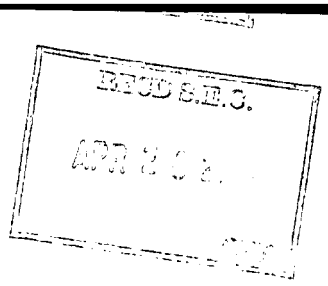

I fight cancer because...


"Because eventually

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

Form 10-K

☑ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934 FOR THE FISCAL YEAR ENDED DECEMBER 31, 2005.**

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934 FOR THE TRANSITION PERIOD FROM TO .**

Commission File No. 0-28298

Onyx Pharmaceuticals, Inc.

(Exact name of registrant as specified in its charter)

Delaware	**94-3154463**
(State or other jurisdiction of Incorporation or Organization)	*(I.R.S. Employer Identification No.)*

2100 Powell Street
Emeryville, California 94608
(510) 597-6500
(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

Securities Registered Pursuant to Section 12(b) of the Act: None

Securities Registered Pursuant to Section 12(g) of the Act:

Title of Each Class	Name of Each Exchange on Which Registered
Common Stock $0.001 par value	Nasdaq National Market

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ☐ No ☑

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes ☐ No ☑

Indicate by check mark whether the Registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the Registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ☑ No ☐

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (Section 229.405 of this chapter) is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer or a non-accelerated filer. See definition of "accelerated filer and large accelerated filer" in Rule 12b-2 of the Act).

Large accelerated filer ☐ Accelerated filer ☑ Non-accelerated filer ☐

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act): Yes ☐ No ☑

The aggregate market value of the voting stock held by nonaffiliates of the Registrant based upon the last trade price of the common stock reported on the Nasdaq National Market on June 30, 2005 was approximately $446,996,878.*

The number of shares of common stock outstanding as of March 8, 2006 was 41,359,343.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's Definitive Proxy Statement for its 2006 Annual Meeting of Shareholders (which will be filed with the Commission within 120 days of December 31, 2005), are incorporated herein by reference into Part III of this Annual Report on Form 10-K.

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* Excludes 16,581,418 shares of Common Stock held by directors, officers and stockholders whose beneficial ownership exceeds 5% of the Registrant's Common Stock outstanding. The number of shares owned by stockholders whose beneficial ownership exceeds 5% was determined based upon information supplied by such persons and upon Schedules 13D and 13G, if any, filed with the SEC. Exclusion of shares held by any person should not be construed to indicate that such person possesses the power, direct or indirect, to direct or cause the direction of the management or policies of the Registrant, that such person is controlled by or under common control with the Registrant, or that such persons are affiliates for any other purpose.

PART I.

This Annual Report on Form 10-K contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934. These statements involve known and unknown risks, uncertainties and other factors that may cause our or our industry's results, levels of activity, or achievements to differ significantly and materially from that expressed or implied by such forward-looking statements. These factors include, among others, those set forth in Item 1A "Risk Factors" and elsewhere in this Annual Report on Form 10-K. In some cases, you can identify forward-looking statements by terminology such as "may," "will," "should," "intend," "expect," "plan," "anticipate," "believe," "estimate," "predict," "potential," or "continue," or the negative of such terms or other comparable terminology.

Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee future results, events, levels of activity, performance or achievements. We do not assume responsibility for the accuracy and completeness of the forward-looking statements. We do not intend to update any of the forward-looking statements after the date of this Annual Report on Form 10-K to conform these statements to actual results, unless required by law.

Unless the context otherwise requires, all references to "the Company," "Onyx," "we," "our," and "us" in this Annual Report on Form 10-K refer to Onyx Pharmaceuticals, Inc.

Item 1. *Business*

Overview

We are a biopharmaceutical company building an oncology business by developing innovative therapies that target the molecular mechanisms implicated in cancer. With our collaborators, we are developing small molecule drugs with the goal of *changing the way cancer is treated*™. A common feature of cancer cells is the excessive activation of signaling pathways that cause abnormal cell proliferation. In addition, tumors require oxygen and nutrients from newly formed blood vessels to support their growth. The formation of these new blood vessels is a process called angiogenesis. We are applying our expertise to develop oral anticancer therapies designed to prevent cancer cell proliferation and angiogenesis by inhibiting proteins that signal or support tumor growth. By exploiting the genetic differences between cancer cells and normal cells, we aim to create novel anticancer agents that minimize damage to healthy tissue.

Our lead product, Nexavar® (sorafenib) tablets, being developed with our collaborator, Bayer Pharmaceuticals Corporation, or Bayer, was approved by the U.S. Food and Drug Administration, or FDA, in December 2005 for the treatment of individuals with advanced kidney cancer. This approval marked the first newly approved drug for patients with this disease in over a decade. Nexavar is a novel, orally available multi-kinase inhibitor and is one of a new class of anticancer treatments that target growth signaling.

The approval of Nexavar was based on data from our ongoing pivotal Phase III trial in patients with advanced kidney cancer. Study results demonstrated that there was statistically significant longer progression-free survival in those patients administered Nexavar versus those patients administered placebo. Progression-free survival is a measure of the time that a patient lives without evident tumor growth. Based on these data and discussions with the FDA, we and Bayer offered access to Nexavar to all patients in the Phase III kidney cancer trial. As a result, patients who were previously administered placebo in the trial could elect to receive Nexavar.

The two companies also made Nexavar available through a treatment protocol for all eligible individuals with advanced kidney cancer in the United States. Through this program more than 2,000 patients with advanced kidney cancer were treated with Nexavar at approximately 300 sites throughout the U.S. With the approval of Nexavar by the FDA, this program is now ending, and patients are being transitioned to commercial product.

An interim analysis on overall survival of patients in the Phase III trial has also been conducted. Based on the data, there was an estimated 28 percent reduction in the risk of death for patients receiving Nexavar

compared to those receiving placebo. The analysis was based on the 220 survival events (patient deaths) that had occurred by May 31, 2005. While the findings of the interim analysis did not reach statistical significance as prespecified in the protocol, these early results suggest a favorable survival trend for patients who received Nexavar. As the data mature, survival analyses will be released at the appropriate scientific meetings.

We and Bayer are jointly marketing Nexavar in the U.S. under our collaboration agreement. In September 2005, we and Bayer also announced that Bayer had submitted a Marketing Authorization Application, or MAA, to the European Medicines Agency, or EMEA, to market Nexavar within the European Union for the treatment of advanced kidney cancer. In more than ten European countries, eligible individuals are now being treated through an expanded access program. In addition, regulatory filings have been completed in Switzerland, Australia, Brazil, Canada, Mexico and Turkey.

In addition, we are conducting multiple clinical trials of Nexavar in other tumor types, including pivotal studies in advanced hepatocellular carcinoma, also known as liver cancer, metastatic melanoma, or advanced skin cancer, and non-small cell lung cancer. We and Bayer are undertaking a wide variety of early stage studies, as well as studies being conducted by independent investigators, to evaluate the safety and effectiveness of Nexavar in combination with other therapies in a wide variety of cancers. To date, we and Bayer have also reported results from several early stage studies combining Nexavar with a range of chemotherapeutic agents.

With Bayer, we share a vision of rapidly making Nexavar available to patients with advanced kidney cancer. It is also our intention to invest significantly in Nexavar in order to assess its possible use in the treatment of other cancers. We believe that Nexavar has the potential to *change the way cancer is treated* ™ by offering patients an effective oral agent that is generally well tolerated, and can be combined with current standards of care and thus improve the length and quality of patient survival.

In a previous collaboration with Warner-Lambert Company, now a subsidiary of Pfizer Inc, we identified a number of lead compounds that modulate the activity of key enzymes that regulate the process whereby a single cell replicates itself and divides into two identical new cells, a process known as the cell cycle. Mutations in genes that regulate the cell cycle are present in a majority of human cancers. Warner-Lambert is currently advancing a lead candidate from that collaboration, PD 332991, a small molecule cell cycle inhibitor targeting a cyclin-dependent kinase, or CDK. In September 2004, we announced that Pfizer initiated Phase I clinical testing of this CDK4 inhibitor.

Our Product Candidates

Certain trials of our product candidates, sponsored by either Onyx or our collaborators, are listed below.

Product/Program	Technology	Indication	Current Status
Nexavar (sorafenib) Tablets	Small molecule inhibitor of tumor cell proliferation and angiogenesis, targeting RAF, VEGFR-2, PDGFR-ß, KIT, FLT-3, and RET.	Advanced kidney cancer	Approved in U.S. Applications pending in Europe and other territories
		Single-agent trial for liver cancer	Phase III
		Combination trials for metastatic melanoma	Phase III
		Combination trial for non-small cell lung cancer	Phase III
		Various single-agent trials for kidney and liver cancer	Phase II — some complete and some ongoing
		Combination trials for kidney and liver cancer, as well as metastatic melanoma	Phase II
		Single-agent trials for breast, non-small cell lung and other cancers	Phase II
		Combination trials with standard chemotherapies for melanoma, colorectal, non-small cell lung, ovarian and other cancers	Phase II and Ib Extension
		Additional combination trials with other anticancer agents	Phase Ib
PD 332991 (licensed to Pfizer)	Small molecule inhibitor of cyclin-dependent kinase 4	Multiple cancer types	Phase I

Nexavar

Nexavar is designed to operate through dual mechanisms of action by inhibiting angiogenesis, as well as the proliferation of cancer cells.

Nexavar inhibits the signaling of VEGFR-2 and PDGFR-ß, key receptors of Vascular Endothelial Growth Factor, or VEGF, and Platelet-Derived Growth Factor, or PDGF. Both receptors play a role in angiogenesis, which is the formation of blood vessels required to support tumor growth. In addition, in preclinical models the inhibition of RAF kinase, an enzyme in the RAS signaling pathway, has also been shown to have antiangiogenic effects. The *RAS* signaling pathway is known to play a key role in cell proliferation. In normal cell proliferation, when the RAS signaling pathway is activated, or turned "on," it sends a signal telling the cell to grow and divide. When a gene in the RAS signaling pathway is mutated, the signal may not turn "off" as it should, causing the cell to continuously reproduce itself. The RAS signaling pathway plays an integral role in the growth of some tumor types, and we believe that inhibiting this pathway could have an effect on tumor growth. Nexavar is an orally active agent designed to block inappropriate

growth signaling in cancer by inhibiting RAF kinase. Nexavar also inhibits other kinases involved in cancer, such as KIT, FLT-3 and RET.

Commercialization Status

In December 2005, we and Bayer announced that the FDA had approved Nexavar for the treatment of patients with advanced kidney cancer. Consistent with our international commercialization strategy, applications are also pending with regulatory agencies in other parts of the world, including Europe, where an MAA was submitted to the EMEA in September 2005. In addition, filings have been completed in Switzerland, Australia, Brazil, Canada, Mexico and Turkey.

Clinical Trials

Under our collaboration agreement with Bayer, we are conducting multiple clinical trials of Nexavar. In addition, we and Bayer are jointly developing and intend to commercialize Nexavar internationally, with the exception of Japan. In Japan, Bayer is responsible for funding and conducting all product development activities and will pay us a royalty on any sales.

Kidney Cancer Program

Phase III in Kidney Cancer. In October 2003, we and Bayer announced the initiation of an international, placebo-controlled, multicenter Phase III clinical trial to evaluate the safety and efficacy of Nexavar in the treatment of advanced kidney cancer. More than 900 people have participated in the Phase III study at sites worldwide. Enrollment was completed in March 2005.

In the first quarter of 2005, we and Bayer announced that an independent Data Monitoring Committee, or DMC, had reviewed the safety and efficacy data from the trial. The DMC concluded that Nexavar significantly prolonged progression-free survival. This result was discussed with medical experts, patient advocacy groups and health authorities. It was concluded that the results reflected a clinically meaningful benefit for patients. Subsequently, we and Bayer allowed all patients in the Phase III kidney cancer trial to be offered access to Nexavar.

Results from the Phase III trial were presented at the 2005 annual meeting of the American Society of Clinical Oncology, or ASCO, in May 2005. It was reported that progression-free survival was significantly prolonged by Nexavar. As assessed by independent radiologic review, progression-free survival doubled to a median value of 24 weeks (167 days) in patients receiving Nexavar as compared to 12 weeks (84 days) for patients receiving placebo (p-value$<$ 0.000001).

In addition, an interim analysis on overall survival of patients in the Phase III trial was presented at the thirteenth European Cancer Conference, or ECCO, in November 2005. Based on the interim analysis, there was an estimated 28 percent reduction in the risk of death for patients receiving Nexavar compared to those who did not (hazard ratio 0.72). The analysis was based on the 220 patients who died by May 31, 2005. While the findings did not reach statistical significance for an interim analysis (which required a p value of less than 0.0005), these early results suggest a favorable survival trend for patients who received Nexavar. P-values are used to indicate the probability that results observed in two different samples are different due to chance alone, as opposed to a benefit due to the intervention, such as treatment with Nexavar. As the data mature, survival data from additional analyses will be released at the appropriate scientific meetings.

The approved Nexavar package insert for the treatment of patients with advanced kidney cancer warns of a number of observed adverse side effects:

- Hypertension may occur early in the course of therapy and blood pressure should be monitored weekly during the first six weeks of therapy and treated as needed.
- Incidence of bleeding regardless of causality was 15 percent for Nexavar vs. 8 percent for placebo and the incidence of treatment-emergent cardiac ischemia/infarction was 2.9 percent for Nexavar vs. 0.4 percent for placebo.

- Most common treatment-emergent adverse events with Nexavar were diarrhea, rash/desquamation, fatigue, hand-foot skin reaction, alopecia, and nausea. Grade 3/4 adverse events were 38 percent for Nexavar vs. 28 percent for placebo.
- Women of child-bearing potential should be advised to avoid becoming pregnant and advised against breast-feeding.

In cases of any severe or persistent side effects, temporary treatment interruption, dose modification or permanent discontinuation should be considered.

We and Bayer have previously announced that Nexavar has been granted orphan drug status for the treatment of kidney cancer by the Committee for Orphan Medicinal Products, or COMP, of the EMEA in August 2004, and in October 2004 by the FDA. Orphan Drug designation provides incentives to companies that develop drugs for diseases affecting small numbers of patients.

Phase II Randomized Discontinuation Trial Results in Kidney Cancer. Since our preclinical data demonstrated that Nexavar works primarily by preventing tumor growth rather than tumor shrinkage, a study was performed to test whether Nexavar could cause disease stabilization. The study included patients with advanced solid tumors of multiple types. Final summary trial results for participants with advanced kidney cancer were presented in May 2005 at the ASCO meeting.

Analysis of the Phase II randomized discontinuation trial of Nexavar administered as a single agent showed activity in patients with advanced kidney cancer. Of the 502 patients enrolled in the study, 202 had kidney cancer. As assessed by investigators, 73 patients achieved at least 25 percent reduction in their tumor size and 69 patients achieved stable disease, defined as tumor growth or shrinkage of less than 25 percent. After the assessment, 65 participants determined to have stable disease were randomized to receive, in a blinded fashion, either placebo or Nexavar.

After a second 12-week treatment period, the blind was broken on the randomized group of 65 patients. The study achieved its primary endpoint, as 16 patients (50%) treated with Nexavar were progression-free compared with 6 patients (18%) treated with placebo ($p=0.0077$). In addition, Nexavar significantly prolonged median progression-free survival to 24 weeks as compared to six weeks for patients treated with placebo ($p=0.0087$). In addition, Nexavar was restarted in 28 patients who progressed on placebo. The median time from restarting Nexavar to the end of treatment in these patients was 24 weeks. The most commonly reported drug-related adverse events in the Phase II kidney cancer population included skin reactions such as hand-foot syndrome and rash, diarrhea, fatigue, weight loss and hypertension, which were shown to be generally manageable and reversible.

Liver Cancer Program

Phase III Trial. In March 2005, we and Bayer initiated a randomized, double-blind, placebo-controlled Phase III clinical trial of Nexavar administered as a single agent in patients with advanced hepatocellular carcinoma, also known as HCC or liver cancer. The Phase III study is designed to measure differences in overall survival, time to symptom progression, and time to tumor progression of Nexavar versus placebo in patients with advanced HCC. Approximately 560 patients with advanced HCC, who have not received previous systemic treatment for their disease, are being randomized to receive 400 mg of Nexavar twice daily or matching placebo. This study is expected to enroll patients in the Americas, Europe and Australia/New Zealand. We expect to complete enrollment in the study in 2006. At the same time, we and Bayer announced a randomized Phase II trial evaluating Nexavar in this disease in combination with doxorubicin, a chemotherapeutic agent commonly used to treat liver cancer.

Phase II Trial. The decision to begin the Phase III liver cancer study was based upon data from a Phase II clinical trial. In September 2004, the data from this Phase II trial were presented at the 16th American Association for Cancer Research-National Cancer Institute-European Organization for Research and Treatment of Cancer, or AACR-NCI-EORTC, meeting in Geneva, Switzerland. Of 137 patients enrolled in the study, investigators reported median overall survival for all patients was 9.2 months and median time-to-tumor progression was 4.2 months (or 5.7 months in patients with good hepatic function). In

the study, safety data generated showed that Nexavar's side effect profile was generally well tolerated and predictable. The most common grade 3/4 drug-related toxicities, all less than ten percent, were fatigue, diarrhea and hand-foot skin reaction.

Metastatic Melanoma Program

Phase III Trials. In May 2005, we and Bayer commenced a randomized, double-blind Phase III trial administering Nexavar in combination with the chemotherapeutic agents carboplatin and paclitaxel in patients with advanced metastatic melanoma. The trial, which is expected to enroll approximately 250 patients, has progression-free survival as its primary endpoint. Participating patients must have failed no more than one previous systemic chemotherapeutic treatment with either dacarbazine, also known as DTIC, or temozolomide. Patients are being randomized to receive 400 mg of Nexavar twice daily or matching placebo, in addition to a standard dosing schedule of carboplatin (AUC 6) and paclitaxel (225 mg/m2). The study includes sites in the United States, Canada, Europe and Australia. We expect to complete enrollment in the study in 2006. Subsequently, a second Phase III study was initiated under the sponsorship of the Eastern Cooperative Oncology Group, or ECOG. This trial has overall survival as its primary endpoint, and is expected to enroll approximately 800 patients with advanced metastatic melanoma. Participants in this study may not have had prior systemic chemotherapy.

Phase I/II Trial. The decision to conduct Phase III trials in patients with metastatic melanoma was based upon data from a Phase Ib combination trial evaluating Nexavar in combination with these agents. By the fall of 2005, investigators had reported on a total of 77 melanoma patients enrolled in the trial at two different sites. At the time of the report, progression-free survival was more than six months in the majority of patients, and these patients had the most advanced form of melanoma, the disease having spread to their internal organs. It was also reported that Nexavar was generally well tolerated when combined with full dose paclitaxel and carboplatin. In addition to side effects normally expected with paclitaxel and carboplatin, toxicities believed to be attributable to Nexavar, including skin rash and hand-foot syndrome, resolved themselves when treatment was halted or Nexavar dosages were reduced. As this investigator-initiated analysis was not reviewed by the sponsors, the results are subject to change until the database is finalized. Since only a limited number of studies have been conducted using paclitaxel and/or carboplatin in melanoma patients, and at doses and administration regimes different from ours, the randomized studies described above are being conducted to assess the efficacy of the combination with Nexavar.

Lung Cancer Program

Phase III Trial. In February 2006, we and Bayer initiated a randomized, double-blind, placebo-controlled pivotal clinical trial studying Nexavar administered in combination with the chemotherapeutic agents carboplatin and paclitaxel in patients with non-small cell lung cancer, or NSCLC. The multicenter study will compare Nexavar when co-administered with the two agents versus carboplatin and paclitaxel alone. The study, which is expected to enroll approximately 900 patients, will assess overall survival as the primary endpoint. Secondary endpoints include progression-free survival, tumor response and safety. Participating patients may not have received prior systemic anticancer treatment. Additionally, the study is open to patients with all histologies, or types, of NSCLC. Patients will be randomized to receive 400 mg of oral Nexavar twice daily or matching placebo, in addition to carboplatin and paclitaxel for six cycles. Subsequently, patients will continue in a maintenance phase where Nexavar or placebo will be administered as a single agent. The study will be conducted at over 100 sites in North America, South America, Europe and the Asia Pacific region.

Phase I/Phase II Trials. We and Bayer generated lung cancer data in several additional studies. We and Bayer conducted a 54 patient, single-agent Nexavar trial in second or third-line NSCLC patients. The median progression-free survival in this refractory population was approximately three months. We and Bayer also obtained additional data from a subset of 14 evaluable NSCLC first-line patients enrolled in a single-arm Phase I study administering the combination of carboplatin, paclitaxel and Nexavar. For the lung cancer patients on the combination therapy, the investigator reported an overall median progression-free survival of

approximately 245 days, or eight months. As this investigator-initiated analysis was not reviewed by the sponsors, the results are subject to change until the database is finalized.

Earlier Stage Clinical Development

Phase II in Multiple Tumor Types. With Bayer we have multiple ongoing Phase II studies evaluating Nexavar as a single agent in tumors such as breast, prostate, ovarian and other cancers. As these studies are completed, we intend to present data at scientific meetings. In addition, based on the results of these ongoing trials, we plan to identify additional potential registration paths for Nexavar.

Phase Ib in Combination with Anticancer Agents in Multiple Tumor Types. Together with Bayer, we are conducting multiple Phase Ib clinical trials evaluating Nexavar in combination with a range of standard chemotherapies, as well as with other anticancer agents. To date, results have been reported from more than ten of these trials, specifically for the use of Nexavar in combination with paclitaxel/carboplatin, gemcitabine, oxaliplatin, doxorubicin, irinotecan, 5-FU/leucovorin, capecitabine, DTIC, taxotere, Iressa, interferon and Avastin. Additional combination trials are planned and decisions about future randomized Phase II trials are pending.

Phase I. Final data from the original single-agent trial was presented at the 2003 ASCO annual meeting. We reported that in an analysis of 118 patients with advanced malignancies who received Nexavar in initial doses of 200 mg or more twice daily, 29 patients, or 25 percent, remained on Nexavar for more than six months, and nine of these patients remained in treatment for more than one year. Most of the dose-limiting toxicities were seen at dose levels of 600 mg twice daily or greater and included diarrhea and skin toxicity, including hand-foot syndrome. Based on these results, we selected a dose of 400 mg twice daily to use in our Phase II and Phase III clinical trials.

Cell Cycle Program

In collaboration with Warner-Lambert, we identified a number of lead compounds that modulate the activity of key enzymes that regulate the process whereby a single cell replicates itself and divides into two identical new cells, a process known as the cell cycle. Mutations in genes that regulate the cell cycle are present in a majority of human cancers. Our small molecule discovery collaboration with Warner-Lambert ended in August 2001. However, Warner-Lambert, now a subsidiary of Pfizer, is currently advancing a lead candidate from that collaboration, PD 332991, a small molecule cell cycle inhibitor targeting cyclin-dependent kinase 4. Pfizer entered Phase I clinical testing with this candidate in 2004.

