key and Mary Lynn Key JTWROS	1,001	1,001	0	--
Joel Braun	5,798	5,798	0	--
Johanna Guttman & Robert Herskowitz JTEN	10,750	10,750	0	--
John and Debbra Landsberger Family Trust	12,524	12,524	0	--
John Best	1,822	1,822	0	-
John Cipriano	5,465	5,465	0	-
John Cleaver & Karen Cleaver JTEN	100	100	0	--
John Knox	19,470	9,108	0	*
John O. Dunkin	6,011	6,012	0	--
John Papadimitropoulos	3,036	3,036	0	-
Joseph Friedman Trust	1,252	1,252	0	--
Joseph J. Vale	115,965	115,966	0	--
Joseph Sorbara	6,480	0	6,480	--
Joseph Strassman and Barbara Strassman	6,957	6,957	0	--
Joshua Kazam and Joia Kazam JTWROS	12,145	12,145	0	-
Judah Schorr	34,790	34,790	0	--
Kanter Family Foundation	1,878	1,878	0	--
Karl Ruggeberg	9,368	1,518	7,850	--
Kathleen Fogerty	1,518	1,518	0	-
Keith Rubenstein	5,798	5,798	0	--
Kinder Investments L.P.	34,789	34,789	0	--
Klaus Kretschmer	74,667	46,590	0	*
Kristen Plonisch	1,518	1,518	0	-
Kyle Kuhn	6,072	6,072	0	-
Lamar F Schild	500	500	0	--
Lawrence Alpert	500	500	0	--
Laya Perlysky 2003 Grantor Retained Annuity Trust	23,193	23,193	0	--
Lillian Hahn	3,131	3,131	0	--
Lind Family Investments LP	5,117	5,117	0	--
Lindsay A. Rosenwald	1,573,794(3)	476,678	221,011	5.46%
Louis R. Reif	22,543	22,543	0	--
Louis Sanzo, Jr.	5,010	5,010	0	--
Louis Smookler	17,326	12,145	0	*
Lucile Slocum	10,019	10,019	0	--
Lyn C Wilkerson	30	30	0	--
Mario Pasquel and Begona Miranda JTWROS	23,254	16,235	0	*
Marion Birch	1,518	1,518	0	-
Mark J. Ahn	5,798	5,798	0	--
Mark Mazzer	6,262	6,262	0	--
Mark O. Thornton	8,370	8,370	0	-
Matador Investments Pte Ltd.	16,235	16,235	0	--
Mathew Meister c/o Beeman Holdings	25	25	0	--
Mega International Corporation	8,581	8,581	0	--
Mibars, LLC	1,214,456	1,214,456	0	-
Michael Blechman and Barry J. Lind, Tenants in Common	9,596	9,596	0	--
Michael Gundzik C. Eugene Gronning	100	100	0	--
Michael J Stallone	200	200	0	--

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Michael Luftman	5,798	5,798	0	--
Michael M Edmonds	100	100	0	--
Michael Mullen	13,534	0	13,534	--
Michael Rosenman	64,797	12,145	19,709	*
Michael S. Walsh	5,798	5,798	0	--
Michael Weiser	159,845	83,445	35,566	*
Michele Markowitz	5,798	5,798	0	--
Millennium Partners, L.P.	793,486	231,931	0	3.54%

