



## **To Our Stockholders:**

2005 marked the first full year of operations for ZIOPHARM. We are pleased to report a year of significant milestones and remarkable progress on both the clinical and financial fronts. As we focus on our mission of developing safer and more effective cancer therapies, we continue to increase stockholder value.

### **We have continued to pursue our strategy of in-licensing promising oncology drug candidates in order to build a strong pipeline.**

Our drug development strategy, which consists of developing products to address unmet medical needs in cancer therapy by in-licensing drug candidates related to cancer therapeutics already on the market, is designed to shield stockholders from the inherent risks of investing in novel entities with unproven mechanisms of action or activity. We currently have two promising compounds in clinical development, ZIO-101 and ZIO-201. Because the biology underlying existing products related to ZIO-101 and ZIO-201 have been established and their clinical activities proven, we are able to focus on and streamline their clinical development without the constraints of resource-consuming basic research. As a result, we have been able to progress our products through clinical development predictably and rapidly.

Applying this strategy, we advanced ZIO-101 (organic arsenic) from phase I to phase I/II clinical trials in less than nine months. We are currently dosing ZIO-101 at high doses with minimal toxicities in the ongoing phase I trial, particularly as contrasted with inorganic arsenic. We are encouraged that the phase II data for ZIO-101 may exhibit efficacy at a higher dose with less side effects than that of currently approved inorganic arsenic.

We intend to apply for Fast Track status from the U.S. Food and Drug Administration (FDA) for one or both of our lead products, ZIO-101 and ZIO-201. If designated, the FDA would perform an expedited review of data upon completion of clinical trials further accelerating market access.

### **Our clinical development programs are progressing rapidly.**

In 2005, we initiated two clinical trials for ZIO-101 in patients with advanced cancers (hematological and solid cancers). At the AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics, held in Philadelphia in November 2005, we announced that ZIO-101 had demonstrated safety at the doses tested up to that point and that one patient with metastatic kidney cancer had resolution of brain metastasis and overall stable disease. While preliminary, we believe these data indicate the promise of

ZIO-101. We have since accelerated our planned development program by commencing a phase I/II trial for ZIO-101 in advanced multiple myeloma. This multinational trial began enrolling patients in early 2006.

ZIO-201 (isophosphoramidate mustard or IPM) is also showing evidence of clinical activity in an ongoing phase I trial: one patient with mesothelioma had stable disease for more than a year without significant toxicity. Like ZIO-101, we have accelerated our clinical development program for ZIO-201 by initiating a phase I/II trial with ZIO-201 in patients with advanced sarcoma. This trial also began enrolling patients in early 2006.

Looking ahead, we continue to advance another organic arsenic compound, ZIO-102, in preclinical studies. Results of some of these studies were also presented at the AACR-NCI-EORTC International Conference. Several other novel organic arsenics developed in our collaboration with Texas A&M University have been identified as potential clinical candidates. Also in preclinical studies, we have established anti-tumor activity of an orally available form of ZIO-101.

Preclinical research with IPM analogs is ongoing in collaboration with Southern Research Institute in Birmingham, Alabama, with the objective of identifying a ZIO-202 clinical candidate.

### **We became a public company and solidified our financial position.**

On the business front, 2005 has been a year of remarkable progress, setting a firm foundation for the Company in 2006. In May, we completed a Series A Convertible Preferred Stock offering, with gross proceeds of approximately \$18.1 million. These proceeds have been and continue to be used for the clinical development of ZIO-101 and ZIO-201. Maintaining adequate funding for our ongoing clinical trials is a key component that will enable us to keep our clinical development plan on track for initiating pivotal trials with both products in 2007. Following our preferred stock financing, we completed a transaction in which we became a publicly reporting company currently trading under the stock symbol ZIOP.OB. We believe ZIO-101 and ZIO-201 will address unmet medical needs in multiple myeloma and sarcoma, respectively; if commercialized, our forecasted combined sales for the products in these lead indications may be in excess of \$800 million.

### **We're focusing on continuing our progress in 2006.**

We begin 2006 on track with our development strategy and we continue to set our sights high. We currently have five clinical trials ongoing for our two lead product candidates, and we plan to commence additional phase II trials with both candidates in 2006. For both products, we also expect to announce phase I clinical trial data in the first half of the year and phase II interim data by year's end. We expect 2006 to be a year of data-generated news, and we anticipate entering pivotal trials for ZIO-101 and ZIO-201 in 2007.

We continue to be actively engaged in discussions around future in-licensing opportunities and commercial partners. We are receptive to the growing interest in our programs and our management's development expertise, and we will be active participants in several scientific, clinical and partnering meetings and forums in 2006.

We have developed a solid foundation from which to continue to build value, generate data, help people with cancer, and attract investors. We look forward to continuing our journey with you.

Sincerely,

Jonathan Lewis, M.D., Ph.D.  
Chief Executive Officer