Virus Platform

Prior to June 2003, in addition to our small molecule program, we were developing therapeutic viruses that selectively replicate in cells with cancer-causing genetic mutations. In June 2003, we announced that we were discontinuing this program as part of a business realignment that placed an increased priority on the development of Nexavar. Effective January 2005, Onyx licensed exclusive rights to our p53-selective virus, ONYX-015, to Shanghai Sunway Biotech Co. Ltd. headquartered in Shanghai, People's Republic of China. Under this agreement, Shanghai Sunway is responsible for the research, development, manufacture and commercialization of ONYX-015 worldwide. Onyx received an initial payment of $1.0 million and will receive additional milestone payments on achievement of clinical, regulatory and commercial events. We will also receive royalties on net sales of ONYX-015 in the U.S., Europe and certain other foreign countries, but excluding China.

Collaborations

Bayer

Effective February 1994, we established a research and development collaboration agreement with Bayer to discover, develop and market compounds that inhibit the function, or modulate the activity, of the RAS signaling pathway to treat cancer and other diseases. Together with Bayer, we concluded collaborative

research under this agreement in 1999, and based on this research, a product development candidate, Nexavar, was identified.

Bayer paid all the costs of research and preclinical development of Nexavar until the Investigational New Drug application, or IND, was filed in May 2000. Under our agreement with Bayer, we are currently funding 50 percent of mutually agreed development costs worldwide, excluding Japan. Bayer is funding 100 percent of development costs in Japan and will pay us a royalty on any sales in Japan. We are co-promoting Nexavar in the United States and, if we continue to co-fund development and co-promote in the United States, we will share equally in profits or losses, if any, in the United States. If we continue to co-fund but do not co-promote in the United States, Bayer would first receive a portion of the product revenues to repay Bayer for its commercialization infrastructure, before determining our share of profits and losses. We also share profits and losses with Bayer in the rest of the world (outside of Japan), but as we do not have the right to co-promote Nexavar outside the United States, Bayer would also receive this preferential distribution in all other parts of the world, except Japan where we would receive a royalty on any sales.

On March 6, 2006, we and Bayer entered into a Co-Promotion Agreement to co-promote Nexavar in the United States. This agreement supersedes those provisions of the original 1994 Collaboration Agreement that relate to the co-promotion of Nexavar in the United States between Bayer and us. Outside of the United States, the terms of the Collaboration Agreement continue to govern. Under the terms of the Co-Promotion Agreement and consistent with the Collaboration Agreement, we will share equally in the profits or losses of Nexavar, if any, in the United States, subject only to our continued co-funding of the development costs of Nexavar worldwide, excluding Japan.

Our collaboration agreement with Bayer calls for creditable milestone-based payments. These amounts are interest-free and will be repayable to Bayer from a portion of any of our future profits and royalties. We received $5.0 million in the third quarter of 2002 upon initiation of Phase II clinical studies and $15.0 million in the fourth quarter of 2003 based upon the initiation of a Phase III study. Based on the July 2005 NDA filing, we received the third milestone advance for $10.0 million in the third quarter of 2005. In addition, in January 2006, we received the final $10.0 million milestone advance as a result of the U.S. approval in December 2005. At any time during product development, either company may terminate its participation in development costs, in which case the terminating party would retain rights to the product on a royalty-bearing basis. If we do not continue to bear 50 percent of product development costs, Bayer would retain exclusive, worldwide rights to this product candidate and would pay royalties to us based on net sales.

Warner-Lambert

In May 1995, we entered into a research and development collaboration agreement with Warner-Lambert, now a subsidiary of Pfizer, to discover and commercialize small molecule drugs that restore control of, or otherwise intervene in, the misregulated cell cycle in tumor cells. Under this agreement, we developed screening tests, or assays, for jointly selected targets, and transferred these assays to Warner-Lambert for screening of their compound library to identify active compounds. The discovery research term under the agreement ended in August 2001. Warner-Lambert is responsible for subsequent medicinal chemistry and preclinical investigations on the active compounds. In addition, Warner-Lambert is obligated to conduct and fund all clinical development, make regulatory filings and manufacture for sale any approved collaboration compounds. We will receive milestone payments on clinical development and registration of any resulting products and would receive royalties on worldwide sales of the products. Warner-Lambert has identified a small molecule lead compound, PD 332991, an inhibitor of cyclin-dependent kinase 4, and began clinical testing with this drug candidate in 2004. As a result of this, we received a $500,000 milestone payment from Warner-Lambert, which we recorded as revenue in 2004.

Research and Development

The majority of our operating expenses to date have been related to research and development, or R&D. In 2005, R&D expenses consisted of costs associated with collaborative R&D as we do not have internal research capabilities and have only a limited development staff. We anticipate that a significant percentage of

our operating expenses will continue to be related to R&D in 2006, specifically the clinical development of Nexavar as both we and Bayer have agreed to continued substantial investment in this drug.

Marketing and Sales

Since our first product, Nexavar, was recently approved by the FDA, and because we have retained U.S. co-promotion rights, we have added sales, marketing and medical affairs capabilities with particular expertise in commercializing oncology products. We and Bayer are each providing one-half of the field-based staffing in the U.S. to satisfy commercial demand for this product and to provide medical affairs support for Nexavar. All the individuals hired into this organization have significant experience relevant to the field of pharmaceuticals in general and to the specialty of oncology in particular. We and Bayer have also established comprehensive patient support services to maximize access to Nexavar. This includes REACH, an acronym for Resources for Expert Assistance and Care Hotline, which provides a single point-of-contact for most patients. In addition, REACH helps link patients to specialty pharmacies for direct product distribution. Bayer currently has multiple specialty pharmacies under contract that are shipping drug directly to patients' homes.

Manufacturing

At this time, we do not have any internal manufacturing capability for any of our product candidates, and we rely on others to provide manufacturing services. To manufacture our product candidates for clinical trials or on a commercial scale, if we are required to or choose to do so, we would have to build or gain access to a manufacturing facility, which will require significant funds.

Under our collaboration agreement with Bayer, Bayer has the manufacturing responsibility to supply Nexavar for clinical trials and to support any commercial requirements. To date, Bayer has manufactured sufficient drug supply to support the current needs of clinical trials in progress and commercial activity since approval of Nexavar in December 2005. We believe that Bayer has the capability to meet all future drug supply needs and meet the FDA and other regulatory agency requirements for commercialization. However, Bayer may, for reasons beyond our control, become unable or unwilling to provide sufficient future drug supply or to meet these requirements. If this were to happen, we would be forced to incur additional expenses to pay for the manufacture of Nexavar or to develop our own manufacturing capabilities. Under our license agreement with Warner-Lambert, Warner-Lambert is obligated to manufacture all small molecule drugs for clinical development and commercialization.

Patents and Proprietary Rights

We believe that patent and trade secret protection is crucial to our business and that our future will depend in part on our ability to obtain patents, maintain trade secret protection and operate without infringing the proprietary rights of others, both in the United States and other countries. The patent applications covering Nexavar are owned by Bayer, but licensed to us in conjunction with our collaboration agreement with Bayer. We currently anticipate that, if issued, the United States patent related to Nexavar will expire in 2022, subject to possible patent-term extension, the entitlement to which and the term of which cannot be presently calculated. Patent applications for Nexavar are also pending throughout the world. As of December 31, 2005, we owned or had licensed rights to 51 United States patents and 34 United States patent applications, and generally, foreign counterparts of these filings. Most of these patents or patent applications cover protein targets used to identify product candidates during the research phase of our collaborative agreements with Warner-Lambert or Bayer, or aspects of our now discontinued therapeutic virus program.

Generally, patent applications in the United States are maintained in secrecy for a period of 18 months or more. Since publication of discoveries in the scientific or patent literature often lag behind actual discoveries, we are not certain that we were the first to make the inventions covered by each of our pending patent applications or that we were the first to file those patent applications. The patent positions of biotechnology and pharmaceutical companies are highly uncertain and involve complex legal and factual questions. Therefore, we cannot predict the breadth of claims allowed in biotechnology and pharmaceutical patents, or their enforceability. To date, there has been no consistent policy regarding the breadth of claims allowed in

biotechnology patents. Third parties or competitors may challenge or circumvent our patents or patent applications, if issued. Because of the extensive time required for development, testing and regulatory review of a potential product, it is possible that before we commercialize any of our products, any related patent may expire, or remain in existence for only a short period following commercialization, thus reducing any advantage of the patent.

If patents are issued to others containing preclusive or conflicting claims and these claims are ultimately determined to be valid, we may be required to obtain licenses to these patents or to develop or obtain alternative technology. Our breach of an existing license or failure to obtain a license to technology required to commercialize our products may seriously harm our business. We also may need to commence litigation to enforce any patents issued to us or to determine the scope and validity of third-party proprietary rights. Litigation would create substantial costs. If our competitors prepare and file patent applications in the United States that claim technology also claimed by us, we may have to participate in interference proceedings declared by the United States Patent and Trademark Office to determine priority of invention, which could result in substantial cost, even if the eventual outcome is favorable to us. An adverse outcome in litigation could subject us to significant liabilities to third parties and require us to seek licenses of the disputed rights from third parties or to cease using the technology if such licenses are unavailable.

Together with our licensors, we also rely on trade secrets to protect our combined technology especially where we do not believe patent protection is appropriate or obtainable. However, trade secrets are difficult to protect. We protect our proprietary technology and processes, in part, by confidentiality agreements with our employees, consultants and collaborators. These parties may breach these agreements, and we may not have adequate remedies for any breach. Our trade secrets may otherwise become known or be independently discovered by competitors. To the extent that we or our consultants or collaborators use intellectual property owned by others in their work for us, we may have disputes with them or other third parties as to the rights in related or resulting know-how and inventions.

Government Regulation

Regulation by government authorities in the United States and other countries will be a significant factor in the manufacturing and marketing of any products that may be developed by us. We must obtain the requisite regulatory approvals by government agencies prior to commercialization of any product. This is true internationally and for any additional indications, if any. We anticipate that any product candidate will be subject to rigorous preclinical and clinical testing and premarket approval procedures by the FDA and similar health authorities in foreign countries. Various federal statutes and regulations also govern or influence the manufacturing, testing, labeling, storage, record-keeping, marketing and promotion of products and product candidates.

The steps ordinarily required before a drug or biological product may be marketed in the United States include:

- preclinical studies;
- the submission to the FDA of an IND that must become effective before human clinical trials may commence;
- adequate and well-controlled human clinical trials to establish the safety and efficacy of the product candidate;
- the submission of an NDA to the FDA; and
- FDA approval of the NDA, including inspection and approval of the product manufacturing facility.

Preclinical trials involve laboratory evaluation of product candidate chemistry, formulation and stability, as well as animal studies to assess the potential safety and efficacy of each product candidate. Preclinical safety trials must be conducted by laboratories that comply with FDA regulations regarding Good Laboratory Practice. The results of the preclinical trials are submitted to the FDA as part of an IND and are reviewed by the FDA before the commencement of clinical trials. Unless the FDA objects to an IND, the IND will

become effective 30 days following its receipt by the FDA. Submission of an IND may not result in FDA clearance to commence clinical trials, and the FDA's failure to object to an IND does not guarantee FDA approval of a marketing application.

Clinical trials involve the administration of the product candidate to humans under the supervision of a qualified principal investigator. In the United States, clinical trials must be conducted in accordance with Good Clinical Practices under protocols submitted to the FDA as part of the IND. In addition, each clinical trial must be approved and conducted under the auspices of an Institutional Review Board, or IRB, and with the patient's informed consent. The IRB will consider, among other things, ethical factors, the safety of human subjects and the possible liability of the institution conducting the clinical trial. The United Kingdom and many other European and Asian countries have similar regulations.

The goal of Phase I clinical trials is to establish initial data about safety and tolerability of the product candidate in humans. The goal of Phase II clinical trials is to provide evidence about the desired therapeutic efficacy of the product candidate in limited studies with small numbers of carefully selected subjects. The investigators seek to evaluate the effects of various dosages and to establish an optimal dosage level and dosage schedule. Investigators also gather additional safety data from these studies. Phase III clinical trials consist of expanded, large-scale, multicenter studies in the target patient population. This phase further tests the product's effectiveness, monitors side effects, and, in some cases, compares the product's effects to a standard treatment, if one is already available.

We would need to submit all data obtained from this comprehensive development program as an NDA to the FDA, and to the corresponding agencies in other countries for review and approval, before marketing product candidates. These regulations define not only the form and content of the development of safety and efficacy data regarding the proposed product, but also impose specific requirements regarding:

- manufacture of the product;
- testing;
- quality assurance;
- packaging;
- storage;
- documentation;
- record-keeping;
- labeling;
- advertising; and
- marketing procedures.

The process of obtaining FDA approval can be costly, time consuming and subject to unanticipated delays. The FDA may refuse to approve an application if it believes that applicable regulatory criteria are not satisfied. The FDA may also require additional testing for safety and efficacy of the product candidate. In some instances, regulatory approval may be granted with the condition that confirmatory Phase IV clinical trials are carried out. If these Phase IV clinical trials do not confirm the results of previous studies, regulatory approval for marketing may be withdrawn. Moreover, if regulatory approval of a product is granted, the approval will be limited to specific indications. Approvals of our proposed products, processes, or facilities may not be granted on a timely basis, if at all. Any failure to obtain, or delay in obtaining, such approvals would seriously harm our business, financial condition and results of operations. Facilities used to manufacture drugs are subject to periodic inspection by the FDA and other authorities where applicable, and must comply with the FDA's current Good Manufacturing Practice, or cGMP, regulations. Failure to comply with the statutory and regulatory requirements subjects the manufacturer to possible legal action, such as suspension of manufacturing, seizure of product or voluntary recall of a product. Adverse experiences with the product must be reported to the FDA and could result in the imposition of market restrictions through labeling changes or in

product removal. Product approvals may be withdrawn if compliance with regulatory requirements is not maintained or if problems concerning safety or efficacy of the product occur following approval. Failure to comply with FDA and other applicable regulatory requirements may result in, among other things:

- warning letters;
- civil penalties;
- criminal prosecution;
- injunctions;
- seizure or recall of products;
- total or partial suspension of production;
- refusal of the government to grant approval; or
- withdrawal of approval of products.

Even though we have obtained FDA approval, approval of a product candidate by comparable regulatory authorities will be necessary in foreign countries prior to the commencement of marketing of the product candidate in these countries. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval may differ from that required for FDA approval. Although there is now a centralized European Union approval mechanism in place, each European country may nonetheless impose its own procedures and requirements, many of which are time consuming and expensive. Thus, there can be substantial delays in obtaining required approvals from both the FDA and foreign regulatory authorities after the relevant applications are filed. We expect to rely on our collaborators and licensees, along with our own expertise, to obtain governmental approval in foreign countries of product candidates discovered by us or arising from our programs.

We are subject to various federal and state laws pertaining to healthcare "fraud and abuse," including anti-kickback and false claims laws. The federal Anti-Kickback Law makes it illegal for any person, including a prescription drug manufacturer, or a party acting on its behalf, to knowingly and willfully solicit, offer, receive or pay any remuneration, directly or indirectly, in exchange for, or to induce, the referral of business, including the purchase, order or prescription of a particular drug, for which payment may be made under federal healthcare programs such as Medicare and Medicaid. The federal government has issued regulations, commonly known as safe harbors, that set forth certain provisions which, if fully met, will assure healthcare providers and other parties that they will not be prosecuted under the federal Anti-Kickback Law. Although full compliance with these provisions ensures against prosecution under the federal Anti-Kickback Law, the failure of a transaction or arrangement to fit within a specific safe harbor does not necessarily mean that the transaction or arrangement is illegal or that prosecution under the federal Anti-Kickback Law will be pursued. Violations of the law are punishable by up to five years in prison, criminal fines, administrative civil money penalties and exclusion from participation in federal healthcare programs. In addition, many states have adopted laws similar to the federal Anti-Kickback Law. Some of these state prohibitions apply to referral of patients for healthcare services reimbursed by any source, not only the Medicare and Medicaid programs. Due to the breadth of these laws, and the potential for additional legal or regulatory change addressing some of our practices, it is possible that our sales and marketing practices or our relationships with physicians might be challenged under anti-kickback laws, which could harm us. We have developed a comprehensive compliance program that will seek to establish internal controls to facilitate adherence to the rules and program requirements to which we may be or may become subject.

In the course of practicing medicine, physicians may legally prescribe FDA approved drugs for an indication that has not been approved by the FDA and which, therefore, is not described in the product's approved labeling — a so-called "off-label use." The FDA does not regulate the behavior of physicians in their choice of treatments. The FDA and other governmental agencies do, however, restrict communications on the subject of off-label use by a manufacturer or those acting on behalf of a manufacturer. Companies may not promote FDA-approved drugs for off-label uses. The FDA has not approved the use of Nexavar for the

treatment of any disease other than advanced kidney cancer and neither we nor Bayer market Nexavar for the treatment of any disease other than advanced kidney cancer. The FDA and other governmental agencies do permit a manufacturer (and those acting on its behalf) to engage in some limited, non-misleading, non-promotional exchanges of scientific information regarding unapproved indications. We believe that our pre-approval educational communications constitute lawful activities, and we have policies and procedures in place to regulate them. In addition, we periodically review and update these policies and procedures to ensure that our pre-approval activities comply with current applicable law. However, while we believe that we are currently in compliance with the FDA guidelines which govern medical education and the FDA regulations which prohibit off-label promotion, the guidelines and regulations are subject to varying interpretations, which are evolving, and the FDA may disagree that all of our activities comply with applicable restrictions on pre-approval promotion. Failure to comply with these requirements in the past or with respect to future activities can result in enforcement action, including civil and criminal sanctions by the FDA and other federal and state governmental bodies, such as the Department of Justice and the Office of the Inspector General of the Department of Health and Human Services, which would harm our business and could have a material adverse effect on our business, financial condition and profitability.

Competition

We are engaged in a rapidly changing and highly competitive field. We are seeking to develop and market product candidates that will compete with other products and therapies that currently exist or are being developed. Many other companies are actively seeking to develop products that have disease targets similar to those we are pursuing. Some of these competitive product candidates are in clinical trials, and others are approved. Competitors that target the same tumor types as our Nexavar program and that have commercial products or product candidates in clinical development include Pfizer, Novartis International AG, AstraZeneca PLC, OSI Pharmaceuticals, Inc., Genentech, Inc., Chiron Corporation, and Abgenix, Inc., among others. A number of companies have agents targeting Vascular Endothelial Growth Factor, or VEGF; VEGF receptors; Epidermal Growth Factor, or EGF; EGF receptors; and other enzymes. These agents include antibodies and small molecules. OSI Pharmaceuticals with Tarceva™ a small molecule inhibitor of the EGF receptor has been approved in the U.S. for treatment of NSCLC and pancreatic cancer in combination with gemcitabine. Companies working on developing antibody approaches include ImClone Systems, Inc. and Abgenix. Imclone has developed Erbitux, which is an antibody targeting the EGF receptor. Erbitux has been approved in the U.S. and the European Union for treatment of colorectal cancer, as well as in the U.S. for the treatment of most types of head and neck cancer. Genentech has Avastin™, an antibody targeting VEGF, which has received approvals in the U.S. and the European Union for treatment of colorectal cancer. In addition, many other pharmaceutical companies are developing novel cancer therapies that, if successful, would also provide competition for Nexavar.

Historically, the most commonly used therapeutic agents for patients suffering from advanced kidney cancer were interleukin-2 or interferon-alpha. With the development and approval of new anticancer therapies, it is anticipated that the initial, or first-line, treatment for many of these patients will become targeted agents. For example, Genentech's Avastin has been reported to have activity in kidney cancer, and Genentech has indicated that Avastin is now being used off-label for treatment of some kidney cancer patients. In addition, Avastin is currently in a Phase III trial for kidney cancer, which, if successful, could result in marketing approval in this indication.

Pfizer's drug, Sutent, a multi-kinase inhibitor, was recently approved by the FDA for treating patients with Gleevec-resistant gastrointestinal stromal tumors, or GIST. Sutent also received accelerated approval for advanced kidney cancer. Pfizer has also submitted an MAA to the EMEA for Sutent. In addition, Wyeth is conducting a Phase III study of CCI-779, an mTOR inhibitor, in patients with advanced kidney cancer. Pfizer also has an earlier stage compound, AG-013736, a multi-kinase inhibitor, which has been evaluated in kidney cancer patients, in clinical development. Many other pharmaceutical and biotechnology companies have multi-targeted kinase inhibitors that could be competitive with Nexavar.

We compete with alternative therapies based on a variety of factors, including:

- product efficacy and safety;
- availability of patients for clinical trials;
- the timing and scope of regulatory approvals;
- availability of supply;
- marketing and sales capability;
- reimbursement coverage;
- price; and
- patent position.

Employees

As of December 31, 2005, we had 100 full-time employees of whom 12 hold Ph.D., M.D. or Pharm.D. degrees. Of our employees, 12 are in research and development, 63 are in sales and marketing and 25 are in corporate development, finance and administration. No employee of ours is represented by a labor union.

Company Information

We were incorporated in California in February 1992 and reincorporated in Delaware in May 1996. Our principal office is located at 2100 Powell Street, Emeryville, California 94608 and our telephone number is (510) 597-6500. Our website is located at *http://www.onyx-pharm.com.*

Available Information

We file electronically with the Securities and Exchange Commission, or SEC, our annual reports on Form 10-K, quarterly interim reports on Form 10-Q, current reports on Form 8-K, and amendments to those reports pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934. We maintain a site on the worldwide web at http://www.onyx-pharm.com; however, information found on our website is not incorporated by reference into this report. We make available free of charge on or through our website our SEC filings, including our annual report on Form 10-K, quarterly interim reports on Form 10-Q, current reports on Form 8-K and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC. Further, a copy of this Annual Report on Form 10-K is located at the Securities and Exchange Commission's Public Reference Rooms at 100 F Street, N.E., Washington, D. C. 20549. Information on the operation of the Public Reference Room can be obtained by calling the Securities and Exchange Commission at 1-800-SEC-0330. The Securities and Exchange Commission maintains a website that contains reports, proxy and information statements and other information regarding our filings at http://www.sec.gov.

Code of Ethics

In 2003, we adopted a code of ethics that applies to our principal officers, directors and employees. We have posted the text of our code of ethics on our website at http://www.onyx-pharm.com in connection with "Investors" materials. In addition, we intend to promptly disclose (1) the nature of any amendment to our code of ethics that applies to our principal executive officer, principal financial officer, principal accounting officer, or persons performing similar functions and (2) the nature of any waiver, including an implicit waiver, from a provision of our code of ethics that is granted to one of these specified officers, the name of such person who is granted the waiver and the date of the waiver on our website in the future.

Item 1A. ***Risk Factors***

In addition to the risks discussed in "Business" and "Management's Discussion and Analysis of Financial Condition and Results of Operations," our business is subject to the risks set forth below.

Nexavar® (sorafenib) tablets is our only product, and we do not have any other product candidates in Phase II or Phase III clinical development. If Nexavar is not commercially successful, we may be unable to identify and promote alternative product candidates and our business would fail.