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Morri L Namaste	100	100	0	--
Murry J. McCabe	104,541	34,789	0	*
National Financial Services LLC	25	25	0	--
National Investors Services Corp. FBO Stephen J. Nelson	23,193	23,193	0	--
Neel B. Ackerman and Martha N. Ackerman JTWROS	25,048	25,048	0	--
Neil Herskowitz	25,805	6,262	0	*
Neil J. Laird	6,011	6,011	0	--
Nicholas Ponzio	24,048	24,048	0	--
Nicole Berg	169,923	57,612	0	*
Nicole Netolicky	1,517	1,517	0	-
Nora O'Donoghue	5,798	5,798	0	--
NTP Partners	3,131	3,131	0	--
OZF Investments LLC	115,965	115,965	0	--
Paramount BioCapital, Inc.	62,621	0	62,621	--
Paul Bermanski and Barbara Bermanski JTWROS	11,596	11,596	0	--
Paul D. Newman and Judith E. Newman JTWROS	6,011	6,011	0	--
Paul F. Berlin	5,798	5,798	0	--
Paul J. Solit	14,221	5,798	0	*
Paul Sallwasser and Teri Sallwasser JTWROS	17,394	17,394	0	--
Pearl Capital LP (f/k/a Weisenberg Real Estate LP)	1,252	1,252	0	--
Peter Barber	3,288	3,036	0	-
Peter Kash	83,445	83,445	0	-
Phil Lifshitz	4,095	4,095	0	--
Philip J. Abdalla and Joyce V. Abdalla JTWROS	6,011	6,011	0	--
Praful Desai	5,009	5,009	0	--
Rachel Family Partnership	34,789	34,789	0	--
Ramsay Investments Pte. Ltd.	2,319	2,319	0	--
Rick J. Goad	10,019	10,019	0	--
Riverside Contracting LLC	25,805	12,524	0	*
RL Capital Partners, LP	11,597	11,597	0	--
Robert D. Millstone	3,479	0	3,479	--
Robert E Ohman	25	25	0	--
Robert Falk	1,252	1,252	0	--
Robert Guercio	7,514	7,514	0	--
Robert Herskowitz	1,875	1,875	0	--
Robert J. Sechan II	5,798	5,798	0	--
Robert J. Whetten	11,596	11,596	0	--
Robert J. Zappa	23,000	23,000	0	--
Robert Klein	1,252	1,252	0	--
Robert Masters	11,596	11,596	0	--
Robert McEntire	10,000	10,000	0	--
Robert Petrozzo	11,083	0	11,083	--
S. Alan Lisenby	25,048	25,048	0	--
Sandgrain Securities, Inc.	579	0	579	--
Sanford Schwartz	25	25	0	--
Scot Bryant	100	100	0	--

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Scott D. Whitaker	11,596	11,596	0	--
Scott Katzmann	65,760	9,108	19,709	*
Scott Shovea	50	50	0	--
Shea Ventures, LLC	23,193	23,193	0	--
Shoup Revocable Trust DTD April 29, 2003	11,597	11,597	0	--
Smithfield Fiduciary LLC	512,708	231,931	0	1.78%
Stephen C. Rabbitt	10,019	10,019	0	--
Stephen H. Lebovitz	1,001	1,001	0	--
Stephen N. Kitchens and Martha M. Kitchens JTWROS	11,193	11,193	0	--
Stephen Rocamboli	51,039	40,677	0	*
Steven A. Sherman	1,739	0	1,739	--
Steven Lisi	14,027	14,027	0	--
Steven Markowitz	6,480	0	6,480	--
Summit Financial Relations Inc.	11,314	11,314	0	--
Susan Schwartz	25	25	0	--
Suzanne Schiller	5,009	5,009	0	--
Suzette T. Seigel	5,798	5,798	0	--