Nexavar is our only product. In June 2003, following an unsuccessful search for new collaboration partners for our therapeutic virus product candidates, including ONYX-015 and ONYX-411, we announced that we were discontinuing the development of all therapeutic virus product candidates, eliminating all employee positions related to these candidates and terminating all related research and manufacturing capabilities. As a result, we do not have internal research and preclinical development capabilities. Our scientific and administrative employees are dedicated to managing our relationship with Bayer, and the development and commercialization of Nexavar, but are not actively discovering or developing new product candidates. As a result of the termination of our therapeutic virus program and drug discovery programs, we do not have a clinical development pipeline beyond Nexavar. If Nexavar is not commercially successful, we may be unable to identify and promote alternative product candidates to later stage clinical development, which would cause our business to fail.

Our clinical trial of Nexavar in kidney cancer may not yield statistically significant overall survival data, which may negatively impact the commercialization of Nexavar.

In March 2005, an independent data monitoring committee reviewed the safety and efficacy data from our ongoing Phase III trial of Nexavar in kidney cancer and concluded that the trial met its co-primary endpoint, resulting in statistically significant longer progression-free survival in those patients administered Nexavar versus those patients administered placebo. As a result, in July 2005, we and Bayer filed an NDA seeking approval of Nexavar to treat patients with kidney cancer in the United States. In September 2005, Bayer also filed a Marketing Authorization Application, or MAA, to the European Medicines Agency, or EMEA, for the approval to market Nexavar within the European Union to treat patients with kidney cancer.

In April 2005, we and Bayer recommended that all patients in our ongoing Phase III kidney cancer trial be offered access to Nexavar. This decision followed further review of the progression-free survival data, as well as additional discussions with the principal investigators, an independent data monitoring committee, and the FDA. As a result, patients who were previously administered placebo in the trial could have elected to receive Nexavar. This action has reduced the number of patients in the trial receiving placebo and is expected to negatively impact our ability to obtain statistically significant data on overall survival of patients with kidney cancer participating in this clinical trial.

In November 2005, an investigator-reported interim analysis on overall survival of patients in the Phase III kidney cancer trial was presented at the thirteenth European Cancer Conference, or ECCO. The analysis, which was based on the 220 deaths that had occurred by May 31, 2005, was conducted while the Phase III kidney cancer study was ongoing and soon after we and Bayer offered access to Nexavar to all patients in the trial, including those who had been receiving placebo. The investigator reported there was a 28% reduction in the risk of dying for patients receiving Nexavar compared to those who were not. While this represents a positive trend, with a p-value of 0.018, the data was not sufficient to be considered statistically significant according to the predefined specifications for this interim analysis. P-values are used to indicate the probability that results observed in two different samples are different due to chance alone, as opposed to a benefit due to the intervention, such as treatment with Nexavar. In order for the interim analysis of survival data reported by the investigator to be considered statistically significant, the p-value would have had to be less than 0.0005. The final survival analysis, which is planned when 540 deaths have occurred, is not expected for some time. Cross over of patients from placebo to Nexavar is likely to negatively impact our ability to obtain statistically significant overall survival data. Nexavar may be at a competitive disadvantage to third

parties' drugs if they generate statistically significant overall survival data which could impair our ability to successfully market Nexavar.

Nexavar has not been approved for sale outside of the United States, and may never receive foreign marketing approval.

In July 2005, we and Bayer filed for approval of Nexavar based on the progression-free survival data. While the FDA granted full approval in December 2005, we and Bayer do not know whether foreign regulatory authorities will grant approval to Nexavar as a treatment for kidney cancer. The foreign regulatory authorities may not be satisfied with the safety and efficacy data submitted in support of the foreign applications, which could result in either non-approval or a requirement of additional clinical trials or further analysis of existing data. Lack of marketing approval in a particular country would prevent us from selling Nexavar in that country, which could harm our business. In particular, if we do not receive approval from the EMEA to sell Nexavar in Europe, we will be prevented from selling into this potentially large market.

Nexavar was approved by the FDA for the treatment of advanced kidney cancer on the basis of the progression-free survival endpoint. Since we have not yet performed the final analysis on overall survival, we do not know whether we will achieve a statistically significant outcome on this endpoint. We expect that our ability to obtain statistically significant overall survival data will be negatively impacted by our April 2005 decision to allow patients that had been receiving placebo to elect to receive Nexavar. The EMEA and other regulatory authorities may have concerns or require further analysis of the manner in which tumor progression was determined. It is possible that in the absence of statistically significant overall survival data, Nexavar will not receive marketing approval by the EMEA or in individual countries, or will receive more limited approval than that granted by the FDA. In addition to the question of whether Nexavar has demonstrated sufficient efficacy in the treatment of kidney cancer, the EMEA and other regulatory authorities may have questions about the safety of the drug. For example, there were instances of greater adverse events in the treatment arm relative to the placebo arm of the most recent Phase III trial. In addition, as an element of the foreign approval process, the applicable regulatory authority must be satisfied with the processes and facilities for drug manufacture, which includes a physical inspection of those facilities. Any conclusion that there are shortcomings in the processes, facilities, or quality control procedures related to manufacture of the drug could result in a significant delay in foreign approval. For these or other reasons, there is no assurance that Nexavar will receive foreign approval on the basis of the current application without amendment, if it is approved at all.

There is a competing therapy approved for the treatment of advanced kidney cancer, and we expect the number of approved therapies could rapidly increase, which could harm the prospects for Nexavar in this indication.

Pfizer's drug, Sutent, a multi-kinase inhibitor, was recently approved by the FDA for treating patients with Gleevec-resistant gastrointestinal stromal tumors, or GIST, and Sutent also received accelerated approval for advanced kidney cancer. Pfizer has also submitted an MAA to the EMEA for Sutent. The FDA approval of Nexavar permits Nexavar to be used as a first-line therapy for the treatment of advanced kidney cancer. Similarly, Sutent can also be used to treat first-line patients. Moreover, Genentech's Avastin has been reported to have activity in kidney cancer, and Genentech has indicated that Avastin is now being used off-label for treatment of some kidney cancer patients. Both Genentech and Pfizer have pivotal Phase III kidney cancer studies underway in first-line patients that may include superior progression-free survival or overall survival data. It is not currently known which of Nexavar and these potential new kidney cancer products, if any, will be accepted by the medical community as the standard of care. The use of any particular therapy may limit the use of a competing therapy with a similar mechanism of action.

In addition, Wyeth is conducting a Phase III study of CCI-779, an mTOR inhibitor, in patients with advanced kidney cancer. Pfizer also has an earlier stage compound, AG-013736, a multi-kinase inhibitor, which is in clinical development and being evaluated in kidney cancer patients. Historically, the most commonly used therapeutic agents for patients suffering from metastatic kidney cancer were interleukin-2 (IL-2) and interferon-alpha (IFN).

With the development and approval of new anticancer therapies, it is anticipated that the initial, or first-line, treatment for many of these patients could shift to the new therapeutic products. The successful introduction of new therapies could significantly reduce the potential market for Nexavar in this indication. Decreased demand or price for Nexavar would harm our ability to realize revenue and profits from Nexavar which could cause our stock price to fall.

If our clinical trials fail to demonstrate that Nexavar is safe and effective for cancer types other than kidney cancer, we will be unable to broadly commercialize Nexavar as a treatment for cancer, and our business may fail.

In collaboration with Bayer, we are conducting multiple clinical trials of Nexavar. We have completed Phase I single-agent clinical trials of Nexavar. We are currently conducting a number of Phase Ib clinical trials of Nexavar in combination with other anticancer agents. Phase I trials are not designed to test the efficacy of a drug candidate but rather to test safety; to study pharmacokinetics, or how drug concentrations in the body change over time; to study pharmacodynamics, or how the drug candidate acts on the body over a period of time; and to understand the drug candidate's side effects at various doses and schedules.

With Bayer, we have completed Phase II clinical trials of Nexavar in kidney and liver cancer and are currently conducting Phase II clinical trials in breast, non-small cell lung, melanoma and other cancers. Phase II trials are designed to explore the efficacy of a product candidate in several different types of cancers and may be randomized and double-blinded to ensure that the results are due to the effects of the drug. In addition, in March 2005, we and Bayer initiated a Phase III clinical trial of Nexavar in patients with liver cancer. In May 2005, we and Bayer initiated a Phase III clinical trial of Nexavar in combination with the chemotherapeutic agents carboplatin and paclitaxel in patients with malignant melanoma. In February 2006, we and Bayer initiated a Phase III clinical trial of Nexavar in combination with carboplatin and paclitaxel in patients with NSCLC. Phase III trials are designed to more rigorously test the efficacy of a product candidate and are normally randomized and double-blinded.

Although we have received FDA approval for the use of Nexavar in the treatment of patients with advanced kidney cancer, the efficacy of Nexavar has not been proven in other types of cancer. Historically, many companies have failed to demonstrate the effectiveness of pharmaceutical product candidates in Phase III clinical trials notwithstanding favorable results in Phase I or Phase II clinical trials. In addition, if previously unforeseen and unacceptable side effects are observed, we may not proceed with further clinical trials of Nexavar. In our clinical trials, we treat patients who have failed conventional treatments and who are in advanced stages of cancer. During the course of treatment, these patients may die or suffer adverse medical effects for reasons unrelated to Nexavar. These adverse effects may impact the interpretation of clinical trial results, which could lead to an erroneous conclusion regarding the toxicity or efficacy of Nexavar.

Our clinical trials may fail to demonstrate that Nexavar is safe and effective as a treatment for types of cancer other than kidney cancer, which would prevent us from marketing Nexavar as a treatment for those other types of cancer, limiting the potential market for the product, which may cause our business to fail.

If serious adverse side effects are associated with Nexavar, approval for Nexavar could be revoked, sales of Nexavar could decline, and we may be unable to develop Nexavar as a treatment for other types of cancer.

The approved package insert for Nexavar for the treatment of patients with advanced kidney cancer warns of a number of observed adverse side effects:

- Hypertension may occur early in the course of therapy and blood pressure should be monitored weekly during the first six weeks of therapy and treated as needed.
- Incidence of bleeding, regardless of causality, was 15 percent for Nexavar vs. 8 percent for placebo and the incidence of treatment-emergent cardiac ischemia/infarction was 2.9 percent for Nexavar vs. 0.4 percent for placebo.

- Most common treatment-emergent adverse events with Nexavar were diarrhea, rash/desquamation, fatigue, hand-foot skin reaction, alopecia and nausea. Grade 3/4 adverse events were 38 percent for Nexavar vs. 28 percent for placebo.
- Women of child-bearing potential should be advised to avoid becoming pregnant and advised against breast-feeding.

In cases of any severe or persistent side effects, temporary treatment interruption, dose modification or permanent discontinuation should be considered.

If additional adverse side effects emerge, or a pattern of severe or persistent previously observed side effects is observed in the Nexavar patient population, the FDA could modify or revoke its approval of Nexavar or we may choose to withdraw it from the market. If this were to occur, we may be unable to obtain approval of Nexavar in additional indications and foreign regulatory agencies may decline to approve Nexavar for use in any indication. Any of these outcomes would have a material adverse impact on our business. In addition, if patients receiving Nexavar were to suffer harm as a result of their use of Nexavar, these patients or their representatives may bring claims against us. These claims, or the mere threat of these claims, could have a material adverse effect on our business and results of operations.

We are dependent upon our collaborative relationship with Bayer to manufacture and to further develop and commercialize Nexavar. There may be circumstances that delay or prevent the development and commercialization of Nexavar.

Our strategy for manufacturing and further developing and commercializing Nexavar depends in large part upon our relationship with Bayer. If we are unable to maintain our collaborative relationship with Bayer, we would need to undertake development, manufacturing and marketing activities at our own expense, which would significantly increase our capital requirements and limit the indications we are able to pursue and could prevent us from further commercializing Nexavar.

Under the terms of the collaboration agreement, we and Bayer are conducting multiple clinical trials of Nexavar. We and Bayer must agree on the development plan for Nexavar. If we and Bayer cannot agree, clinical trial progress could be significantly delayed or halted.

Under our agreement with Bayer, we have the opportunity to fund 50 percent of clinical development costs worldwide except in Japan, where Bayer will fund 100 percent of development costs and pay us a royalty on net sales. We are currently funding 50 percent of development costs for Nexavar and depend on Bayer to fund the balance of these costs. Our collaboration agreement with Bayer does not, however, create an obligation for either us or Bayer to fund additional development of Nexavar, or any other product candidate. If a party declines to fund development or ceases to fund development of a product candidate under the collaboration agreement, then that party will be entitled to receive a royalty on any product that is ultimately commercialized, but not to share in profits. Bayer could, upon 60 days notice, elect at any time to terminate its co-funding of the development of Nexavar. If Bayer terminates its co-funding of Nexavar development, we may be unable to fund the development costs on our own and may be unable to find a new collaborator, which could cause our business to fail.

Bayer has been the sponsor for all regulatory filings with the FDA. As a result, we have been dependent on Bayer's experience in filing and pursuing applications necessary to gain regulatory approvals. Bayer has limited experience in developing drugs for the treatment of cancer.

Our collaboration agreement with Bayer provides for Bayer to advance us creditable milestone-based payments. Bayer advanced us a total of $40.0 million pursuant to this provision. These funds are repayable out of a portion of our future profits and royalties, if any, from any of our products.

Our collaboration agreement with Bayer terminates when patents expire that were issued in connection with product candidates discovered under that agreement, or upon the time when neither we nor Bayer are entitled to profit sharing under that agreement, whichever is later. Bayer holds the global patent applications related to Nexavar. We currently anticipate that, if issued, the United States patent related to Nexavar will

expire in 2022, subject to possible patent-term extension, the entitlement to which and the term of which cannot presently be calculated.

We are subject to a number of additional risks associated with our dependence on our collaborative relationship with Bayer, including:

- the amount and timing of resource expenditures can vary because of decisions by Bayer;
- possible disagreements as to development plans, including clinical trials or regulatory approval strategy;
- the right of Bayer to terminate its collaboration agreement with us on limited notice and for reasons outside our control;
- loss of significant rights if we fail to meet our obligations under the collaboration agreement;
- withdrawal of support by Bayer following the development or acquisition by it of competing products; and
- possible disagreements with Bayer regarding the collaboration agreement or ownership of proprietary rights.

Due to these factors and other possible disagreements with Bayer, we may be delayed or prevented from further developing or commercializing Nexavar, or we may become involved in litigation or arbitration, which would be time consuming and expensive.

If Bayer's business strategy changes, it may adversely affect our collaborative relationship.

Bayer may change its business strategy. Decisions by Bayer to either reduce or eliminate its participation in the oncology field, or to add competitive agents to its portfolio, could reduce its financial incentive to promote Nexavar. A change in Bayer's business strategy may adversely affect activities under its collaboration agreement with us, which could cause significant delays and funding shortfalls impacting the activities under the collaboration and seriously harming our business.

Provisions in our collaboration agreement with Bayer may prevent or delay a change in control.

Our collaboration agreement with Bayer provides that if Onyx is acquired by another entity by reason of merger, consolidation or sale of all or substantially all of our assets, and Bayer does not consent to the transaction, then for 60 days following the transaction, Bayer may elect to terminate Onyx's co-development and co-promotion rights under the collaboration agreement. If Bayer were to exercise this right, Bayer would gain exclusive development and marketing rights to the product candidates developed under the collaboration agreement, including Nexavar. If this happened, Onyx, or the successor to Onyx, would receive a royalty based on any sales of Nexavar and other collaboration products, rather than a share of any profits. In this case, Onyx or its successor would be permitted to continue co-funding development, and the royalty rate would be adjusted to reflect this continued risk-sharing by Onyx or its successor. These provisions of our collaboration agreement with Bayer may have the effect of delaying or preventing a change in control, or a sale of all or substantially all of our assets, or may reduce the number of companies interested in acquiring Onyx.

Our clinical trials could take longer to complete than we project or may not be completed at all.

Although for planning purposes we project the commencement, continuation and completion of ongoing clinical trials for Nexavar, the actual timing of these events may be subject to significant delays relating to various causes, including actions by Bayer, scheduling conflicts with participating clinicians and clinical institutions, difficulties in identifying and enrolling patients who meet trial eligibility criteria and shortages of available drug supply. We may not complete clinical trials involving Nexavar as projected or at all.

We rely on Bayer, academic institutions and clinical research organizations to conduct, supervise or monitor most clinical trials involving Nexavar. We have less control over the timing and other aspects of these clinical trials than if we conducted them entirely on our own.

We are directly supervising and monitoring on our own certain Phase II and Phase III clinical trials of Nexavar for the treatment of malignant melanoma. Onyx has not conducted a clinical trial that has led to an NDA filing. Consequently, we may not have the necessary capabilities to successfully execute and complete these planned clinical trials in a way that leads to approval of Nexavar for the target indication. Failure to commence or complete, or delays in our planned clinical trials would prevent us from commercializing Nexavar in melanoma, and thus seriously harm our business.

We face intense competition and rapid technological change, and many of our competitors have substantially greater managerial resources than we have.

We are engaged in a rapidly changing and highly competitive field. We are seeking to develop and market product candidates that will compete with other products and therapies that currently exist or are being developed. Many other companies are actively seeking to develop products that have disease targets similar to those we are pursuing. Some of these competitive product candidates are in clinical trials, and others are approved. Competitors that target the same tumor types as our Nexavar program and that have commercial products or product candidates in clinical development include Pfizer, Novartis International AG, AstraZeneca PLC, OSI Pharmaceuticals, Inc., Genentech, Inc., Chiron Corporation and Abgenix, Inc., among others. A number of companies have agents targeting Vascular Endothelial Growth Factor, or VEGF; VEGF receptors; Epidermal Growth Factor, or EGF; EGF receptors; and other enzymes. These agents include antibodies and small molecules. OSI Pharmaceuticals with Tarceva™, a small molecule inhibitor of the EGF receptor has been approved in the United States for treatment of NSCLC and pancreatic cancer in combination with gemcitabine. Companies working on developing antibody approaches include Abgenix and ImClone Systems, Inc. ImClone has developed Erbitux, which is an antibody targeting the EGF receptor. Erbitux has been approved in the United States and the European Union for treatment of colorectal cancer, as well as in the United States for the treatment of most types of head and neck cancer. Genentech has developed Avastin™, an antibody targeting VEGF, which has received approvals in the United States and the European Union for treatment of colorectal cancer and is in clinical development for kidney cancer. In addition, many other pharmaceutical companies are developing novel cancer therapies that, if successful, would also provide competition for Nexavar.

Many of our competitors, either alone or together with collaborators, have substantially greater financial resources and research and development staffs. In addition, many of these competitors, either alone or together with their collaborators, have significantly greater experience than we do in:

- developing products;
- undertaking preclinical testing and human clinical trials;
- obtaining FDA and other regulatory approvals of products; and
- manufacturing and marketing products.

Accordingly, our competitors may succeed in obtaining patent protection, receiving FDA approval or commercializing product candidates before we do. If we receive FDA approval and commence commercial product sales, we will compete against companies with greater marketing and manufacturing capabilities, areas in which we have limited or no experience.

We also face, and will continue to face, competition from academic institutions, government agencies and research institutions. Further, we face numerous competitors working on product candidates to treat each of the diseases for which we are seeking to develop therapeutic products. In addition, our product candidates, if approved, will compete with existing therapies that have long histories of safe and effective use. We may also face competition from other drug development technologies and methods of preventing or reducing the incidence of disease and other classes of therapeutic agents.

Developments by competitors may render our product candidates obsolete or noncompetitive. We face and will continue to face intense competition from other companies for collaborations with pharmaceutical and biotechnology companies, for establishing relationships with academic and research institutions, and for

licenses to proprietary technology. These competitors, either alone or with collaborative parties, may succeed with technologies or products that are more effective than ours.

We anticipate that we will face increased competition in the future as new companies enter our markets and as scientific developments surrounding other cancer therapies continue to accelerate. We have made significant expenditures towards the development of Nexavar and the establishment of a commercialization infrastructure. If Nexavar cannot compete effectively in the marketplace, we may be unable to realize revenue from Nexavar sufficient to offset our expenditures towards its development and commercialization, and our business will suffer.

Our operating results are unpredictable and may fluctuate. If our operating results are below the expectations of securities analysts or investors, the trading price of our stock could decline.

Our operating results will likely fluctuate from fiscal quarter to fiscal quarter, and from year to year, and are difficult to predict. Sales of Nexavar commenced in late December 2005. Our operating expenses are largely independent of Nexavar sales in any particular period. We believe that our quarterly and annual results of operations may be negatively affected by a variety of factors. These factors include, but are not limited to, the level of patient demand for Nexavar, the ability of Bayer's distribution network to process and ship product on a timely basis, fluctuations in foreign exchange rates, investments in sales and marketing efforts to support the sales of Nexavar, investments in the research and development efforts of Nexavar, and expenditures we may incur to acquire additional products. It is, therefore, difficult for us to accurately forecast profits or losses. As a result, it is possible that in some quarters our operating results could be below the expectations of securities analysts or investors, which could cause the trading price of our common stock to decline, perhaps substantially.

We will need substantial additional funds, and our future access to capital is uncertain.

We will require substantial additional funds to conduct the costly and time-consuming clinical trials necessary to develop Nexavar for additional indications, pursue regulatory approval and commercialize this product in Europe and the rest of the world. Our future capital requirements will depend upon a number of factors, including:

- the size and complexity of our Nexavar program;
- decisions made by Bayer and Onyx to alter the size, scope and schedule of clinical development;
- our receipt of milestone-based payments;
- progress with clinical trials;
- the time and costs involved in obtaining regulatory approvals;
- the cost involved in enforcing patent claims against third parties and defending claims by third parties (both of which are shared with Bayer);
- the costs associated with acquisitions or licenses of additional products;
- competing technological and market developments; and
- global product commercialization activities.

We may not be able to raise additional financing on favorable terms, or at all. If we are unable to obtain additional funds, we may not be able to fund our share of commercialization expenses and clinical trials. We may also have to curtail operations or obtain funds through collaborative and licensing arrangements that may require us to relinquish commercial rights or potential markets or grant licenses that are unfavorable to us.

We believe that our existing capital resources and interest thereon will be sufficient to fund our current development plans into 2008. However, if we change our development plans, we may need additional funds sooner than we expect. In addition, we anticipate that our co-development costs for the Nexavar program may increase over the next several years as we continue our share of funding the clinical development program and

prepare for the potential product launches of Nexavar throughout the world. While these costs are unknown at the current time, we expect that we will need to raise substantial additional capital to continue the co-funding of the Nexavar program in future periods through and beyond 2008. We may have to curtail our funding of Nexavar if we cannot raise sufficient capital. If we do not continue to co-fund the further development of Nexavar, we will receive a royalty on future sales of products, instead of a share of profits.

If the specialty pharmacies and distributors that we and Bayer rely upon to sell our products fail to perform, our business may be adversely affected.

Our success depends on the continued customer support efforts of our network of specialty pharmacies and distributors. A specialty pharmacy is a pharmacy that specializes in the dispensing of medications for complex or chronic conditions, which often require a high level of patient education and ongoing management. The use of specialty pharmacies and distributors involves certain risks, including, but not limited to, risks that these specialty pharmacies and distributors will:

- not provide us with accurate or timely information regarding their inventories, the number of patients who are using Nexavar or complaints about Nexavar;
- not effectively sell or support Nexavar;
- reduce their efforts or discontinue to sell or support Nexavar;
- not devote the resources necessary to sell Nexavar in the volumes and within the time frames that we expect;
- be unable to satisfy financial obligations to us or others; or
- cease operations.

Any such failure may result in decreased product sales and profits, which would harm our business.

We have a history of losses, and we expect to continue to incur losses.

Our net loss for the year ended December 31, 2003 was $45.0 million, for the year ended December 31, 2004 was $46.8 million and for the year ended December 31, 2005 was $95.2 million. As of December 31, 2005, we had an accumulated deficit of approximately $345.8 million. We have incurred these losses principally from costs incurred in our research and development programs, from our general and administrative costs and the development of our commercialization infrastructure. It is not unusual for patients to be offered access to investigational compounds in late-stage clinical development. Such programs involve substantial costs. We expect to incur significant and increasing operating losses over the next several years as we continue our clinical trial activities and, with Bayer, establish commercial infrastructure in Europe and other parts of the world. We expect our operating losses to increase with our co-funding of ongoing Nexavar clinical and commercial activities under our collaboration agreement with Bayer.

We and Bayer only began to generate revenues from the sale of Nexavar in December 2005, and we must repay the milestone-based advances we received from Bayer from any future profits and royalties. We have made significant expenditures towards the development and commercialization of Nexavar, and may never realize sufficient product sales to offset these expenditures. Our ability to achieve profitability depends upon success by us and Bayer in completing development of Nexavar, obtaining required regulatory approvals and manufacturing and marketing the approved product.

We do not have manufacturing expertise or capabilities and are dependent on Bayer to fulfill our manufacturing needs, which could result in lost sales and the delay of clinical trials or regulatory approval.

Under our collaboration agreement with Bayer, Bayer has the manufacturing responsibility to supply Nexavar for clinical trials and to support our commercial requirements. However, should Bayer give up its right to co-develop Nexavar, we would have to manufacture Nexavar, or contract with another third party to do so for us. We lack the resources, experience and capabilities to manufacture Nexavar or any future product

candidates on our own and would require substantial funds to establish these capabilities. Consequently, we are, and expect to remain, dependent on third parties to manufacture our product candidates and products. These parties may encounter difficulties in production scale-up, including problems involving production yields, quality control and quality assurance and shortage of qualified personnel. These third parties may not perform as agreed or may not continue to manufacture our products for the time required by us to successfully market our products. These third parties may fail to deliver the required quantities of our products or product candidates on a timely basis and at commercially reasonable prices. Failure by these third parties could impair our ability to meet the market demand for Nexavar, and could delay our ongoing clinical trials and our applications for regulatory approval. If these third parties do not adequately perform, we may be forced to incur additional expenses to pay for the manufacture of products or to develop our own manufacturing capabilities.

We have the right to co-promote Nexavar in the United States, but we do not have proven sales or marketing expertise.

We have the right under our collaboration and co-promotion agreements with Bayer to co-promote Nexavar in the United States in conjunction with Bayer. While we have invested heavily in our commercialization infrastructure and intend to continue doing so, we may not successfully establish adequate marketing and sales capabilities or have sufficient resources to do so. If we do not further develop marketing and sales capabilities, we will be unable to meet our co-promotion obligations under our collaboration agreement, which could result in the loss of our co-promotion rights. If we do develop such capabilities, we will compete with other companies that have experienced and well-funded marketing and sales operations, and we will incur additional expenses.

We will be dependent on the efforts of Bayer to market and promote Nexavar in countries outside the United States where Nexavar may receive approval.

Under our collaboration and co-promotion agreements with Bayer, we and Bayer are co-promoting Nexavar in the United States. If we continue to co-promote Nexavar, and continue to co-fund development in the United States, we will share equally in profits or losses, if any, in the United States.

We do not, however, have the right to co-promote Nexavar in any country outside the United States, and will be dependent solely on Bayer to promote Nexavar in any foreign countries where Nexavar is approved. In all foreign countries, except Japan, Bayer would first receive a portion of the product revenues to repay Bayer for its foreign commercialization infrastructure, before determining our share of profits and losses. In Japan, we would receive a royalty on any sales of Nexavar.

We have limited ability to direct Bayer in its promotion of Nexavar in foreign countries where Nexavar is approved, if any. Bayer may not have sufficient experience to promote oncology products in foreign countries and may fail to devote appropriate resources to this task. If Bayer fails to adequately promote Nexavar in foreign countries, we may be unable to obtain any remedy against Bayer. If this were to happen, sales of Nexavar in any foreign countries where Nexavar is approved may be harmed, which would negatively impact our business.

Similarly, Bayer may establish a sales and marketing infrastructure for Nexavar outside the United States that is too large and expensive in view of the magnitude of the Nexavar sales opportunity or establish this infrastructure too early in view of the ultimate timing of regulatory approval. Since we share in the profits and losses arising from sales of Nexavar outside of the United States, rather than receiving a royalty (except in Japan), we are at risk with respect to the success or failure of Bayer's commercial decisions related to Nexavar as well as the extent to which Bayer succeeds in the execution of its strategy.

If we lose our key employees and consultants or are unable to attract or retain qualified personnel, our business could suffer.

Our future success will depend in large part on the continued services of our management personnel, including Hollings C. Renton, our Chairman, President and Chief Executive Officer, Edward F. Kenney, our

Executive Vice President and Chief Business Officer and Henry J. Fuchs, our Executive Vice President and Chief Medical Officer as well as each of our other executive officers. The loss of the services of one or more of these key employees could have an adverse impact on our business. We do not maintain key person life insurance on any of our officers, employees or consultants, other than for our chief executive officer. Any of our key personnel could terminate their employment with us at any time and without notice. We depend on our continued ability to attract, retain and motivate highly qualified personnel. We face competition for qualified individuals from numerous pharmaceutical and biotechnology companies, universities and other research institutions.

In 2003, we restructured our operations to reflect an increased priority on the development of Nexavar and discontinued our therapeutic virus program. As a result of the restructuring, we eliminated approximately 75 positions, including our entire scientific team associated with the therapeutic virus program. Our remaining scientific and administrative employees are engaged in managing our collaboration with Bayer to develop Nexavar, but are not actively involved in new product candidate discovery. If we resume our research and development of other product candidates, we will need to hire individuals with the appropriate scientific skills. If we cannot hire these individuals in a timely fashion, we will be unable to engage in new product candidate discovery activities.

We have rapidly expanded our sales and marketing operations, and any difficulties managing this growth could disrupt our operations.

During 2005, in anticipation of the commercial launch of Nexavar in the United States, we rapidly expanded and developed our sales and marketing operations. We increased expenditures in these areas, hired additional employees and expanded the scope of our operations. Prior to December 2005, we did not have any products approved for sale, so our sales and marketing operations, and our ability to manage them, are untested. We do not have any history of managing sales and marketing operations, and may be unable to do so. If we are unable to effectively manage our newly expanded sales and marketing capacity, or if this capacity proves inadequate, we may not be able to implement our business plan.

The market may not accept our products and pharmaceutical pricing and reimbursement pressures may reduce profitability.

Nexavar or any future product candidates that we may develop may not gain market acceptance among physicians, patients, healthcare payors and the medical community or the market may not be as large as forecasted. One factor that may affect market acceptance of Nexavar or any future products we may develop is the availability of third-party reimbursement. Our commercial success may depend, in part, on the availability of adequate reimbursement for patients from third-party healthcare payors, such as government and private health insurers and managed care organizations. Third-party payors are increasingly challenging the pricing of medical products and services and their reimbursement practices may affect the price levels for Nexavar. In addition, the market for Nexavar may be limited by third-party payors who establish lists of approved products and do not provide reimbursement for products not listed. If Nexavar is not on the approved lists, our sales may suffer.

If Nexavar is approved in Europe, its success there will also depend largely on obtaining and maintaining government reimbursement because in many European countries patients will not use prescription drugs that are not reimbursed by their governments. In addition, negotiating prices with governmental authorities can delay commercialization by twelve months or more. Even if reimbursement is available, reimbursement policies may adversely affect our ability to sell our products on a profitable basis. For example, in Europe as in many international markets, governments control the prices of prescription pharmaceuticals and expect prices of prescription pharmaceuticals to decline over the life of the product or as volumes increase. We believe that this will continue into the foreseeable future as governments struggle with escalating health care spending.

A number of additional factors may limit the market acceptance of products including the following:

- rate of adoption by healthcare practitioners;
- types of cancer for which the product is approved;
- rate of a product's acceptance by the target population;
- timing of market entry relative to competitive products;
- availability of alternative therapies;
- price of our product relative to alternative therapies;
- extent of marketing efforts by us and third-party distributors or agents retained by us; and
- side effects or unfavorable publicity concerning our products or similar products.

If Nexavar or any future product candidates that we may develop do not achieve market acceptance, we may not realize sufficient revenues from product sales, which may cause our stock price to decline.

We are subject to extensive government regulation, which can be costly, time consuming and subject us to unanticipated delays.

Drug candidates under development are subject to extensive and rigorous domestic and foreign regulation. We have not received regulatory approval in any foreign market for Nexavar or any other product candidate, and have received approval in the United States for the use of Nexavar only in the treatment of advanced kidney cancer.

We expect to rely on Bayer to manage communications with regulatory agencies, including filing new drug applications and generally directing the regulatory approval process for Nexavar. We and Bayer may not obtain necessary additional approvals from the FDA or other regulatory authorities. If we fail to obtain required governmental approvals, we will experience delays in or be precluded from marketing Nexavar in particular indications or countries. The FDA or other regulatory authorities may approve only limited label information for the product. The label information describes the indications and methods of use for which the product is authorized, and if overly restrictive may limit our and Bayer's ability to successfully market any approved product. If we have disagreements as to ownership of clinical trial results or regulatory approvals, and the FDA refuses to recognize us as holding, or having access to, the regulatory approvals necessary to commercialize our product candidates, we may experience delays in or be precluded from marketing products.

The regulatory review and approval process takes many years, requires the expenditure of substantial resources, involves post-marketing surveillance and may involve ongoing requirements for post-marketing studies. Additional or more rigorous governmental regulations may be promulgated that could delay regulatory approval of Nexavar. Delays in obtaining regulatory approvals may:

- adversely affect the successful commercialization of Nexavar;
- impose costly procedures on us;
- diminish any competitive advantages that we may attain; and
- adversely affect our receipt of revenues or royalties.

Even after Nexavar and any other products we may develop are marketed, the products and their manufacturers are subject to continual review. Later discovery of previously unknown problems with Nexavar or manufacturing and production by Bayer or other third parties may result in restrictions on Nexavar, including withdrawal of Nexavar from the market. In addition, problems or failures with the products of others, before or after regulatory approval, including our competitors, could have an adverse effect on our ability to obtain or maintain regulatory approval for Nexavar. If we fail to comply with applicable regulatory requirements, we could be subject to penalties, including fines, suspensions of regulatory approval, product recall, seizure of products and criminal prosecution.

We may incur significant liability if it is determined that we are promoting the "off-label" use of drugs or are otherwise found in violation of federal and state regulations in the United States or elsewhere.

Physicians may prescribe drug products for uses that are not described in the product's labeling and that differ from those approved by the FDA or other applicable regulatory agencies. Off-label uses are common across medical specialties. Physicians may prescribe Nexavar for the treatment of cancers other than advanced kidney cancer, although neither we nor Bayer are permitted to promote Nexavar for the treatment of any indication other than kidney cancer, and the FDA and other regulatory agencies have not approved the use of Nexavar for any other indication. Although the FDA and other regulatory agencies do not regulate a physician's choice of treatments, the FDA and other regulatory agencies do restrict communications on the subject of off-label use. Companies may not promote drugs for off-label uses. Accordingly, prior to approval of Nexavar for use in any indications other than advanced kidney cancer, we may not promote Nexavar for these indications. The FDA and other regulatory agencies actively enforce regulations prohibiting promotion of off-label uses and the promotion of products for which marketing clearance has not been obtained. A company that is found to have improperly promoted off-label uses may be subject to significant liability, including civil and administrative remedies as well as criminal sanctions.

Notwithstanding the regulatory restrictions on off-label promotion, the FDA and other regulatory authorities allow companies to engage in truthful, non-misleading, and non-promotional speech concerning their products. We engage in medical education activities and communicate with investigators and potential investigators regarding our clinical trials. Although we believe that all of our communications regarding Nexavar are in compliance with the relevant regulatory requirements, the FDA or another regulatory authority may disagree, and we may be subject to significant liability, including civil and administrative remedies as well as criminal sanctions.

We may not be able to protect our intellectual property or operate our business without infringing upon the intellectual property rights of others.

We can protect our technology from unauthorized use by others only to the extent that our technology is covered by valid and enforceable patents or effectively maintained as trade secrets. As a result, we depend in part on our ability to:

- obtain patents;
- license technology rights from others;
- protect trade secrets;
- operate without infringing upon the proprietary rights of others; and
- prevent others from infringing on our proprietary rights.

In the case of Nexavar, the global patent applications related to this product candidate are held by Bayer, but licensed to us in conjunction with our collaboration agreement with Bayer. We currently anticipate that, if issued, the United States patent related to Nexavar will expire in 2022, subject to possible patent-term extension, the entitlement to which and the term of which cannot presently be calculated. Patent applications for Nexavar are also pending throughout the world. As of December 31, 2005, we owned or had licensed rights to 51 United States patents and 34 United States patent applications and, generally, foreign counterparts of these filings. Most of these patents or patent applications cover protein targets used to identify product candidates during the research phase of our collaborative agreements with Warner-Lambert Company or Bayer, or aspects of our now discontinued virus program. Additionally, we have corresponding patents or patent applications pending or granted in certain foreign jurisdictions.

The patent positions of biotechnology and pharmaceutical companies are highly uncertain and involve complex legal and factual questions. Our patents, or patents that we license from others, may not provide us with proprietary protection or competitive advantages against competitors with similar technologies. Competitors may challenge or circumvent our patents or patent applications. Courts may find our patents invalid. Due to the extensive time required for development, testing and regulatory review of our potential products, our

patents may expire or remain in existence for only a short period following commercialization, which would reduce or eliminate any advantage the patents may give us.

We may not have been the first to make the inventions covered by each of our issued or pending patent applications, or we may not have been the first to file patent applications for these inventions. Competitors may have independently developed technologies similar to ours. We may need to license the right to use third-party patents and intellectual property to develop and market our product candidates. We may not acquire required licenses on acceptable terms, if at all. If we do not obtain these required licenses, we may need to design around other parties' patents, or we may not be able to proceed with the development, manufacture or, if approved, sale of our product candidates. We may face litigation to defend against claims of infringement, assert claims of infringement, enforce our patents, protect our trade secrets or know-how, or determine the scope and validity of others' proprietary rights. In addition, we may require interference proceedings declared by the United States Patent and Trademark Office to determine the priority of inventions relating to our patent applications. These activities, and especially patent litigation, are costly.

Bayer may have rights to publish data and information in which we have rights. In addition, we sometimes engage individuals, entities or consultants to conduct research that may be relevant to our business. The ability of these individuals, entities or consultants to publish or otherwise publicly disclose data and other information generated during the course of their research is subject to certain contractual limitations. The nature of the limitations depends on various factors, including the type of research being conducted, the ownership of the data and information and the nature of the individual, entity or consultant. In most cases, these individuals, entities or consultants are, at the least, precluded from publicly disclosing our confidential information and are only allowed to disclose other data or information generated during the course of the research after we have been afforded an opportunity to consider whether patent and/or other proprietary protection should be sought. If we do not apply for patent protection prior to publication or if we cannot otherwise maintain the confidentiality of our technology and other confidential information, then our ability to receive patent protection or protect our proprietary information will be harmed.

We face product liability risks and may not be able to obtain adequate insurance.

The sale of Nexavar and its ongoing use in clinical trials, and the sale of any approved products, exposes us to liability claims. Although we are not aware of any historical or anticipated product liability claims against us, if we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of Nexavar.

We believe that we have obtained reasonably adequate product liability insurance coverage that includes the commercial sale of Nexavar and our clinical trials. However, the cost of insurance coverage is rising. We may not be able to maintain insurance coverage at a reasonable cost. We may not be able to obtain additional insurance coverage that will be adequate to cover product liability risks that may arise should a future product candidate receive marketing approval. Regardless of merit or eventual outcome, product liability claims may result in:

- decreased demand for a product;
- injury to our reputation;
- withdrawal of clinical trial volunteers; and
- loss of revenues.

Thus, whether or not we are insured, a product liability claim or product recall may result in losses that could be material.

Our stock price is volatile.

The market price of our common stock has been volatile and is likely to continue to be volatile. For example, during the period beginning January 1, 2003 and ending December 31, 2005, the closing sales price

for one share of our common stock reached a high of $58.75 and a low of $4.65. Factors affecting our stock price include:

- interim or final results of, or speculation about, clinical trials from Nexavar;
- changes in the regulatory approval requirements;
- ability to accrue patients into clinical trials;
- success or failure in, or speculation about, obtaining regulatory approval by us or our competitors;
- public concern as to the safety and efficacy of our product candidates;
- developments in our relationship with Bayer;
- developments in patent or other proprietary rights;
- additions or departures of key personnel;
- announcements by us or our competitors of technological innovations or new commercial therapeutic products;
- published reports by securities analysts;
- statements of governmental officials; and
- changes in healthcare reimbursement policies.

Existing stockholders have significant influence over us.

Our executive officers, directors and five-percent stockholders own, in the aggregate, approximately 24 percent of our outstanding common stock. As a result, these stockholders will be able to exercise substantial influence over all matters requiring stockholder approval, including the election of directors and approval of significant corporate transactions. This could have the effect of delaying or preventing a change in control of our company and will make some transactions difficult or impossible to accomplish without the support of these stockholders.

Bayer, a collaborative party, has the right, which it is not currently exercising, to have its nominee elected to our board of directors as long as we continue to collaborate on the development of a compound. Because of these rights, ownership and voting arrangements, our officers, directors, principal stockholders and collaborator may be able to effectively control the election of all members of the board of directors and determine all corporate actions.

We are at risk of securities class action litigation due to our expected stock price volatility.

In the past, stockholders have often brought securities class action litigation against a company following a decline in the market price of its securities. This risk is especially acute for us, because biotechnology companies have experienced greater than average stock price volatility in recent years and, as a result, have been subject to, on average, a greater number of securities class action claims than companies in other industries. Following our announcement in October 2004 of Phase II clinical trial data in patients with advanced kidney cancer, our stock price declined significantly. Our closing stock price on the last trading day before the announcement was $40.81, and our closing stock price on the day of the announcement was $27.34. We may in the future be the target of securities class action litigation. Securities litigation could result in substantial costs, could divert management's attention and resources, and could seriously harm our business, financial condition and results of operations.

Provisions in Delaware law, our charter and executive change of control agreements we have entered into may prevent or delay a change of control.

We are subject to the Delaware anti-takeover laws regulating corporate takeovers. These anti-takeover laws prevent Delaware corporations from engaging in a merger or sale of more than ten percent of its assets

with any stockholder, including all affiliates and associates of the stockholder, who owns 15 percent or more of the corporation's outstanding voting stock, for three years following the date that the stockholder acquired 15 percent or more of the corporation's stock unless:

- the board of directors approved the transaction where the stockholder acquired 15 percent or more of the corporation's stock;
- after the transaction in which the stockholder acquired 15 percent or more of the corporation's stock, the stockholder owned at least 85 percent of the corporation's outstanding voting stock, excluding shares owned by directors, officers and employee stock plans in which employee participants do not have the right to determine confidentially whether shares held under the plan will be tendered in a tender or exchange offer; or
- on or after this date, the merger or sale is approved by the board of directors and the holders of at least two-thirds of the outstanding voting stock that is not owned by the stockholder.

As such, these laws could prohibit or delay mergers or a change of control of us and may discourage attempts by other companies to acquire us.

Our certificate of incorporation and bylaws include a number of provisions that may deter or impede hostile takeovers or changes of control or management. These provisions include:

- our board is classified into three classes of directors as nearly equal in size as possible with staggered three-year terms;
- the authority of our board to issue up to 5,000,000 shares of preferred stock and to determine the price, rights, preferences and privileges of these shares, without stockholder approval;
- all stockholder actions must be effected at a duly called meeting of stockholders and not by written consent;
- special meetings of the stockholders may be called only by the chairman of the board, the chief executive officer, the board or ten percent or more of the stockholders entitled to vote at the meeting; and
- no cumulative voting.

These provisions may have the effect of delaying or preventing a change in control, even at stock prices higher than the then current stock price.

We have entered into change in control severance agreements with each of our executive officers. These agreements provide for the payment of severance benefits and the acceleration of stock option vesting if the executive officer's employment is terminated within 24 months of a change in control of Onyx. These change in control severance agreements may have the effect of preventing a change in control.

Accounting pronouncements may affect our future financial position and results of operations.

There may be new accounting pronouncements or regulatory rulings, which may have an effect on our future financial position and results of operations. In December 2004, the Financial Accounting Standards Board, or FASB, issued a revision of Statement of Financial Accounting Standards, or FAS, No. 123, "Accounting for Stock-Based Compensation." The revision is referred to as "FAS 123(R) — Share-Based Payment", which supersedes Accounting Principles Board Opinion No. 25, "Accounting for Stock Issued to Employees," and will require companies to recognize compensation expense, using a fair-value based method, for costs related to share-based payments including stock options and stock issued under our employee stock plans. We will adopt FAS 123(R) using the modified prospective basis on January 1, 2006. We expect that the adoption of FAS 123(R) will have a material adverse impact on our results of operations and our net loss per share. However, our estimate of future stock-based compensation expense will be affected by a number of items including our stock price, the number of stock options our board of directors may grant in 2006, as well as a number of complex and subjective valuation adjustments and the related tax impact. These valuation assumptions include, but are not limited to, the volatility of our stock price and employee stock option exercise behaviors.

Item 1B. ***Unresolved Staff Comments***

None

Item 2. ***Properties***

We occupy 23,000 square feet of office space in our primary facility in Emeryville, California, which we began occupying in December 2004. The lease expires in February 2010 with an option to extend the lease for an additional three years. Previously we occupied approximately 50,000 square feet of office and laboratory space in Richmond, California. The lease for that facility expired in April 2005.

We also lease an additional 9,000 square feet of space in a secondary facility in Richmond, California. The lease for this facility expires in September 2010 with renewal options at the end of the lease for two subsequent five-year terms. We are currently subleasing this facility. Please refer to Note 6 of the accompanying financial statements for further information regarding our lease obligations.

Item 3. ***Legal Proceedings***

We are not a party to any material legal proceedings.

Item 4. ***Submission of Matters to a Vote of Securities Holders***

No matters were submitted to a vote of the Company's stockholders during the quarter ended December 31, 2005.

PART II.

Item 5. ***Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities***

Our common stock is traded on the Nasdaq National Market (NASDAQ) under the symbol "ONXX." We commenced trading on NASDAQ on May 9, 1996. The following table presents the high and low closing sales prices per share of our common stock reported on NASDAQ.

	Common Stock			
	2005		2004	
	High	Low	High	Low
First Quarter	$33.77	$25.30	$41.53	$28.75
Second Quarter	33.46	23.70	58.75	37.80
Third Quarter	27.66	19.30	43.16	30.60
Fourth Quarter	30.14	22.45	44.65	26.72

On March 8, 2006, the last reported sales price of our common stock on NASDAQ was $28.20 per share.

Holders

There were approximately 236 holders of record of our common stock as of March 8, 2006.