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The Bahr Family Limited Partnership	11,596	11,596	0	--
The Henry H. Bahr QTIP Trust Dated 2/22/88	11,596	11,596	0	--
The Holding Company	4,383	4,383	0	--
The Lindsay A. Rosenwald 2000 Irrevocable Trust U/A dated 5/24/2000	231,931	231,931	0	--
The Lindsay Rosenwald 2000 Family Trust U/A dated 12/15/00	231,932	231,932	0	--
The University of Texas M.D. Anderson	250,487	250,487	0	--
Thomas B. Olson	5,000	5,000	0	--
Thomas M. Vickers	5,000	5,000	0	--
Thomas M. Vickers	5,250	5,250	0	--
Tim P. Cooper	4,634	4,634	0	--
Timothy McInerney	183,224	59,204	20,767	*
Timothy S Greufe	150	150	0	--
Timothy Shands	3,036	3,036	0	-
Tisu Investment Ltd.	17,394	17,394	0	--
Tokenhouse Trading Pte. Ltd.	46,386	46,386	0	--
Ursuline Co.	12,524	12,524	0	--
Valeo Partners, LLC	6,262	6,262	0	--
Vicki D E Barone	25	25	0	--
VLA LLP	50	50	0	--
Walter B. Martin and Paloma Munoz JTWROS	5,798	5,798	0	--
Waterspout Investments Pte Ltd	4,638	4,638	0	--
William Corcoran	12,145	12,145	0	-
William D. Cronin	100	100	0	--
William McCahey and Lisa Krivacka JTWROS	5,798	5,798	0	--
William R Going	25	25	0	--
William S. Silver and Elinor Silver JTWROS	6,011	6,011	0	--
Wolcot Capital, Inc.	24,048	24,048	0	--
Yitzhak Nissan	1,252	1,252	0	--
		6,658,295	482,407	

\*

Less than one percent.

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

(2) Assumes sales of all shares by the selling stockholders.

(3) Includes 563,296 shares that the selling stockholder has the right to acquire from existing stockholders under certain circumstances pursuant to pledge agreements between the selling stockholder and such existing stockholders.

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## PLAN OF DISTRIBUTION

We are registering the resale of certain shares of common stock offered by this prospectus on behalf of the selling stockholders. As used in this prospectus, the term “selling stockholders” include donees, pledges, transferees and other successors in interest selling shares received from the selling stockholders after the date of this prospectus, whether as a gift, pledge, partnership distribution or other form of transfer. All costs, expenses and fees in connection with the registration of the shares of common stock offered hereby will be borne by the Company. Brokerage commissions and similar selling expenses, if any, attributable to the sale of shares of common stock will be borne by the selling stockholders.

Sales of shares of common stock offered hereby may be effected by the selling stockholders from time to time in one or more types of transactions (which may include block transactions):

- 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;
- short sales;
- through the writing or settlement of options or other hedging transactions, whether through an options exchange or otherwise;
- broker-dealers may agree with the selling stockholders 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 effect sales of shares of common stock offered hereby at fixed prices, at prevailing market prices at the time of sale, at prices related to the prevailing market price, at varying prices determined at the time of sale, or at privately negotiated prices. Any of these transactions may or may not involve brokers or dealers. Any such broker-dealers may receive compensation in the form of discounts, concessions or commissions from the selling stockholders and/or the purchaser(s) of shares of common stock for whom those broker-dealers may act as agents or to whom they sell as principals, or both (which compensation as to a particular broker-dealer might be in excess of customary commissions). The selling stockholders have advised us that they have not entered into any agreements, understandings or arrangements with any underwriters or broker-dealers regarding the sale of their securities, nor is there any underwriter or coordinating broker acting in connection with the proposed sale of shares of common stock by the selling stockholders.

The selling stockholders may, from time to time, pledge or grant a security interest in some or all of the shares of common stock owned by them and registered hereby and, if any such selling stockholder defaults in the performance of its secured obligations, the pledgees or secured parties may offer and sell the shares of common stock, from time to time, under this prospectus, or under an amendment to this prospectus or other applicable provision of the Securities Act amending the list of selling stockholders to include the pledgee, transferee or other successors in interest as selling stockholders under this prospectus. The selling stockholders also may transfer the shares of common stock in other circumstances, in which case the transferees, pledgees or other successors in interest will be the selling beneficial owners for purposes of this prospectus.