Dividends

Onyx has not paid cash dividends on its common stock and does not plan to pay any cash dividends in the foreseeable future.

Securities Authorized for Issuance Under Equity Compensation Plans as of December 31, 2005

Plan Category (1)	Number of securities to be issued upon exercise of outstanding options, warrants and rights	Weighted-average exercise price of outstanding options, warrants and rights	Number of securities remaining available for future issuance under equity compensation plans (excluding securities reflected in column a)
	Column a	Column b	Column c
Equity compensation plans approved by security holders...	3,806,081	$21.17	3,649,049(2)

(1) We have no equity compensation plans not approved by security holders.

(2) Of these securities, 38,588 shares remain available for purchase under our Employee Stock Purchase Plan.

Recent Sales of Unregistered Securities

On November 14, 2005, Onyx issued an aggregate of 18,518 shares of its common stock to DKR Soundshore Private Investors Holding Fund Ltd. pursuant to the cash exercise of a warrant dated May 7, 2002. The warrant was exercisable for 18,518 shares of common stock and had an exercise price of $9.59 per share. The issuance of the shares pursuant to this warrant was exempt from registration under the Securities Act of 1933 in reliance on Section 4(2) promulgated thereunder.

Issuer Purchases of Equity Securities

We did not repurchase any of our equity securities during the fiscal year ended December 31, 2005.

Item 6. ***Selected Financial Data***

This section presents our selected historical financial data. You should read carefully the financial statements and the notes thereto included in this report and "Management's Discussion and Analysis of Financial Condition and Results of Operations."

The Statement of Operations data for the years ended December 31, 2005, 2004, and 2003 and the Balance Sheet data as of December 31, 2005 and 2004 have been derived from our audited financial statements included elsewhere in this report. The Statement of Operations data for the years ended December 31, 2002 and 2001 and the Balance Sheet data as of December 31, 2003, 2002 and 2001 have been derived from our audited financial statements that are not included in this report. Historical results are not necessarily indicative of future results. See the Notes to Financial Statements for an explanation of the method used to determine the number of shares used in computing basic and diluted net loss per share.

	Year Ended December 31,				
	2005	2004	2003	2002	2001
	(In thousands, except per share data)				
Statement of Operations Data:					
Total revenue	$ 1,000	$ 500	$ —	$ 2,715	$ 15,846
Operating expenses:					
Research and development	63,120	35,846	32,059	43,604	39,530
Selling, general and administrative	39,671	14,316	7,939	6,192	7,049
Restructuring	—	258	5,530	—	812
Loss from operations	(101,791)	(49,920)	(45,528)	(47,081)	(31,545)
Interest and other income and expense, net	6,617	3,164	559	1,294	3,973
Net loss	$ (95,174)	$(46,756)	$(44,969)	$(45,787)	$(27,572)
Basic and diluted net loss per share	$ (2.64)	$ (1.36)	$ (1.73)	$ (2.23)	$ (1.50)
Shares used in computing basic and diluted net loss per share	36,039	34,342	25,953	20,535	18,385

	December 31,				
	2005	2004	2003	2002	2001
			(In thousands)		
Balance Sheet Data:					
Cash, cash equivalents, and marketable securities	$ 284,680	$ 209,624	$ 105,400	$ 39,833	$ 58,466
Total assets	294,665	215,546	109,138	46,241	65,782
Working capital	241,678	197,873	92,826	28,727	48,669
Advance from collaboration partner	30,000	20,000	20,000	5,000	—
Accumulated deficit	(345,810)	(250,636)	(203,880)	(158,911)	(113,124)
Total stockholders' equity	223,240	179,988	73,519	28,784	55,085

Item 7. *Management's Discussion and Analysis of Financial Condition and Results of Operations*

The following Management's Discussion and Analysis of Financial Condition and Results of Operations contains forward-looking statements that involve risks and uncertainties. We use words such as "may," "will," "expect," "anticipate," "estimate," "intend," "plan," "predict," "potential," "believe," "should" and similar expressions to identify forward-looking statements. These statements appearing throughout our 10-K are statements regarding our intent, belief, or current expectations, primarily regarding our operations. You should not place undue reliance on these forward-looking statements, which apply only as of the date of this Annual Report on Form 10-K. Our actual results could differ materially from those anticipated in these forward-looking statements for many reasons, including those set forth under "Business" Item 1A "Risk Factors" and elsewhere in this Annual Report on Form 10-K.

Overview

We are a biopharmaceutical company building an oncology business by developing innovative therapies that target the molecular mechanisms implicated in cancer. With our collaborators, we are developing small molecule drugs with the goal of *changing the way cancer is treated*™. A common feature of cancer cells is the excessive activation of signaling pathways that cause abnormal cell proliferation. In addition, tumors require oxygen and nutrients from newly formed blood vessels to support their growth. The formation of these new blood vessels is a process called angiogenesis. We are applying our expertise to develop oral anticancer therapies designed to prevent cancer cell proliferation and angiogenesis by inhibiting proteins that signal or support tumor growth. By exploiting the genetic differences between cancer cells and normal cells, we aim to create novel anticancer agents that minimize damage to healthy tissue.

Our lead product, Nexavar® (sorafenib) tablets, being developed with our collaborator, Bayer Pharmaceuticals Corporation, or Bayer, was approved by the U.S. Food and Drug Administration, or FDA, in December 2005 for the treatment of individuals with advanced kidney cancer. This approval marked the first newly approved drug for patients with this disease in over a decade. Nexavar is a novel, orally available multi-kinase inhibitor and is one of a new class of anticancer treatments that target growth signaling.

In August 2005, we received the third milestone advance from Bayer for $10.0 million in connection with the filing of the New Drug Application, or NDA, for Nexavar. In January 2006, we received the fourth and final $10.0 million milestone advance from Bayer as a result of the FDA approval.

In November 2005, we sold 5,000,000 shares of our common stock at $25.25 per share in an underwritten public offering pursuant to an effective registration statement previously filed with the Securities and Exchange Commission. Also in November 2005, the underwriters for the offering exercised their over-allotment option and purchased an additional 750,000 shares of our common stock to cover over-allotments at a price of $25.25 per share. We received aggregate net cash proceeds of approximately $136.2 million from this public offering.

On March 6, 2006, we and Bayer entered into a Co-Promotion Agreement to co-promote Nexavar in the United States. This agreement supersedes those provisions of the original 1994 Collaboration Agreement that relate to the co-promotion of Nexavar in the United States between Bayer and us. Outside of the United States, the terms of the Collaboration Agreement continue to govern. Under the terms of the Co-Promotion Agreement and consistent with the Collaboration Agreement, we will share equally in the profits or losses of Nexavar, if any, in the United States, subject only to our continued co-funding of the development costs of Nexavar worldwide, excluding Japan. Please read Note 13 of the Notes to Financial Statements included in Item 8 of this Form 10-K for further information.

We have not been profitable since inception and expect to incur substantial and potentially increasing losses for the foreseeable future, due to expenses associated with the continuing development and commercialization of Nexavar. We expect that losses will fluctuate from quarter to quarter and that such fluctuations may be substantial. As of December 31, 2005, our accumulated deficit was approximately $345.8 million.

Our business is subject to significant risks, including the risks inherent in our development efforts, the results of the Nexavar clinical trials, the marketing of Nexavar as a treatment for patients with advanced kidney cancer, our dependence on collaborative parties, uncertainties associated with obtaining and enforcing patents, the lengthy and expensive regulatory approval process and competition from other products. For a discussion of these and some of the other risks and uncertainties affecting our business, see Item 1A "Risk Factors" of this Annual Report on Form 10-K.

Critical Accounting Policies and the Use of Estimates

The accompanying discussion and analysis of our financial condition and results of operations are based upon our financial statements and the related disclosures, which have been prepared in accordance with accounting principles generally accepted in the United States. The preparation of these financial statements requires us to make estimates, assumptions and judgments that affect the reported amounts in our financial statements and accompanying notes. These estimates form the basis for making judgments about the carrying values of assets and liabilities. We base our estimates and judgments on historical experience and on various other assumptions that we believe to be reasonable under the circumstances. Significant estimates used in 2005 included assumptions used in the determination of stock-based compensation related to all stock options granted. Actual results could differ materially from these estimates.

We believe the following policies to be the most critical to an understanding of our financial condition and results of operations, because they require us to make estimates, assumptions and judgments about matters that are inherently uncertain.

Stock-Based Compensation: The preparation of the financial statement footnotes requires us to estimate the fair value of all stock options granted. While fair value may be readily determinable for awards of stock, market quotes are not available for long-term, nontransferable stock options because these instruments are not traded. We currently use the Black-Scholes option-pricing model to estimate the fair value of stock options. However, the Black-Scholes model was developed for use in estimating the fair value of traded options, which have no vesting restrictions and are fully transferable. Option valuation models require the input of highly subjective assumptions, including but not limited to stock price volatility and stock option exercise behavior. We are currently evaluating our option valuation methodologies and assumptions in light of evolving accounting standards related to accounting for stock-based compensation. We expect to continue to use the Black-Scholes model for valuing our stock-based compensation expense. However, our estimate of future stock-based compensation expense will be affected by a number of items including our stock price, the number of stock options our board of directors may grant in 2006, as well as a number of complex and subjective valuation adjustments and the related tax effect. These valuation assumptions include, but are not limited to, the volatility of our stock price and stock option exercise behaviors. Actual results could differ materially from these estimates.

Research and Development Expense: In accordance with Financial Accounting Standards Board, or FASB, Statement of Financial Accounting Standards, or FAS, No. 2, "Accounting for Research and Development Costs," research and development costs are charged to expense when incurred. The major components of research and development costs include clinical manufacturing costs, clinical trial expenses, consulting and other third-party costs, salaries and employee benefits, supplies and materials and allocations of various overhead and occupancy costs. Not all research and development costs are incurred by us. A significant portion of our research and development expenses, approximately 83 percent in 2005, 93 percent in 2004 and 60 percent in 2003, relates to our cost sharing arrangement with Bayer and represents our share of the research and development costs incurred by Bayer. Such amounts are recorded based on invoices and other information we receive from Bayer. When such invoices have not been received, we must estimate the amounts owed to Bayer based on discussions with Bayer. In addition, research and development costs incurred by us and reimbursed by Bayer are recorded as a reduction to research and development expense.

In instances where we enter into agreements with third parties for clinical trials and other consulting activities, costs are expensed upon the earlier of when non-refundable amounts are due or as services are

performed. Amounts due under such arrangements may be either fixed fee or fee for service, and may include upfront payments, monthly payments, and payments upon the completion of milestones or receipt of deliverables.

Our cost accruals for clinical trials are based on estimates of the services received and efforts expended pursuant to contracts with numerous clinical trial sites and clinical research organizations. In the normal course of business we contract with third parties to perform various clinical trial activities in the on-going development of potential products. The financial terms of these agreements are subject to negotiation and variation from contract to contract and may result in uneven payment flows. Payments under the contracts depend on factors such as the achievement of certain events, the successful enrollment of patients, and the completion of portions of the clinical trial or similar conditions. The objective of our accrual policy is to match the recording of expenses in our consolidated financial statements to the actual services received and efforts expended. As such, expense accruals related to clinical trials are recognized based on our estimate of the degree of completion of the event or events specified in the specific clinical study or trial contract. We monitor service provider activities to the extent possible; however, if we underestimated activity levels associated with various studies at a given point in time, we could record significant research and development expenses in future periods.

Results of Operations

Years Ended December 31, 2005, 2004 and 2003

Total Revenue. Total revenue was $1.0 million in 2005, $500,000 in 2004, and zero in 2003. Total revenue in 2005 represented a payment from Shanghai Sunway Biotech Co. Ltd. in exchange for the transfer to Shanghai Sunway of the intellectual property and know-how related to ONYX-015. We have no ongoing performance obligations under this agreement. Total revenue in 2004 of $500,000 represented a milestone payment from Warner-Lambert, now a subsidiary of Pfizer Inc, when they initiated Phase I clinical testing advancing a lead candidate from our previous cell cycle kinase discovery collaboration. We had no revenue in 2003. Nexavar was approved in late December 2005 and product revenue, if any, will likely fluctuate from fiscal quarter to fiscal quarter and from year to year, and is difficult to predict.

Research and Development Expenses. Research and development expenses were $63.1 million in 2005, a net increase of $27.3 million, or 76 percent, from 2004. In 2005, the increase in research and development expenses were primarily driven by a $28.7 million increase in Onyx's share of codevelopment costs for the Nexavar program, principally for the clinical trial program which included the expanded access program in the Phase III kidney cancer trial initiated in the second quarter of 2005. In addition, 2005 Nexavar development costs reflect the ongoing pivotal Phase III kidney cancer trial, a Phase III trial in liver cancer initiated in the first quarter of 2005 and a Phase III trial in metastatic melanoma initiated in May 2005, as well as several Phase Ib and II clinical trials. This increase was partially offset by a decrease of $1.4 million from the therapeutic virus program, which was terminated in 2003.

Research and development expenses were $35.8 million in 2004, a net increase of $3.8 million, or 12 percent, from 2003. The increase in 2004 was primarily due to a $14.0 million increase in Onyx's share of codevelopment costs for the Nexavar program, which expanded into the Phase III kidney cancer trial in the fourth quarter of 2003. This increase was partially offset by a decrease of $10.2 million of expenses from the therapeutic virus program. It is anticipated that research and development expenditures will continue at 2005 levels or increase as we continue with our clinical trials of Nexavar and as we add additional Phase III clinical trials of Nexavar, including a pivotal trial in lung cancer announced in the first quarter of 2006. However, the presentation of our Statement of Operations will change in future periods as we reflect Nexavar's commercial status and present our share of the profits or losses from Nexavar.

The major components of research and development costs include clinical manufacturing costs, clinical trial expenses, consulting and other third-party costs, salaries and employee benefits, supplies and materials and allocations of various overhead and occupancy costs. The scope and magnitude of future research and

development expenses are difficult to predict at this time given the number of studies that will need to be conducted for any of our potential product candidates. In general, biopharmaceutical development involves a series of steps beginning with identification of a potential target and includes proof of concept in animals and Phase I, II and III clinical studies in humans, each of which is typically more expensive than the previous step.

The following table summarizes our principal product development initiatives, including the related stages of development for each product in development and the research and development expenses recognized in connection with each product. The information in the column labeled "Phase of Development - Estimated Completion" is only our estimate of the timing of completion of the current in-process development phases based on current information. The actual timing of completion of those phases could differ materially from the estimates provided in the table. We cannot reasonably estimate the timing of completion of each clinical phase of our development programs due to the risks and uncertainties associated with developing pharmaceutical product candidates. The clinical development portion of these programs may span as many as seven to ten years, and estimation of completion dates or costs to complete would be highly speculative and subjective due to the numerous risks and uncertainties associated with developing biopharmaceutical products, including significant and changing government regulation, the uncertainty of future preclinical and clinical study results and uncertainties associated with process development and manufacturing as well as marketing. For a discussion of the risks and uncertainties associated with the timing and cost of completing a product development phase, see Item 1A "Risk Factors" of this Annual Report on Form 10-K.

Product	Description	Collaborator	Phase of Development – Estimated Completion	Research and Development Expenses for the year ended December 31, 2005	2004	2003
				(In millions)		
Nexavar (sorafenib) Tablets (1)	Small molecule inhibitor of tumor cell proliferation and angiogenesis; targeting RAF, VEGFR-2, PDGFR-ß, KIT, FLT-3, and RET.	Bayer	Phase I – 2004 Phase II – Unknown Phase III – Unknown	$62.1	$33.4	$19.4
Therapeutic Virus Programs (2)	Programs discontinued during the second quarter of 2003. See Note 10 to our Financial Statements	—	—	1.0	2.4	12.7
			Total Research and Development Expenses	$63.1	$35.8	$32.1

(1) Aggregate research and development costs-to-date through December 31, 2005 incurred by Onyx since fiscal year 2000 for the Nexavar project is $134.8 million.

(2) Costs in 2005 were comprised of:

a. stock-based compensation;

b. consulting fees for consultants retained in connection with the orderly wind-down of the virus programs and preservation of related assets for potential future divestiture or commercialization;

c. outside services related to stability testing and storage of virus product related to the programs.

Selling, General and Administrative Expenses. Selling, general and administrative expenses were $39.7 million in 2005, a net increase of $25.4 million, or 177 percent, from 2004. The increase primarily relates to increased selling and marketing costs of $24.1 million due to employee related costs for hiring our sales and marketing personnel as we establish our commercial infrastructure as well as third-party costs incurred by Onyx and Bayer to support our product launch of Nexavar in the U.S. Additionally, general and administrative costs increased $1.3 million primarily due to employee-related costs as a result of headcount increases to support our planned commercialization of Nexavar. Nexavar, being developed with our collaborator Bayer,

was approved by the FDA on December 20, 2005 for the treatment of individuals with advanced kidney cancer. This is the only product for which we have received marketing approval. Sales of Nexavar were nominal in 2005, and our share of the product sales were offset against our selling, general and administrative expenses.

Selling, general and administrative expenses were $14.3 million in 2004, an increase of $6.4 million, or 80 percent, from 2003. The increase primarily related to increased selling and marketing costs of $4.0 million related to increased headcount and third-party costs for precommercial marketing activities for Nexavar, $700,000 related to consulting expenses for information systems, increased overhead and occupancy costs of $800,000 and $400,000 of external costs incurred to satisfy the requirements of Section 404 of the Sarbanes-Oxley Act of 2002. We anticipate that selling, general and administrative expenses will continue to increase significantly in 2006 as Onyx and Bayer support U.S. sales and marketing efforts as well as invest in pre-launch preparations in Europe and other territories worldwide. However, the presentation of our Statement of Operations will change in future periods as we reflect Nexavar's commercial status and present our share of the profits or losses from Nexavar.

Selling, general and administrative expenses consist primarily of salaries, employee benefits, consulting, other third party costs, corporate functional expenses and allocations for overhead and occupancy costs. Not all selling costs are incurred by us. A significant portion of our selling expenses, approximately 53 percent in 2005, 28 percent in 2004 and 10 percent in 2003, relates to our cost sharing arrangement with Bayer and represents our share of the selling costs incurred by Bayer. Such amounts are recorded based on invoices and other information we receive from Bayer. When such invoices have not been received, we must estimate the amounts owed to Bayer based on discussions with Bayer. In addition, selling costs incurred by us and reimbursed by Bayer are recorded as a reduction to selling, general and administrative expenses.

Restructuring. Prior to June 2003, in addition to our small molecule program, we were developing therapeutic viruses that selectively replicate in cells with cancer-causing genetic mutations. In June 2003, we announced that we were discontinuing this program as part of a business realignment that placed an increased priority on the development of Nexavar. During 2003, we recorded aggregate charges of $5.5 million associated with the restructuring. These charges consist of $1.6 million related to employee severance benefits and $2.5 million related to the early termination of a process development and manufacturing agreement with XOMA (US) LLC. In addition, we incurred aggregate charges of $1.4 million related to the discontinued use of a portion of our leased facilities and the disposal of certain property and equipment. We reclassified $350,000 from property and equipment to other current assets for equipment held-for-sale at December 31, 2003. Had this equipment not been reclassified to other current assets, we would have recorded an additional $27,000 of depreciation expense in 2003.

In 2004, we recorded an additional restructuring charge of $258,000 due to a change in estimate related to the discontinued use and inability to sublet a portion of our leased facility in Richmond, California. As of December 31, 2005, all restructuring costs have been fully paid.

Interest Income, Net. We had net interest income of $6.2 million in 2005, an increase of $3.1 million from 2004, primarily due to higher interest rates in 2005 as compared to 2004. In addition, our average cash balances in 2005 benefited from our November 2005 sale of equity securities from which we received approximately $136.2 million in net cash proceeds. We had net interest income of $3.2 million in 2004, an increase of $2.3 million from 2003, primarily due to the cash received from our February 2004 sale of equity securities. Interest expense was immaterial for the periods presented.

Other Expense — Related Party. In November 2001, we sold and licensed to Syrrx, Inc. assets from our small molecules discovery program, including drug targets, related reagents and assays, compound libraries and certain intellectual property rights in exchange for preferred stock valued at $750,000. The entire amount was recorded as "Other income-related party" on the date of sale. The value of the preferred stock was initially determined based on similar sales of Syrrx preferred stock to unrelated third parties for cash. In 2002, due to a further round of financing completed by Syrrx, we recorded $100,000 as "Other expense-related party" to recognize a permanent impairment in the carrying value of the investment. In 2003, based on a

further round of financing completed by Syrrx in April 2003, we recorded an additional impairment charge of $275,000 as "Other expense-related party" to reduce the carrying value of the investment. We considered the reduction in value of the Syrrx investment to be other than temporary. We did not record any write-downs in 2005 and 2004. At the time of the transactions mentioned above, a member of the board of directors of Onyx was a director and officer of Syrrx. This board member is no longer an officer of Syrrx.

Other Income. In April 2005, we redeemed our investment in Syrrx, Inc. as a result of the acquisition of Syrrx by Takeda Pharmaceutical Company Limited. We received cash of $750,000 as a result of the redemption, which resulted in a gain of $375,000. This amount was recorded as "Other income." No similar items were recorded in fiscal years 2004 and 2003.

Income Taxes

Since our inception, we have incurred operating losses and accordingly have not recorded a provision for income taxes for any of the periods presented and since inception. As of December 31, 2005, our net operating loss carryforwards for federal income tax purposes were approximately $321.0 million and for state income tax purposes were approximately $234.9 million. We also had federal research and development tax credit carryforwards of approximately $8.3 million and state research and development tax credit carryforwards of approximately $3.8 million. Realization of these deferred tax assets is dependent upon future earnings, if any, the timing and amount of which are uncertain. Accordingly, the net deferred tax assets have been fully offset by a valuation allowance. If not utilized, the net operating loss and credit carryforwards will expire at various dates beginning in 2007. Utilization of net operating losses and credits may be subject to substantial annual limitations due to ownership change limitations provided by the Internal Revenue Code of 1986. The annual limitation may result in the expiration of our net operating loss and credit carryforwards before they can be used. Please read Note 11 of the Notes to Financial Statements included in Item 8 of this Form 10-K for further information.

Related Party Transactions

We had a loan with a former employee of which approximately $275,000 was outstanding at December 31, 2003. This loan bore interest at 5.98% per annum; however, we had forgiven $82,000 of interest over the term of the loan through August 2004. This loan was repaid in August 2004 in accordance with the terms of the loan agreement.

Liquidity and Capital Resources

Since our inception, our cash expenditures have substantially exceeded our revenues, and we have relied primarily on the proceeds from the sale of equity securities to fund our operations.

At December 31, 2005, we had cash, cash equivalents, and marketable securities of $284.7 million, compared to $209.6 million at December 31, 2004 and $105.4 million at December 31, 2003. The increase in cash, cash equivalents, and marketable securities in 2005 of $75.1 million was attributable to our public offering completed in November 2005, which raised aggregate net cash proceeds of $136.2 million, as well as $1.4 million received from the exercise of stock options and warrants and $750,000 received from the redemption of our investment in Syrxx. In addition, we received a $10.0 million creditable milestone-based payment from Bayer in August 2005 as a result of the NDA filing for Nexavar. This payment, in addition to $20.0 million of milestones received in previous years, and $10.0 million received from Bayer in January 2006 in connection with the approval of Nexavar by the FDA, will be repayable to Bayer from a portion of any of Onyx's future profits and royalties. If Onyx does not receive any profits or royalties on any products, Onyx will not have to repay Bayer any creditable milestone-based payments. These sources of cash were partially offset by net cash used in operating activities of $72.6 million and capital expenditures of $624,000.

The increase in cash, cash equivalents and marketable securities of $104.2 million in 2004 was attributable to our public offering completed in February 2004, which raised aggregate net cash proceeds of

$148.3 million; $4.0 million received from the exercise of stock options and warrants; and $595,000 received from the sale of fixed assets of laboratory equipment associated with our restructuring in 2003. These sources of cash were partially offset by cash used in operations of $46.9 million and capital expenditures of $1.6 million primarily related to the move of our office facility from Richmond to Emeryville.

Our cash used in operations was $72.6 million in 2005, $46.9 million in 2004 and $37.8 million in 2003. In 2005, the cash was used primarily for co-funding clinical development programs for Nexavar, establishing sales and marketing infrastructure at Onyx and Bayer to prepare for the commercial launch of Nexavar in the U.S., and for third-party pre-commercial marketing activities. In 2004, the cash was used primarily for co-funding the clinical development program with Bayer for Nexavar. In 2003, the cash was used primarily for co-funding clinical development costs with Bayer for Nexavar and to fund development expenses including manufacturing and clinical trial costs for ONYX-015. Expenditures for capital equipment amounted to $624,000 in 2005, $1.6 million in 2004, and $157,000 in 2003. Capital expenditures in 2005 were primarily for equipment to accommodate our employee growth. Capital expenditures in 2004 were primarily for upgrades to our information technology equipment and leasehold improvements and furniture related to our move in December 2004 into our new corporate headquarters. We currently expect to make expenditures for capital equipment and leasehold improvements of up to $600,000 in 2006 primarily for information technology software and equipment.

We believe that our existing capital resources, including the approximately $136.2 million in net proceeds from our public offering closed in November 2005 and interest thereon, will be sufficient to fund our current and planned operations into 2008. However, this is dependent upon the revenue potential of Nexavar in the United States, pending regulatory approvals and revenue potential for Nexavar in Europe and other territories throughout the world as well as the ongoing clinical trial program. If we change our commercialization or development plans, we may need additional funds sooner than we expect. In addition, we are conducting multiple clinical trials of Nexavar in other tumor types, including pivotal studies in liver cancer and metastatic melanoma, and in February 2006, we and Bayer began a Phase III trial of Nexavar in combination with other anticancer agents in non-small cell lung cancer. While we received approval for Nexavar for treatment of individuals with advanced kidney cancer in the U.S., the revenue potential in the first year of an evolving market is not determinable. It is also our intention to invest significantly in Nexavar in order to assess its possible use in the treatment of other cancers. We also maintain an active business development program to identify additional product candidates that we may seek to acquire or license, which would also increase our future development expenses.

While these costs are unknown at the current time, we may need to raise additional capital to continue the co-funding of the programs in future periods beyond 2008. We intend to seek this additional funding through collaborations, public and private equity or debt financings, capital lease transactions or other available financing sources. Additional financing may not be available on acceptable terms, if at all. If additional funds are raised by issuing equity securities, substantial dilution to existing stockholders may result. If adequate funds are not available, we may be required to delay, reduce the scope of or eliminate one or more of our research or development programs or to obtain funds through collaborations with others that are on unfavorable terms or that may require us to relinquish rights to certain of our technologies, product candidates or products that we would otherwise seek to develop on our own.

Contractual Obligations and Commitments

Our contractual obligations for the next five years and thereafter are as follows:

	Payments Due by Period				
Contractual Obligations(1)	Total	Less than 1 Year	1-3 Years	3-5 Years	After 5 Years
		(In thousands)			
Operating leases, net of sublease income	$2,378	$547	$1,136	$695	$—

(1) This table does not include any payments under research and development collaborations, as the amount and timing of such payments are not known. This table also does not include the obligation to repay the $30.0 million creditable milestone-based payments that we received from Bayer as of December 31, 2005 or the additional $10.0 million we received in January 2006, because the repayment of these amounts is contingent upon Onyx generating profits or royalties on any products. Whether Onyx will ever generate any profits or royalties is not known at this time.

In 2004, we entered into a new operating lease for 23,000 square feet of office space in Emeryville, California, which now serves as our corporate headquarters. The lease expires on February 28, 2010. When we moved into this new facility in December 2004, we vacated our 50,000 square foot facility in Richmond, California. The lease for this facility expired in April 2005, and we did not renew this lease. We also have a lease for 9,000 square feet of space in a secondary facility in Richmond, California. In December 2001, we determined that we no longer required the secondary facility because of a reduction in force. In September 2002, the Company entered into a sublease agreement for this space through September 2010.

Recently Issued Accounting Standards

In December 2004, the FASB issued FAS No. 123(R), *Share-Based Payment,* ("FAS 123(R)"), a revision to FAS No. 123 *Accounting for Stock-Based Compensation,* effective for reporting periods beginning after June 15, 2005. FAS 123(R) supersedes Accounting Principles Board Opinion, or APB, No. 25 and amends FAS No. 95, *Statement of Cash Flows.* Generally, the approach in FAS 123(R) is similar to the approach described in FAS 123. However, FAS 123(R) requires all share-based payments to employees, including grants of employee stock options and employee stock purchase plans to be recognized in the income statement based on their fair values. The pro forma disclosures previously permitted under FAS 123 no longer will be an alternative to financial statement recognition. The Company is required to adopt the new standard no later than January 1, 2006. FAS 123(R) permits public companies to adopt its requirements using one of two methods:

1. A "modified prospective" method in which compensation cost is recognized beginning with the effective date (a) based on the requirements of FAS 123(R) for all share-based payments granted after the effective date and (b) based on the requirements of FAS 123 for all awards granted to employees prior to the effective date of FAS 123(R) that remain unvested on the effective date.

2. A "modified retrospective" method which includes the requirements of the modified prospective method described above, but also permits entities to restate based on the amounts previously recognized under FAS 123 for purposes of pro forma disclosures either (a) all prior periods presented or (b) prior interim periods of the year of adoption.

We will adopt FAS 123(R) using the modified prospective basis on January 1, 2006. Our adoption of FAS 123(R) will have a material impact on our statement of operations and our net loss per share. We expect to continue to use the Black-Scholes model for valuing our stock-based compensation. However, our estimate of future stock-based compensation expense will be affected by a number of items including our stock price, the number of stock options our board of directors may grant in 2006, as well as a number of complex and subjective valuation adjustments and the related tax effect. These valuation assumptions include, but are not limited to, the volatility of our stock price and employee stock option exercise behaviors.

In May 2005, the FASB issued FAS No. 154, "Accounting Changes and Error Corrections" ("FAS No. 154"). FAS No. 154 is a replacement of APB No. 20, "Accounting Changes" and FAS No. 3, "Reporting of Accounting Changes in Interim Financial Statements." FAS No. 154 provides guidance on the accounting for and reporting of accounting changes and error corrections. It establishes retrospective application as the required method for reporting a change in accounting principle. FAS No. 154 provides guidance for determining whether retrospective application of a change in accounting principle is impracticable and for reporting a change when retrospective application is impracticable. FAS No. 154 also addresses the

reporting of a correction of an error by restating previously issued financial statements. FAS No. 154 is effective for accounting changes and corrections of errors made in fiscal years beginning after December 15, 2005. We will be adopting this pronouncement beginning in our fiscal year 2006 and do not currently believe that it will have a material impact on our financial statements.

In November 2005, the FASB issued FASB Staff Position, or FSP, FAS 123(R)-3, "Transition Election Related to Accounting for the Tax Effects of Share-Based Payment Awards" ("FSP 123(R)-3"). FSP 123(R)-3 provides an elective alternative method that establishes a computational component to arrive at the beginning balance of the accumulated paid-in capital pool related to employee compensation and a simplified method to determine the subsequent impact on the accumulated paid-in capital pool of employee awards that are fully vested and outstanding upon the adoption of FAS No. 123(R). We are currently evaluating this transition method.

In November 2005, the FASB issued FSP FAS 115-1 and FAS 124-1, "The Meaning of Other-Than-Temporary Impairment and Its Application to Certain Investments" ("FSP 115-1 and 124-1"), which clarifies when an investment is considered impaired, whether the impairment is other than temporary, and the measurement of an impairment loss. It also includes accounting considerations subsequent to the recognition of an other-than-temporary impairment and requires certain disclosures about unrealized losses that have not been recognized as other-than-temporary impairments. FSP 115-1 and 124-1 are effective for all reporting periods beginning after December 15, 2005. At December 31, 2005, we had no unrealized investment losses that we have deemed to be other-than-temporary impairments in our available-for-sale securities.

Item 7A. *Quantitative and Qualitative Disclosures about Market Risk*

Interest Rate Risk

The primary objective of our investment activities is to preserve principal while at the same time maximize the income we receive from our investments without significantly increasing risk. Our exposure to market rate risk for changes in interest rates relates primarily to our investment portfolio. This means that a change in prevailing interest rates may cause the principal amount of the investments to fluctuate. By policy, we minimize risk by placing our investments with high quality debt security issuers, limit the amount of credit exposure to any one issuer, limit duration by restricting the term, and hold investments to maturity except under rare circumstances. We maintain our portfolio of cash equivalents and marketable securities in a variety of securities, including commercial paper, money market funds, and investment grade government and non-government debt securities. Through our money managers, we maintain risk management control systems to monitor interest rate risk. The risk management control systems use analytical techniques, including sensitivity analysis. If market interest rates were to increase by 100 basis points, or 1%, as of December 31, 2005, the fair value of our portfolio would decline by approximately $1.6 million.

The table below presents the amounts and related weighted interest rates of our cash equivalents and marketable securities at December 31:

	2005			2004		
	Maturity	Fair Value ($ in millions)	Average Interest Rate	Maturity	Fair Value ($ in millions)	Average Interest Rate
Cash equivalents, fixed rate	0 – 2 months	$ 45.4	3.97%	0 – 2 months	$ 74.2	2.09%
Marketable securities, fixed rate...	0 – 23 months	$238.6	4.66%	0 – 16 months	$135.4	2.18%

We did not hold any derivative instruments as of December 31, 2005, and we have not held derivative instruments in the past. However, our investment policy does allow us to use derivative financial instruments for the purposes of hedging foreign currency denominated obligations. Our cash flows are denominated in U.S. dollars.

Item 8. *Financial Statements and Supplementary Data*

Our Financial Statements and notes thereto appear on pages 51 to 70 of this Annual Report on Form 10-K.

Item 9. *Changes In and Disagreements With Accountants on Accounting and Financial Disclosure*

Not applicable.

Item 9A. *Controls and Procedures*

Evaluation of Disclosure Controls and Procedures: The Company's chief executive officer and principal financial officer reviewed and evaluated the Company's disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended). Based on that evaluation, the Company's chief executive officer and principal financial officer concluded that the Company's disclosure controls and procedures were effective as of December 31, 2005 to ensure the information required to be disclosed by the Company in this Annual Report on Form 10-K is recorded, processed, summarized and reported within the time periods specified in the Securities and Exchange Commission's rules and forms.

Management's Report on Internal Control over Financial Reporting: The Company's management is responsible for establishing and maintaining adequate internal control over financial reporting (as defined in Rule 13a-15(f) under the Securities Exchange Act of 1934, as amended). Under the supervision and with the participation of the Company's management, including the chief executive officer and principal financial officer, the Company conducted an evaluation of the effectiveness of internal control over financial reporting as of December 31, 2005. In making this assessment, management used the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission ("COSO") in Internal Control-

Integrated Framework. The Company's management has concluded that, as of December 31, 2005, the Company's internal control over financial reporting is effective based on these criteria.

Management's assessment of the effectiveness of the Company's internal control over financial reporting as of December 31, 2005 has been audited by Ernst & Young LLP, an independent registered public accounting firm, as stated in their report which is included elsewhere herein.

Changes in Internal Control over Financial Reporting: There were no changes in the Company's internal control over financial reporting during the quarter ended December 31, 2005 that have materially affected, or are reasonably likely to materially affect the Company's internal control over financial reporting.

Inherent Limitations on Effectiveness of Controls: Internal control over financial reporting may not prevent or detect all errors and all fraud. Also, projections of any evaluation of effectiveness of internal control to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

The Board of Directors and Stockholders
Onyx Pharmaceuticals, Inc.

We have audited management's assessment, included in the accompanying Management's Annual Report on Internal Control Over Financial Reporting, that Onyx Pharmaceuticals, Inc. maintained effective internal control over financial reporting as of December 31, 2005, based on criteria established in Internal Control — Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (the COSO criteria). Onyx Pharmaceuticals, Inc.'s management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting. Our responsibility is to express an opinion on management's assessment and an opinion on the effectiveness of the company's internal control over financial reporting based on our audit.

We conducted our audit in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects. Our audit included obtaining an understanding of internal control over financial reporting, evaluating management's assessment, testing and evaluating the design and operating effectiveness of internal control, and performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

In our opinion, management's assessment that Onyx Pharmaceuticals, Inc. maintained effective internal control over financial reporting as of December 31, 2005, is fairly stated, in all material respects, based on the COSO criteria. Also, in our opinion, Onyx Pharmaceuticals, Inc. maintained, in all material respects, effective internal control over financial reporting as of December 31, 2005, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the balance sheets of Onyx Pharmaceuticals, Inc. as of December 31, 2005 and 2004, and the related statements of operations, stockholders' equity and cash flows for each of the three years in the period ended December 31, 2005 of Onyx Pharmaceuticals, Inc. and our report dated March 7, 2006 expressed an unqualified opinion thereon.

/S/ ERNST & YOUNG LLP

Palo Alto, California
March 7, 2006

Item 9B. Other information

None.

PART III.

Item 10. ***Directors and Executive Officers of the Registrant***

The information required by this item concerning our directors and executive officers is incorporated by reference from our 2006 Definitive Proxy Statement filed not later than 120 days following the close of the fiscal year ended December 31, 2005.

Item 11. ***Executive Compensation***

The information required under this item is hereby incorporated by reference from our 2006 Definitive Proxy Statement.

Item 12. ***Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters***

The information required under this item is hereby incorporated by reference from our 2006 Definitive Proxy Statement.

Item 13. ***Certain Relationships and Related Transactions***

The information required under this item is hereby incorporated by reference from our 2006 Definitive Proxy Statement.

Item 14. ***Principal Accountant Fees and Services***

The information required under this item is hereby incorporated by reference from our 2006 Definitive Proxy Statement.

Consistent with Section 10A (i) (2) of the Securities Exchange Act of 1934, as added by Section 202 of the Sarbanes-Oxley Act of 2002, we are responsible for listing the non-audit services approved by our Audit Committee to be performed by Ernst & Young LLP, our external auditor. Non-audit services are defined as services other than those provided in connection with an audit or a review of our financial statements. The Audit Committee has approved Ernst & Young LLP for non-audit services related to the preparation of federal and state income tax returns, and tax advice in preparing for and in connection with such filings.

PART IV.

Item 15. ***Exhibits, Financial Statement Schedules***

(a) (1) Index to Financial Statements

The Financial Statements required by this item are submitted in a separate section beginning on page 51 of this Report.

Report of Independent Registered Public Accounting Firm
Balance Sheets
Statements of Operations
Statement of Stockholders' Equity
Statements of Cash Flows
Notes to Financial Statements

(2) Financial Statement Schedules

Financial statement schedules have been omitted because the information required to be set forth therein is not applicable.

(3) Exhibits

Exhibit Number	Description of Document
3.1(1)	Restated Certificate of Incorporation of the Company.
3.2(1)	Bylaws of the Company.
3.3(2)	Certificate of Amendment to Amended and Restated Certificate of Incorporation.
4.1(1)	Reference is made to Exhibits 3.1, 3.2 and 3.3.
4.2(1)	Specimen Stock Certificate.
4.4(1)	Amended and Restated Information and Registration Rights Agreement dated May 30, 1994 and as amended through May 16, 1995.
10.1(1)*	Collaboration Agreement between Bayer Corporation (formerly Miles, Inc.) and the Company dated April 22, 1994.
10.1(i)(1)*	Amendment to Collaboration Agreement between Bayer Corporation and the Company dated April 4, 1996.
10.2(1)*	Research, Development and Marketing Collaboration Agreement between Warner-Lambert Company and the Company, dated May 2, 1995.
10.2(i)(1)	Waiver of Certain Rights under the Research, Development and Marketing Agreement by Warner-Lambert Company dated as of March 28, 1996.
10.3(3)*	Technology Transfer Agreement dated April 24, 1992 between Chiron Corporation and the Company, as amended in the Chiron Onyx HPV Addendum dated December 2, 1992, in the Amendment dated February 1, 1994, in the Letter Agreement dated May 20, 1994 and in the Letter Agreement dated March 29, 1996.
10.4(1)+	Letter Agreement between Dr. Gregory Giotta and the Company dated May 26, 1995.
10.5(1)+	1996 Equity Incentive Plan.
10.6(1)+	1996 Non-Employee Directors' Stock Option Plan.
10.7(1)+	1996 Employee Stock Purchase Plan.
10.8(1)+	Form of Indemnity Agreement to be signed by executive officers and directors of the Company.
10.9(4)*	Amended and restated Research, Development and Marketing Collaboration Agreement dated May 2, 1995 between the Company and Warner-Lambert Company.
10.10(4)*	Research, Development and Marketing Collaboration Agreement dated July 31, 1997 between the Company and Warner-Lambert Company.
10.11(4)*	Amendment to the Amended and Restated Research, Development and Marketing Collaboration Agreement, dated December 15, 1997, between the Company and Warner-Lambert Company.
10.12(5)*	Amendment to Collaboration Agreement between Bayer Corporation and the Company dated February 1, 1999.
10.13(6)*	Collaboration Agreement between the Company and Warner-Lambert Company dated October 13, 1999 and effective September 1, 1999.
10.14(6)	Stock Put and Purchase Agreement between the Company and Warner-Lambert Company dated October 13, 1999 and effective September 1, 1999.
10.15(6)	Stock Purchase Agreement between the Company and the investors dated January 18, 2000.
10.16(4)*	Second Amendment to the Amended and Restated Research, Development and Marketing Agreement between Warner-Lambert and the Company dated May 2, 1995.
10.17(4)*	Second Amendment to Research, Development and Marketing Collaboration Agreement between Warner-Lambert and the Company dated July 31, 1997.
10.18(7)+	Employment Offer Letter between Leonard E. Post, Ph.D. and the Company dated July 28, 2000.
10.19(13)+	Form of Executive Change in Control Severance Benefits Agreement.

Exhibit Number	Description of Document
10.20(8)*	Amendment #1 to the Collaboration Agreement between the Company and Warner-Lambert dated August 6, 2001.
10.21(8)*	Amendment #3 to the Research, Development and Marketing Collaboration Agreement between the Company and Warner-Lambert dated August 6, 2001.
10.22(8)*	Amendment #3 to the Amended and Restated Research, Development and Marketing Collaboration Agreement between the Company and Warner-Lambert dated August 6, 2001.
10.23(9)	Stock and Warrant Purchase Agreement between the Company and the investors dated May 6, 2002.
10.24(10)*	Amendment to the Collaboration Agreement between the Company and Warner-Lambert Company dated September 16, 2002.
10.25(11)	Stock Purchase Agreement between the Company and the investors dated February 13, 2003.
10.26(12)	Sublease between the Company and Siebel Systems dated August 5, 2004.
10.27(14)	2005 Base Salaries for Named Executive Officers.
10.28(15)	Onyx Pharmaceuticals, Inc. 2005 Equity Incentive Plan.
10.29(16)	Separation Agreement between Onyx Pharmaceuticals, Inc. and Leonard E. Post, Ph. D., dated December 5, 2005.
23.1	Consent of Independent Registered Public Accounting Firm.
24.1	Power of Attorney. Reference is made to the signature page.
31.1	Certification required by Rule 13a-14(a) or Rule 15d-14(a).
32.1	Certifications required by Rule 13a-14(b) or Rule 15d-14(b) and Section 1350 of Chapter 63 of Title 18 of the United States Code (18 U.S.C. 1350).

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* Confidential treatment has been received for portions of this document.

\+ Indicates management contract or compensatory plan or arrangement.

(1) Filed as an exhibit to Onyx's Registration Statement on Form SB-2 (No. 333-3176-LA).

(2) Filed as an exhibit to Onyx's Quarterly Report on Form 10-Q for the quarter ended June 30, 2000.

(3) Filed as an exhibit to Onyx's Annual Report on Form 10-K for the year ended December 31, 2001.

(4) Filed as an exhibit to Onyx's Annual Report on Form 10-K for the year ended December 31, 2002.

(5) Filed as an exhibit to Onyx's Quarterly Report on Form 10-Q for the quarter ended March 31, 1999.

(6) Filed as an exhibit to Onyx's Current Report on Form 8-K filed on March 1, 2000.

(7) Filed as an exhibit to Onyx's Quarterly Report on Form 10-Q for the quarter ended September 30, 2000.

(8) Filed as an exhibit to Onyx's Quarterly Report on Form 10-Q for the quarter ended September 30, 2001.

(9) Filed as an exhibit to Onyx's Registration Statement on Form S-3 filed on June 5, 2002 (No. 333-89850).

(10) Filed as an exhibit to Onyx's Quarterly Report on Form 10-Q for the quarter ended September 30, 2002.

(11) Filed as an exhibit to Onyx's Registration Statement on Form S-3 filed on March 25, 2003 (No. 333-104025).

(12) Filed as an exhibit to Onyx's Quarterly Report on Form 10-Q for the quarter ended September 30, 2004.

(13) Filed as an exhibit to Onyx's Quarterly Report on Form 10-Q for the quarter ended September 30, 2005.

(14) Filed as an exhibit to Onyx's Current Report on Form 8-K filed on March 14, 2005.

(15) Filed as an exhibit to Onyx's Current Report on Form 8-K filed on June 7, 2005.

(16) Filed as an exhibit to Onyx's Current Report on Form 8-K filed on December 9, 2005.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Act of 1934, as amended, the Registrant has duly caused this Annual Report on Form 10-K to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Emeryville, County of Alameda, State of California, on the 16th day of March, 2006.

ONYX PHARMACEUTICALS, INC.

BY: /s/ HOLLINGS C. RENTON

Hollings C. Renton
Chairman of the Board,
President and Chief Executive Officer

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Hollings C. Renton and Marilyn E. Wortzman or either of them, his or her attorney-in-fact, each with the power of substitution, for him or her in any and all capacities, to sign any amendments to this Annual Report on Form 10-K, and to file the same, with exhibits thereto and other documents in connections therewith, with the Securities and Exchange Commission, hereby ratifying and confirming all that each of said attorneys-in-fact, or his or her substitute or substitutes, may do or cause to be done by virtue hereof.

In accordance with the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the Registrant in the capacities and on the dates stated.