In connection with the sale of our common stock or interests therein, 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 common stock in the course of hedging the positions they assume. The selling stockholders may also sell shares of our common stock short and deliver these securities to close out their short positions, or loan or pledge the common stock to broker-dealers that in turn may sell these securities. 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 aggregate proceeds to the selling stockholders from the sale of the common stock offered by them will be the purchase price of the common stock less discounts or commissions, if any. The selling stockholders reserve the right to accept and, together with their agents from time to time, to reject, in whole or in part, any proposed purchase of common stock to be made directly or through agents. We will not receive any of the proceeds from this offering.

The selling stockholders may also resell all or a portion of the shares in open market transactions in reliance upon Rule 144 under the Securities Act, provided that they meet the criteria and conform to the requirements of that rule.

The selling stockholders and any broker-dealers, agents or underwriters that participate with the selling stockholders in the distribution of the issued and outstanding shares of common stock or the shares of stock issuable upon the exercise of warrants may be deemed to be “underwriters” within the meaning of the Securities Act, in which event any commissions received by these broker-dealers, agents or underwriters and any profits realized by the selling stockholders on the resales of the securities may be deemed to be underwriting commissions or discounts under the Securities Act. If the selling stockholders are deemed to be underwriters, the selling stockholders may be subject to certain statutory and regulatory liabilities, including liabilities imposed pursuant to Section 11, 12 and 17 of the Securities Act and Rule 10b-5 under the Exchange Act.

To the extent required, the shares of our common stock to be sold, the name of the selling stockholders, the respective purchase prices and public offering prices, the names of any agents, dealer or underwriter, any applicable commissions or discounts with respect to a particular offer will be set forth in an accompanying prospectus supplement or, if appropriate, a post-effective amendment to the registration statement that includes this prospectus.

In order to comply with the securities laws of some states, if applicable, the common stock may be sold in these jurisdictions only through registered or licensed brokers or dealers. In addition, in some states the common stock may not be sold unless it has been registered or qualified for sale or an exemption from registration or qualification requirements is available and is complied with.

We have advised the selling stockholders that the anti-manipulation rules of Regulation M under the Exchange Act may apply to sales of shares in the market and to the activities of the selling stockholders and their affiliates. In addition, we will make copies of this prospectus (as it may be supplemented or amended from time to time) available to the selling stockholders for the purpose of satisfying the prospectus-delivery requirements of the Securities Act. The selling stockholders may indemnify any broker-dealer that participates in transactions involving the sale of the shares against certain liabilities, including liabilities arising under the Securities Act.

We are unable to predict with certainty the effect which sales of the shares of common stock offered by this prospectus might have upon our ability to raise additional capital. Nevertheless, it is possible that the resale of shares offered hereby could adversely affect the trading price of our common stock.

### **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 15,746,655 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, including the 6,967,941 outstanding shares issued in connection with our September 13, 2005 merger transaction with ZIOPHARM, Inc., and the 7,991,256 shares issued in connection with our May 3, 2006 private placement transaction 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, the 6,967,941 restricted shares of our common stock that were issued in connection with the September 13, 2005 merger transaction will first be eligible for resale without registration on September 13, 2006 and the 7,991,256 shares issued in our May 3, 2006 private placement transaction will first be eligible for resale without registration on May 3, 2007.

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 <http://www.sec.gov> 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, 2005, filed on March 20, 2006, as amended by Form 10-KSB/A filed on April 12, 2006;
- Quarterly Report on Form 10-QSB for the quarter ended March 31, 2006, filed on May 15, 2006;
- Current Reports on Form 8-K filed on April 26, 2006 and May 3, 2006, 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.

You may request a copy of these filings 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 and for the years ended December 31, 2005 and 2004 and for the period from September 9, 2003 (date of inception) to December 31, 2003, included in this prospectus, have been included herein in reliance on the report, dated March 9, 2006, of Vitale Caturano & Company, Ltd., independent registered public accounting firm, given on the authority of that firm as experts in auditing and

accounting.

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**7,140,702 Shares**

**Common Stock**

**ZIOPHARM Oncology, Inc.**

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PROSPECTUS

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July 6, 2006

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