Signature	Title	Date
/s/ HOLLINGS C. RENTON Hollings C. Renton	Chairman of the Board, President and Chief Executive Officer (Principal Executive and Financial Officer)	March 16, 2006
/s/ MARILYN E. WORTZMAN Marilyn E. Wortzman	Vice President, Finance and Administration (Principal Accounting Officer)	March 16, 2006
/s/ PAUL GODDARD Paul Goddard, Ph.D.	Director	March 16, 2006
/s/ ANTONIO GRILLO-LÓPEZ Antonio Grillo-López, M.D.	Director	March 16, 2006
/s/ MAGNUS LUNDBERG Magnus Lundberg	Director	March 16, 2006

Signature	Title	Date
/s/ CORINNE LYLE Corinne Lyle	Director	March 16, 2006
/s/ WENDELL WIERENGA Wendell Wierenga, Ph.D.	Director	March 16, 2006
/s/ THOMAS G. WIGGANS Thomas G. Wiggans	Director	March 16, 2006

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

The Board of Directors and Stockholders
Onyx Pharmaceuticals, Inc.

We have audited the accompanying balance sheets of Onyx Pharmaceuticals, Inc. as of December 31, 2005 and 2004, and the related statements of operations, stockholders' equity and cash flows for each of the three years in the period ended December 31, 2005. These financial statements are the responsibility of Onyx Pharmaceuticals' management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the financial position of Onyx Pharmaceuticals, Inc. at December 31, 2005 and 2004, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2005, in conformity with U.S. generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the effectiveness of Onyx Pharmaceuticals, Inc.'s internal control over financial reporting as of December 31, 2005, based on criteria established in Internal Control — Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission and our report dated March 7, 2006 expressed an unqualified opinion thereon.

/S/ ERNST & YOUNG LLP

Palo Alto, California
March 7, 2006

ONYX PHARMACEUTICALS, INC.

BALANCE SHEETS

	December 31, 2005	December 31, 2004
	(In thousands, except share and per share amounts)	
ASSETS		
Current Assets:		
Cash and cash equivalents	$ 46,064	$ 74,243
Short-term marketable securities	228,754	135,381
Receivable from collaboration partner	4,350	1,029
Prepaid expenses and other current assets	3,935	2,778
Total current assets	283,103	213,431
Long-term marketable securities	9,862	—
Property and equipment, net	1,617	1,623
Other assets	83	492
Total assets	$ 294,665	$ 215,546
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current Liabilities:		
Accounts payable	$ 581	$ 1,038
Payable to collaboration partner	30,823	11,520
Accrued liabilities	1,343	1,895
Accrued clinical trials and related expenses	5,567	—
Accrued compensation	3,111	910
Accrued restructuring	—	195
Total current liabilities	41,425	15,558
Advance from collaboration partner	30,000	20,000
Commitments and contingencies		
Stockholders' Equity:		
Preferred stock, $0.001 par value; 5,000,000 shares authorized; none issued and outstanding	—	—
Common stock, $0.001 par value; 50,000,000 shares authorized; 41,210,734 and 35,266,667 shares issued and outstanding as of December 31, 2005 and 2004, respectively	41	35
Additional paid-in capital	569,800	430,966
Receivable from stock option exercises	(24)	—
Accumulated other comprehensive loss	(767)	(377)
Accumulated deficit	(345,810)	(250,636)
Total stockholders' equity	223,240	179,988
Total liabilities and stockholders' equity	$ 294,665	$ 215,546

See accompanying notes.

ONYX PHARMACEUTICALS, INC.

STATEMENTS OF OPERATIONS

	Year Ended December 31,		
	2005	2004	2003
	(In thousands, except per share amounts)		
Revenue:			
Contract revenue	$ 1,000	$ 500	$ —
Total revenue	1,000	500	—
Operating expenses:			
Research and development	63,120	35,846	32,059
Selling, general and administrative	39,671	14,316	7,939
Restructuring	—	258	5,530
Total operating expenses	102,791	50,420	45,528
Loss from operations	(101,791)	(49,920)	(45,528)
Interest income, net	6,242	3,164	834
Other expense — related party	—	—	(275)
Other income	375	—	—
Net loss	$ (95,174)	$(46,756)	$(44,969)
Basic and diluted net loss per share	$ (2.64)	$ (1.36)	$ (1.73)
Shares used in computing basic and diluted net loss per share	36,039	34,342	25,953

See accompanying notes.

ONYX PHARMACEUTICALS, INC.

STATEMENT OF STOCKHOLDERS' EQUITY

	Common Stock		Additional Paid-In Capital	Receivable From Stock Option Exercises	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount					
	(In thousands, except share and per share amounts)						
Balances at December 31, 2002	21,614,624	$22	$187,633	$ —	$ 40	$(158,911)	$ 28,784
Exercise of stock options at prices ranging from $1.07 to $25.63 per share	656,308	1	4,679	(235)	—	—	4,445
Issuance of common stock in private placement, net of costs of $98	2,105,263	2	9,900	—	—	—	9,902
Issuance of common stock in connection with follow-on public offering, net of issuance costs of $5,826	5,179,000	5	73,719	—	—	—	73,724
Stock-based compensation, related to non-employee stock option grants	—	—	1,501	—	—	—	1,501
Issuance of common stock pursuant to employee stock purchase plan	30,827	—	145	—	—	—	145
Comprehensive loss:				—			
Change in unrealized loss on investments	—	—	—	—	(13)	—	(13)
Net loss	—	—	—	—	—	(44,969)	(44,969)
Comprehensive loss	—	—	—	—	—	—	(44,982)
Balances at December 31, 2003	29,586,022	30	277,577	(235)	27	(203,880)	73,519
Exercise of stock options at prices ranging from $1.07 to $38.08 per share	424,265	—	3,275	235	—	—	3,510
Issuance of common stock in connection with follow-on public offering, net of issuance costs of $9,837	4,685,693	5	148,301	—	—	—	148,306
Stock-based compensation, related to non-employee stock option grants	—	—	1,353	—	—	—	1,353
Issuance of common stock pursuant to employee stock purchase plan	16,852	—	105	—	—	—	105
Exercise of warrants	553,835	—	355	—	—	—	355
Comprehensive loss:							
Change in unrealized loss on investments	—	—	—	—	(404)	—	(404)
Net loss	—	—	—	—	—	(46,756)	(46,756)
Comprehensive loss	—	—	—	—	—	—	(47,160)
Balances at December 31, 2004	35,266,667	35	430,966	—	(377)	(250,636)	179,988
Exercise of stock options at prices ranging from $4.00 to $27.34 per share	152,093	—	1,177	(24)	—	—	1,153
Issuance of common stock in connection with follow-on public offering, net of issuance costs of $8,953	5,750,000	6	136,228	—	—	—	136,234
Stock-based compensation, related to non-employee stock option grants	—	—	906	—	—	—	906
Issuance of common stock pursuant to employee stock purchase plan	12,424	—	257	—	—	—	257
Exercise of warrants	29,550	—	266	—	—	—	266
Comprehensive loss:							
Change in unrealized loss on investments	—	—	—	—	(390)	—	(390)
Net loss	—	—	—	—	—	(95,174)	(95,174)
Comprehensive loss	—	—	—	—	—	—	(95,564)
Balances at December 31, 2005	41,210,734	$41	$569,800	$ (24)	$(767)	$(345,810)	$223,240

See accompanying notes.

ONYX PHARMACEUTICALS, INC.

STATEMENTS OF CASH FLOWS

	Year Ended December 31		
	2005	2004	2003
		(In thousands)	
Cash flows from operating activities:			
Net loss	$(95,174)	$(46,756)	$(44,969)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	630	194	1,124
(Gain)/Loss on investment	(375)	—	275
Noncash restructuring charges	—	280	2,341
Gain on sale of fixed assets	(7)	(18)	(9)
Forgiveness of note receivable	—	11	16
Stock-based compensation to consultants	906	1,353	1,501
Changes in assets and liabilities:			
Receivable from collaboration partner	(3,321)	(445)	(584)
Prepaid expenses and other current assets	(1,157)	(1,139)	(345)
Other assets	34	(84)	32
Accounts payable	(457)	739	(437)
Accrued liabilities	(552)	1,121	(599)
Accrued clinical trials and related expenses	5,567	(147)	(2,830)
Payable to collaboration partner	19,303	(2,112)	6,847
Accrued compensation	2,201	188	(438)
Accrued restructuring	(195)	(130)	294
Net cash used in operating activities	(72,597)	(46,945)	(37,781)
Cash flows from investing activities:			
Purchases of marketable securities	(336,645)	(201,304)	(61,568)
Maturities of marketable securities	233,020	115,607	40,286
Proceeds from sale of Syrxx Investment	750	—	—
Capital expenditures	(624)	(1,573)	(157)
Proceeds from sale of fixed assets	7	595	302
Proceeds from repayment of note receivable	—	275	—
Net cash used in investing activities	(103,492)	(86,400)	(21,137)
Cash flows from financing activities:			
Advance from collaboration partner	10,000	—	15,000
Net proceeds from issuances of common stock	137,910	152,276	88,216
Net cash provided by financing activities	147,910	152,276	103,216
Net increase (decrease) in cash and cash equivalents	(28,179)	18,931	44,298
Cash and cash equivalents at beginning of period	74,243	55,312	11,014
Cash and cash equivalents at end of period	$ 46,064	$ 74,243	$ 55,312

See accompanying notes.

Note 1. Summary of Significant Accounting Policies

The Company

Onyx Pharmaceuticals, Inc. ("Onyx" or "the Company") was incorporated in California in February 1992 and reincorporated in Delaware in May 1996. Onyx is a biopharmaceutical company building an oncology business by developing innovative therapies that target the molecular mechanisms implicated in cancer. With the Company's collaborators, the Company is developing small molecule drugs with the goal of changing the way cancer is treated™. The Company is applying expertise to develop oral anticancer therapies designed to prevent cancer cell proliferation and angiogenesis by inhibiting proteins that signal or support tumor growth. By exploiting the genetic differences between cancer cells and normal cells, the Company aims to create novel anticancer agents that minimize damage to healthy tissue.

The Company's lead product, Nexavar® (sorafenib) tablets, being developed in collaboration with Bayer Pharmaceuticals Corporation (Bayer) was approved by the U.S. Food and Drug Administration (FDA) in December 2005 for the treatment of individuals with advanced kidney cancer. This approval marked the first newly approved drug for patients with this disease in over a decade. Nexavar is a novel, orally available multi-kinase inhibitor and is one of a new class of anticancer treatments that target growth signaling.

Revenue Recognition

Revenue is recognized when the related costs are incurred and the four basic criteria of revenue recognition are met: (1) persuasive evidence of an arrangement exists; (2) delivery has occurred or services rendered; (3) the fee is fixed or determinable; and (4) collectibility is reasonably assured. Determination of criteria (3) and (4) are based on management's judgments regarding the nature of the fee charged for products or services delivered and the collectibility of those fees.

Contract Revenue from Collaborations. Revenue from nonrefundable, up-front license or technology access payments under license and collaboration agreements that are not dependent on any future performance by the Company under the arrangements is recognized when such amounts are received. If the Company has continuing obligations to perform, such up-front fees are recognized over the period of continuing performance obligation.

Creditable milestone-based payments that Onyx receives from the Company's collaboration with Bayer are not recorded as revenue. These amounts are interest-free and will be repayable to Bayer from a portion of any of Onyx's future profits and royalties and are shown in the caption "Advance from collaboration partner" on the Company's balance sheet.

Use of Estimates

The preparation of the financial statements in conformity with accounting principles generally accepted in the United States requires management to make estimates and assumptions that affect the amounts reported in the financial statements and accompanying notes. Actual results could differ from those estimates.

Reclassifications

Certain amounts have been reclassified to conform to the current period presentation. Specifically, marketing costs of $5.4 million and $1.4 million for the years ending December 31, 2004 and 2003, respectively have been included in selling, general and administrative expenses.

Research and Development

Research and development costs are charged to expense when incurred. Research and development consists of costs incurred for independent and collaborative research and development activities. The major components of research and development costs include clinical manufacturing costs, clinical trial expenses, consulting and other third-party costs, salaries and employee benefits, supplies and materials, and allocations of various overhead and occupancy costs. Not all research and development costs are incurred by the Company. A significant portion of the Company's research and development expenses, approximately 83 percent in 2005, 93 percent in 2004 and 60 percent in 2003, relates to the cost sharing arrangement with Bayer and represents the Company's share of the research and development costs incurred by Bayer. Such amounts are recorded based on invoices and other information the Company receives from Bayer. When such invoices have not been received, the Company must estimate the amounts owed to Bayer based on discussions with Bayer. In addition, research and development costs incurred by the Company and reimbursed by Bayer are recorded as a reduction to research and development expense.

In instances where the Company enters into agreements with third parties for clinical trial, research and other consulting activities, costs are expensed upon the earlier of when non-refundable amounts are due or as services are performed. Amounts due under such arrangements may be either fixed fee or fee for service, and may include upfront payments, monthly payments, and payments upon the completion of milestones or receipt of deliverables.

The Company's cost accruals for clinical trials are based on estimates of the services received and efforts expended pursuant to contracts with numerous clinical trial sites and clinical research organizations. In the normal course of business the Company contracts with third parties to perform various clinical trial activities in the on-going development of potential products. The financial terms of these agreements are subject to negotiation and variation from contract to contract and may result in uneven payment flows. Payments under the contracts depend on factors such as the achievement of certain events, the successful enrollment of patients, and the completion of portions of the clinical trial or similar conditions. The objective of the Company's accrual policy is to match the recording of expenses in Onyx's financial statements to the actual services received and efforts expended. As such, expense accruals related to clinical trials are recognized based on the Company's estimate of the degree of completion of the event or events specified in the specific clinical study or trial contract. If the Company underestimate activity levels associated with various studies at a given point in time, the Company could record significant research and development expenses in future periods.

Cash Equivalents and Marketable Securities

The Company considers all highly liquid investments with a maturity from the date of purchase of three months or less to be cash equivalents. All other liquid investments are classified as marketable securities. These instruments consist primarily of corporate debt securities, corporate commercial paper, debt securities of U.S. government agencies and money market funds. Concentration of risk is limited by diversifying investments among a variety of industries and issuers.

Management determines the appropriate classification of securities at the time of purchase. At December 31, 2005 and 2004, all securities were designated as available-for-sale. Available-for-sale securities are carried at fair value based on quoted market prices, with any unrealized gains and losses reported in accumulated other comprehensive income. The amortized cost of securities in this category is adjusted for amortization of premiums and accretion of discounts to maturity. Such amortization is included in interest income and (expense), net. The cost of securities sold or the amount reclassified out of accumulated other comprehensive income into earnings is based on the specific identification method. The estimated fair values have been determined by the Company using available market information. Realized gains and losses and declines in value judged to be other than temporary are included in the statements of operations. There were

no realized gains or losses in each of the years ended December 31, 2005, 2004 and 2003. Interest and dividends on securities classified as available-for-sale are included in interest income and (expense), net.

Property and Equipment

Property and equipment are stated on the basis of cost. Depreciation is calculated using the straight-line method over the estimated useful lives of the respective assets, generally two to five years. Leasehold improvements are amortized over the lesser of the lease term or the estimated useful lives of the related assets, generally approximately five years.

Impairment of Long-Lived Assets

Impairment of long-lived assets is performed when events or changes in circumstances indicate that the carrying amount of such assets may not be recoverable. Determination of recoverability is based on an estimate of undiscounted future cash flows resulting from the use of the asset and its eventual disposition. In the event that such cash flows are not expected to be sufficient to recover the carrying amount of the assets, the assets are written down to their estimated fair values. Long-lived assets to be disposed of are reported at the lower of carrying amount or fair value less costs to sell. There were no write-downs in 2005, $40,000 in 2004 and none in 2003. The write-down in 2004 was related to property and equipment abandoned as a result of the Company's facility move, see Note 4 for additional discussion.

Stock-Based Compensation

The Company has elected to continue to follow Accounting Principles Board Opinion, or APB, No. 25, "Accounting for Stock Issued to Employees," ("APB 25") to account for employee stock options because the alternative fair value method of accounting prescribed by Statement of Financial Accounting Standards, or FAS, No. 123, "Accounting for Stock-Based Compensation," ("FAS 123"), requires the use of option valuation models that were not developed for use in valuing employee stock options. Under APB 25, no compensation expense is recognized when the exercise price of employee stock options equals the market price of the underlying stock on the date of grant.

All stock option awards to non-employees are accounted for at the fair value of the consideration received or the fair value of the equity instrument issued, as calculated using the Black-Scholes model, in accordance with FAS 123 and Emerging Issues Task Force Consensus No. 96-18, "Accounting for Equity Instruments that are Issued to Other Than Employees for Acquiring, or in Conjunction with Selling, Goods or Services." The option arrangements are subject to periodic remeasurement over their vesting terms. The Company recorded compensation expense related to option grants to non-employees of $906,000 for the year ended December 31, 2005, $1.4 million for the year ended December 31, 2004 and $1.5 million for the year ended December 31, 2003.

The pro forma information regarding net loss and loss per share prepared in accordance with FAS 123, as amended, has been determined as if the Company had accounted for its employee stock options and employee stock purchase plan under the fair value method prescribed by FAS 123. The fair value of options was

estimated at the date of grant using the Black-Scholes option-valuation model with the following weighted-average assumptions:

	Year Ended December 31,		
	2005	2004	2003
Risk-free interest rate	3.80%	2.92%	2.34%
Expected life	3.8 years	3.7 years	3.0 years
Expected volatility	0.74	0.85	0.89
Expected dividends	None	None	None
Weighted average fair value of options at date of grant	$13.55	$22.93	$3.48

For purposes of pro forma disclosures pursuant to FAS 123, the estimated fair value of employee stock options is amortized to expense over the options' vesting period. The following table illustrates the effect on net loss and loss per share if the Company had applied the fair value recognition provisions of FAS 123 to stock-based employee compensation:

	Year Ended December 31,		
	2005	2004	2003
	(In thousands, except per share amounts)		
Net loss — as reported	$ (95,174)	$(46,756)	$(44,969)
Deduct: Total stock-based employee compensation determined under the fair value based method for all awards, net of related tax effects	(13,333)	(6,071)	(1,277)
Pro forma net loss	$(108,507)	$(52,827)	$(46,246)
Loss per share:			
Basic and diluted net loss per share — as reported	$ (2.64)	$ (1.36)	$ (1.73)
Basic and diluted net loss per share — pro forma	$ (3.01)	$ (1.54)	$ (1.78)

No options were granted at other than fair value for the years ended December 31, 2005, 2004, and 2003.

The Black-Scholes option valuation model was developed for use in estimating the fair value of traded options, which have no vesting restrictions and are fully transferable. In addition, option valuation models require the input of highly subjective assumptions including the expected stock price volatility.

Net Loss Per Share

Basic and diluted net loss per share are presented in conformity with FAS No. 128, "Earnings Per Share." Basic and diluted net loss per share have been computed using the weighted-average number of shares of common stock outstanding during each period. The following potentially dilutive outstanding securities were not considered in the computation of diluted net loss per share because such securities would be antidilutive:

	December 31,		
	2005	2004	2003
	(In thousands)		
Stock options	3,806	2,296	1,984
Stock warrants	9	40	743
	3,815	2,336	2,727

Comprehensive Loss

Comprehensive loss is comprised of net loss and other comprehensive loss. Other comprehensive loss includes certain changes in stockholders' equity that are excluded from net loss. Other comprehensive loss for all periods presented is comprised of unrealized holding gains and losses on the Company's available-for-sale securities, which were reported separately in stockholders' equity.

Concentration of Credit Risk and Significant Research and Development Collaborators

Financial instruments that potentially subject Onyx to concentration of credit risk consist principally of cash equivalents and marketable securities. Onyx invests cash that is not required for immediate operating needs principally in money market funds and corporate securities.

Onyx's research and development collaborators are currently concentrated in the United States and Germany.

Income Taxes

The Company uses the liability method to account for income taxes as required by FAS No. 109, "Accounting for Income Taxes." Under this method, deferred tax assets and liabilities are determined based on differences between financial reporting and tax bases of assets and liabilities. Deferred tax assets and liabilities are measured using enacted tax rates and laws that will be in effect when the differences are expected to reverse.

Segment Reporting

The Company operates in only one segment — the discovery and development of novel cancer therapies.

Recently Issued Accounting Standards

In December 2004, the Financial Accounting Standards Board, or FASB, issued FAS No. 123(R), ("FAS 123(R)"), a revision to FAS 123 "Share-Based Payment." FAS 123(R) supersedes APB 25 and amends FAS No. 95, "Statement of Cash Flows." Generally, the approach in FAS 123(R) is similar to the approach described in FAS 123. However, FAS 123(R) requires all share-based payments to employees, including grants of employee stock options and employee stock purchase plans to be recognized in the income statement based on their fair values. The pro forma disclosures previously permitted under FAS 123 no longer will be an alternative to financial statement recognition. The Company is now required to adopt the new standard no later than January 1, 2006. FAS 123(R) permits public companies to adopt its requirements using one of two methods:

1. A "modified prospective" method in which compensation cost is recognized beginning with the effective date (a) based on the requirements of FAS 123(R) for all share-based payments granted after the effective date and (b) based on the requirements of FAS 123 for all awards granted to employees prior to the effective date of FAS 123(R) that remain unvested on the effective date.

2. A "modified retrospective" method which includes the requirements of the modified prospective method described above, but also permits entities to restate based on the amounts previously recognized under FAS 123 for purposes of pro forma disclosures either (a) all prior periods presented or (b) prior interim periods of the year of adoption.

The Company will adopt FAS 123(R) using the modified prospective basis on January 1, 2006. The Company's adoption of FAS 123(R) will have a material impact on Onyx's statement of operations and Onyx's net loss per share. The Company expects to continue to use the Black-Scholes model for valuing its stock-based compensation. However, the Company's estimate of future stock-based compensation expense

will be affected by a number of items including Onyx's stock price, the number of stock options Onyx's board of directors may grant in 2006, as well as a number of complex and subjective valuation adjustments and the related tax effect. These valuation assumptions include, but are not limited to, the volatility of Onyx's stock price and employee stock option exercise behaviors.

In May 2005, the FASB issued FAS No. 154, "Accounting Changes and Error Corrections" ("FAS No. 154"). FAS No. 154 is a replacement of APB No. 20, "Accounting Changes" and FAS No. 3 "Reporting of Accounting Changes in Interim Financial Statements." FAS No. 154 provides guidance on the accounting for and reporting of accounting changes and error corrections. It establishes retrospective application as the required method for reporting a change in accounting principle. FAS No. 154 provides guidance for determining whether retrospective application of a change in accounting principle is impracticable and for reporting a change when retrospective application is impracticable. FAS No. 154 also addresses the reporting of a correction of an error by restating previously issued financial statements. FAS No. 154 is effective for accounting changes and corrections of errors made in fiscal years beginning after December 15, 2005. Onyx will be adopting this pronouncement beginning in fiscal year 2006 and the Company does not currently believe that it will have a material impact on its financial statements.

In November 2005, the FASB issued FASB Staff Positions, or FSP, FAS 123(R)-3, "Transition Election Related to Accounting for the Tax Effects of Share-Based Payment Awards" ("FSP 123(R)-3"). FSP 123(R)-3 provides an elective alternative method that establishes a computational component to arrive at the beginning balance of the accumulated paid-in capital pool related to employee compensation and a simplified method to determine the subsequent impact on the accumulated paid-in capital pool of employee awards that are fully vested and outstanding upon the adoption of FAS No. 123(R). The Company is currently evaluating this transition method.

In November 2005, the FASB issued FSP FAS 115-1 and FAS 124-1, "The Meaning of Other-Than-Temporary Impairment and Its Application to Certain Investments" ("FSP 115-1 and 124-1"), which clarifies when an investment is considered impaired, whether the impairment is other than temporary, and the measurement of an impairment loss. It also includes accounting considerations subsequent to the recognition of an other-than-temporary impairment and requires certain disclosures about unrealized losses that have not been recognized as other-than-temporary impairments. FSP 115-1 and 124-1 are effective for all reporting periods beginning after December 15, 2005. At December 31, 2005, the Company had no unrealized investment losses that had not been recognized as other-than-temporary impairments in its available-for-sale securities.

Note 2. Collaboration Agreements

Bayer Corporation

Effective February 1994, the Company established a collaboration agreement with Bayer, to discover, develop, and market compounds that inhibit the function, or modulate the activity, of the RAS signaling pathway to treat cancer and other diseases. The Company and Bayer concluded collaborative research under this agreement in 1999, and based on this research, a product development candidate, Nexavar, was identified.

Bayer paid all the costs of research and preclinical development of Nexavar until the Investigational New Drug application, or IND, was filed in May 2000. Under the agreement with Bayer, the Company is currently funding 50 percent of mutually agreed development costs worldwide, excluding Japan. Bayer is funding 100 percent of development costs in Japan and will pay the Company a royalty on any product sales in Japan. The Company is co-promoting Nexavar in the United States and, if the Company continues to co-fund development and co-promote in the United States, profits or losses, if any, will be shared equally in the United States. If Onyx continues to co-fund but does not co-promote in the United States, Bayer would first receive a portion of the product revenues to repay Bayer for its commercialization infrastructure, before determining the

Company's share of profits and losses. As Onyx does not have the right to co-promote Nexavar outside the United States, Bayer would also receive this preferential distribution in all other parts of the world, except Japan where Onyx would receive a royalty on any product sales.

The Company's agreement with Bayer calls for creditable milestone-based payments. These amounts are interest-free and will be repayable to Bayer from a portion of any of Onyx's future profits or royalties. The Company received $5.0 million in the third quarter of 2002 upon initiation of Phase II clinical studies and $15.0 million in the fourth quarter of 2003 based upon the initiation of a Phase III study. Based on the July 2005 New Drug Application, or NDA, filing, the Company received the third milestone payment of $10.0 million in the third quarter of 2005. These payments are shown in the caption "Advance from collaboration partner" on the Company's balance sheet. At any time during product development, either company may terminate its participation in co-funding of development costs, in which case the terminating party would retain rights to receive royalties based on any sales of the product. If Onyx does not continue to bear 50 percent of product development costs, Bayer would retain exclusive, worldwide rights to Nexavar and would pay royalties to Onyx based on net sales. In January 2006, the Company received the final $10.0 million milestone payment as a result of the United States approval of Nexavar in December 2005. On March 6, 2006, Onyx and Bayer entered into a Co-Promotion Agreement to co-promote Onyx's lead product Nexavar in the United States. See Note 13 for additional information.

Onyx's share for funding the development costs of Nexavar, which commenced in fiscal year 2000, was $91.7 million for 2005, $38.8 million for 2004 and $20.8 million for 2003.

Warner-Lambert Company

In May 1995, the Company entered into a research and development collaboration agreement with Warner-Lambert, now a subsidiary of Pfizer, Inc, to discover and commercialize small molecule drugs that restore control of, or otherwise intervene in, the misregulated cell cycle in tumor cells. Under this agreement, the Company developed screening tests, or assays, for jointly selected targets and transferred these assays to Warner-Lambert for screening of their compound library to identify active compounds. The research term under the agreement ended in August 2001. Warner-Lambert is responsible for subsequent medicinal chemistry and preclinical investigations on the active compounds. In addition, Warner-Lambert is obligated to conduct and fund all clinical development, make regulatory filings and manufacture for sale any approved collaboration compounds. The Company will receive milestone payments on clinical development and registration of any resulting products and will receive royalties on worldwide sales of the products. Warner-Lambert identified PD 332991, a small molecule lead compound that inhibits cyclin-dependent kinase 4 and began Phase I clinical trials with this drug candidate in September 2004. The initiation of clinical trials triggered a $500,000 milestone payment to the Company, which Onyx received from Warner-Lambert and recognized as revenue in 2004.

Note 3. Marketable Securities

Investments that are subject to concentration of credit risk are marketable securities. To mitigate this risk, the Company invests its excess cash balance in marketable debt securities, primarily United States government securities and corporate bonds and notes, with investment grade ratings. The Company limits the amount of investment exposure as to institution, maturity, and investment type. The weighted average maturity of the Company's marketable securities as of December 31, 2005 was seven months. Realized gains (losses) on these sales were immaterial for each of the years ended December 31, 2005, 2004 and 2003.

Available-for-sale marketable securities consisted of the following at December 31:

	2005			
	Adjusted Cost	Unrealized Gains	Unrealized (Losses)	Estimated Fair Value
		(In thousands)		
U.S. government investments:				
Maturing within 1 year	$ 20,424	$ 1	$ (65)	$ 20,360
Maturing between 1 and 2 years	15,182	—	(107)	15,075
Total government investments	35,606	1	(172)	35,435
Corporate debt investments:				
Maturing within 1 year	173,460	156	(654)	172,962
Maturing between 1 and 2 years	30,317	—	(98)	30,219
Total corporate investments	203,777	156	(752)	203,181
Total available-for-sale marketable securities	$239,383	$157	$(924)	$238,616

	2004			
	Adjusted Cost	Unrealized Gains	Unrealized (Losses)	Estimated Fair Value
		(In thousands)		
U.S. government investments:				
Maturing within 1 year	$ 41,416	$ 2	$ (44)	$ 41,374
Maturing between 1 and 2 years	10,005	—	(113)	9,892
Total government investments	51,421	2	(157)	51,266
Corporate debt investments:				
Maturing within 1 year	75,594	8	(154)	75,448
Maturing between 1 and 2 years	8,742	—	(75)	8,667
Total corporate investments	84,336	8	(229)	84,115
Total available-for-sale marketable securities	$135,757	$10	$(386)	$135,381

The unrealized losses in 2005 on the Company's investments in United States government investments and corporate debt instruments were caused by interest rate increases. The contractual terms of these investments do not permit the issuer to settle the securities at a price less than the amortized cost of the investment. No significant facts or circumstances have arisen to indicate that there has been any deterioration in the creditworthiness of the issuers of the Company's securities. Approximately $68.6 million of marketable securities, representing 28.7 percent of our total portfolio, has been in an unrealized loss position for greater than nine months. It is our intention and within our ability to hold these securities in an unrealized loss position for a period of time sufficient to allow for an anticipated recovery of fair value up to (or greater than) the cost of the securities and therefore the impairments noted are not other-than-temporary. In 2005, we classified $9.9 million of these marketable securities balance as long-term because these securities carry maturity dates greater than twelve months from the balance sheet date.

Note 4. Property and Equipment

Property and equipment consist of the following:

	December 31,	
	2005	2004
	(In thousands)	
Computers, machinery and equipment	$1,708	$1,174
Furniture and fixtures	413	410
Leasehold improvements	734	647
	2,855	2,231
Less accumulated depreciation and amortization	(1,238)	(608)
	$1,617	$1,623

Depreciation expense was $630,000, $194,000 and $924,000 for the years ended December 31, 2005, 2004 and 2003, respectively.

In December 2004, the Company vacated its Richmond, California headquarters and relocated to Emeryville, California. The Company recorded an impairment charge of $40,000 related to leasehold improvements, equipment and furniture and fixtures that were abandoned as a result of the facility move.

In June 2003, the Company announced the discontinuation of the therapeutic virus program and the termination of all internal research activities. In the second half of 2003, the Company disposed of property and equipment that it no longer used and wrote-off property and equipment that had a net book value of $1.8 million. The Company recorded a net loss of $982,000 from the disposal of property and equipment, which is included in the caption "Restructuring" in the statement of operations for the year ended December 31, 2003. The Company sold property and equipment for $445,000 of which $156,000 remained as a receivable at December 31, 2003. In addition, at December 31, 2003, the Company reclassified $350,000 from property and equipment to other current assets for equipment that remained held-for-sale at December 31, 2003. In 2004, the Company received $595,000 from the sale of these fixed assets.

Note 5. Long-Term Obligations

In July 2005, the Company received a $10.0 million development payment from Bayer under its collaboration agreement as a result of the NDA filing for Nexavar. In December 2003, the Company received a $15.0 million development payment from Bayer for the initiation of Phase III clinical trials of Nexavar. In August 2002, the Company received a $5.0 million development payment from Bayer for the initiation of Phase II clinical trials of Nexavar. Pursuant to its collaboration agreement, these amounts are repayable to Bayer from a portion of any of Onyx's future profits or royalties. These development payments contain no provision for interest. The balances received as of December 31, 2005 and 2004 of $30.0 million and $20.0 million, respectively, are included in the caption "Advance from collaboration partner" in the accompanying balance sheets. In January 2006, the Company received the fourth and final development payment from Bayer for $10.0 million in connection with the approval of Nexavar by the FDA.

Note 6. Facility Leases

In 2004, the Company entered into a new operating lease for 23,000 square feet of office space in Emeryville, California, which serves as the Company's new corporate headquarters. The lease expires on February 28, 2010 with a renewal option at the end of the lease for an additional three years. The lease provides for fixed increases in minimum annual rental payments, as well as rent free periods. The total amount of rental payments due over the lease term is being charged to rent expense on the straight-line method over

the term of the lease. The difference between rent expense recorded and the amount paid is credited or charged to "deferred rent obligations," which is included in the accompanying balance sheets. When the Company moved into this new facility in December 2004, the Company vacated its 50,000 square foot facility in Richmond, California. The lease for this facility expired in April 2005, and the Company did not renew the lease.

The Company also has a lease for 9,000 square feet of space in a secondary facility in Richmond, California. The Company determined that it no longer required this facility due to a reduction in force in December 2001. The lease for this facility expires in September 2010 with renewal options at the end of the lease for two subsequent five-year terms. In September 2002, the Company entered into a sublease agreement for this space through September 2010.

Minimum annual rental commitments, net of sublease income, under all operating leases at December 31, 2005 are as follows (in thousands):

Year ending December 31:	
2006	$ 547
2007	561
2008	575
2009	589
2010	106
Thereafter	—
	$2,378

Rent expense, net of sublease income and restructuring, for the years ended December 31, 2005, 2004 and 2003 was approximately $490,000, $343,000 and $577,000, respectively. Sublease income was $102,000, $99,000 and $110,000 for the years ended December 31, 2005, 2004 and 2003, respectively.

Note 7. Related Party Transactions

The Company had a loan receivable from a former employee of which approximately $275,000 was outstanding at December 31, 2003. This loan bore interest at 5.98% per annum; however, the Company had forgiven $82,000 of interest over the term of the loan through August 31, 2004. This loan was repaid in full in August 2004 per the terms of the loan agreement.

Note 8. 401(k) Plan

The Company has a 401(k) Plan that covers substantially all of its employees. Under the 401(k) Plan, eligible employees may contribute up to 15 percent of their eligible compensation, subject to certain Internal Revenue Service restrictions. The Company does not match employee contributions in the 401(k) Plan.

Note 9. Stockholders' Equity

Stock Options and Employee Stock Purchase Plan

In March 1996, the Board of Directors adopted the Employee Stock Purchase Plan (the "Purchase Plan") covering an aggregate of 100,000 shares of common stock. At the Company's annual meetings of stockholders in subsequent years, the stockholders approved reserving an additional 225,000 shares of common stock for issuance under the Purchase Plan. The Purchase Plan is designed to allow eligible employees of the Company to purchase shares of common stock through periodic payroll deductions. The price of common stock purchased under the Purchase Plan will be equal to 85 percent of the lower of the fair market value of

the common stock on the commencement date of each offering period or the specified purchase date. Purchases of common stock shares made under the Purchase Plan were 12,424 shares in 2005, 16,852 shares in 2004 and 30,827 shares in 2003. Since inception, a total of 286,412 shares have been issued under the Purchase Plan.

In March 1996, the Board amended and restated the 1992 Incentive Stock Plan, renamed it as the 1996 Equity Incentive Plan (the "Incentive Plan") and reserved 1,725,000 shares of common stock for issuance under the Incentive Plan. At the Company's annual meetings of stockholders in subsequent years, stockholders approved reserving an additional 4,100,000 shares of common stock for issuance under the Incentive Plan. The Incentive Plan provides for grants to employees of either nonqualified or incentive options and provides for the grant to consultants of the Company of nonqualified options. The exercise price of options granted under the Incentive Plan is determined by the Board of Directors, but cannot be less than 100 percent of the fair market value of the common stock on the date of grant.

In March 1996, the Board adopted the 1996 Non-Employee Directors' Stock Option Plan (the "Directors' Plan") and reserved 175,000 shares for issuance to provide for the automatic grant of nonqualified options to purchase shares of common stock to non-employee directors of the Company. At the Company's annual meetings of stockholders in subsequent years, stockholders approved reserving an additional 250,000 shares of common stock for issuance under the Directors' Plan.

In June 2005, the 2005 Equity Incentive Plan was approved at the Company's annual meeting of stockholders to supersede and replace prior plans and reserved 7,560,045 shares of common stock for issuance under the Plan, consisting of (a) the number of shares remaining available for grant under the Incentive Plan and the Directors' Plan, including shares subject to outstanding stock awards under those plans, and (b) an additional 3,990,000 shares.

The following table summarizes option activity under all option plans:

		Outstanding Stock Options	
	Shares Available for Grant	Number of Shares	Weighted Average Exercise Price
Balances at December 31, 2002	609,257	2,749,951	$ 7.57
Shares authorized	700,000	—	$ —
Options granted	(446,973)	446,973	$ 6.34
Options exercised	—	(656,308)	$ 7.13
Options forfeited	556,932	(556,932)	$ 6.83
Balances at December 31, 2003	1,419,216	1,983,684	$ 7.65
Shares authorized	600,000	—	$ —
Options granted	(802,925)	802,925	$38.27
Options exercised	—	(424,265)	$ 7.72
Options forfeited	65,902	(65,902)	$19.85
Balances at December 31, 2004	1,282,193	2,296,442	$17.99
Shares authorized	3,990,000	—	$ —
Options granted	(1,718,000)	1,718,000	$24.52
Options exercised	—	(152,093)	$ 7.73
Options forfeited/expired	56,268	(56,268)	$29.85
Balances at December 31, 2005	3,610,461	3,806,081	$21.17

The following table summarizes information about options outstanding and exercisable at December 31, 2005:

	Options Outstanding			Options Exercisable	
Range of Exercise Prices	Number Outstanding	Weighted Average Contractual Life Remaining (In years)	Weighted Average Exercise Price	Number Exercisable	Weighted Average Exercise Price
$ 3.82 - $ 5.00	469,406	6.7	$ 4.56	369,279	$ 4.54
$ 5.02 - $ 7.88	382,503	4.7	$ 6.58	344,586	$ 6.65
$ 8.15 - $12.00	426,989	4.4	$10.38	400,427	$10.47
$12.11 - $21.01	637,697	9.0	$20.04	83,010	$16.16
$21.56 - $25.23	233,542	9.5	$23.43	2,042	$21.60
$25.30	542,073	9.2	$25.30	88,389	$25.30
$25.44 - $31.85	383,271	9.3	$29.54	9,708	$27.51
$32.00 - $38.08	380,650	8.3	$36.98	171,543	$36.89
$38.33 - $48.19	333,950	8.5	$39.75	121,737	$39.63
$53.37	16,000	8.3	$53.37	6,333	$53.37
Total	3,806,081	7.7	$21.17	1,597,054	$14.74

At December 31, 2005, 2004 and 2003, there were no shares subject to repurchase. The Company has reserved common shares for future issuances under all stock option plans and the employee stock purchase plan as follows:

	December 31, 2005
Stock options available for issuance	3,610,461
Stock options outstanding	3,806,081
Employee stock purchase plan	38,588
Total	7,455,130

In December 2005 and 2003, stock options were exercised that were not settled prior to December 31, 2005 and 2003, respectively. The Company recorded a receivable from stock option exercises of $24,000 and $235,000 as of December 31, 2005 and 2003, respectively, related to these stock options. This is included in the caption "Receivable from stock option exercises" in the accompanying balance sheets and Statement of Stockholders' Equity as of December 31, 2005 and 2003. There were no such amounts as of December 31, 2004.

Preferred Stock

The Company's amended and restated certificate of incorporation provides that the Company's Board of Directors has the authority, without further action by the stockholders, to issue up to 5,000,000 shares of preferred stock in one or more series and to fix the rights, preferences, privileges and restrictions thereof, including dividend rights, conversion rights, voting rights, terms of redemption, liquidation preferences, sinking fund terms and the number of shares constituting any series or the designation of such series, without further vote or action by the stockholders. As of December 31, 2005, the Company had 5,000,000 shares of preferred stock authorized at $0.001 par value, and no shares were issued or outstanding.

Warrants

A total of 743,229 warrants were issued in connection with a private placement financing in May 2002. The exercise price of these warrants is $9.59 per share. The $4.4 million fair value of the warrants was estimated on the date of grant using the Black-Scholes option valuation model with the following assumptions: a weighted-average risk-free interest rate of 4.29%, a contractual life of seven years, a volatility of 0.94 and no dividend yield, and accounted for as a stock issuance cost. Any of the outstanding warrants may be exercised by applying the value of a portion of the warrant, which is equal to the number of shares issuable under the warrant being exercised multiplied by the fair market value of the security receivable upon the exercise of the warrant, less the per share price, in lieu of payment of the exercise price per share. In 2004, the Company issued 553,835 shares of the Company's common stock upon the exercise of 703,689 warrants, on both a cash and net exercise basis. The Company received approximately $355,000 in net cash proceeds from the exercise of warrants in 2004. In 2005, the Company issued 29,550 shares of the Company's common stock upon the exercise of 30,277 warrants, on both a cash and net exercise basis. The Company received approximately $266,000 in net cash proceeds from the exercise of warrants in 2005.

As of December 31, 2005, there are outstanding warrants to purchase an aggregate of 9,263 shares of the Company's common stock, which will expire in May 2009, unless earlier exercised. The Company has reserved 9,263 common shares for future issuance for these warrants.

Note 10. Restructuring

In June 2003, the Company announced the discontinuation of its therapeutic virus program as part of a business realignment that placed an increased priority on the development of Nexavar, Onyx's lead product candidate that is being developed jointly with Bayer. During 2003, the Company recorded an aggregate charge of $5.5 million associated with the restructuring. These charges consist of $1.6 million related to employee severance benefits and $2.5 million related to the early termination of a process development and manufacturing agreement with XOMA US (LLC). In addition, the Company incurred aggregate charges of $1.4 million related to the discontinued use of a portion of its leased facilities and the disposal of certain property and equipment. As of December 31, 2005, all restructuring costs have been fully paid.

In 2004, the Company recorded an additional restructuring charge of $258,000 due to a change in estimate related to the discontinued use and inability to sublet a portion of the Company's leased facility in Richmond, California. For the year ended December 31, 2004, the accrual for restructuring, consisting of charges related to the discontinued use of the Company's leased facilities in Richmond and employee severance benefits, was $195,000.

For the year ended December 31, 2003, the accrual for restructuring, consisting of charges related to the discontinued use of a portion of the Company's leased facilities and employee severance benefits, was $325,000.

Note 11. Income Taxes

There is no provision for income taxes, because the Company has incurred operating losses since inception.

Significant components of the Company's deferred tax assets are as follows:

	December 31,	
	2005	2004
	(In thousands)	
Net operating loss carryforwards	$ 122,900	$ 86,400
Tax credit carryforwards	12,300	8,200
Capitalized research and development	4,000	6,900
Deferred revenue	12,000	8,000
Other	400	400
Total deferred tax assets	151,600	109,900
Valuation allowance	(151,600)	(109,900)
Net deferred tax assets	$ —	$ —

Realization of deferred tax assets is dependent upon future earnings, if any, the timing and amount of which are uncertain. Accordingly, the net deferred tax assets have been fully offset by a valuation allowance. The valuation allowance increased by $41.7 million, $28.2 million and $17.9 million in 2005, 2004 and 2003, respectively.

At December 31, 2005, the Company has net operating loss carryforwards for federal and state income tax purposes of approximately $321.0 million and $234.9 million, respectively, which expire beginning in 2007 if not utilized. At December 31, 2005, the Company has research and development credit carryforwards for federal income tax purposes of approximately $8.3 million, which expire beginning in 2008 if not utilized. At December 31, 2005, the Company has research and development credit carryforwards for state income tax purposes of approximately $3.8 million, which do not expire.

Utilization of the net operating loss and tax credit carryforwards may be subject to a substantial annual limitation due to the ownership change limitations provided by the Internal Revenue Code of 1986, as amended, and similar state provisions. The annual limitation may result in the expiration of net operating loss and tax credit carryforwards before utilization.

Note 12. Guarantees, Indemnifications and Contingencies

Guarantees and Indemnifications

The Company has entered into indemnity agreements with certain of its officers and directors, which provide for indemnification to the fullest extent authorized and permitted by Delaware law and the Company's Bylaws. The agreements also provide that the Company will indemnify, subject to certain limitations, the officer or director for expenses, damages, judgments, fines and settlements he or she may be required to pay in actions or proceedings to which he or she is or may be a party because such person is or was a director, officer or other agent of the Company. The term of the indemnification is for so long as the officer or director is subject to any possible claim, or threatened, pending or completed action or proceeding, by reason of the fact that such officer or director was serving the Company as a director, officer or other agent. The rights conferred on the officer or director shall continue after such person has ceased to be an officer or director as provided in the indemnity agreement. The maximum amount of potential future indemnification is unlimited; however, the Company has a director and officer insurance policy that limits its exposure and may enable it to recover a portion of any future amounts paid under the indemnity agreements. The Company has not recorded any amounts as liabilities as of December 31, 2005 as the value of the indemnification obligations, if any, is not estimable.

Contingencies

From time to time, the Company may become involved in claims and other legal matters arising in the ordinary course of business. Management is not currently aware of any matters that could have a material adverse affect on the financial position, results of operations or cash flows of the Company.

Note 13. Subsequent Event

On March 6, 2006, Onyx and Bayer entered into a Co-Promotion Agreement to co-promote Onyx's lead product Nexavar in the United States. This agreement supersedes those provisions of the original 1994 Collaboration Agreement that relate to the co-promotion of Nexavar in the United States between Bayer and Onyx.

Under the terms of the Co-Promotion Agreement and consistent with the terms of the Collaboration Agreement, Onyx will share equally in the profits or losses of Nexavar, if any, in the United States, subject only to Onyx's continued co-funding of the development costs of Nexavar worldwide, excluding Japan. Outside of the United States, the terms of the Collaboration Agreement continue to govern.

Onyx and Bayer will each contribute half of the overall number of sales force personnel required to market and promote Nexavar in the United States and half of the medical science liaisons to support Nexavar in the United States. Onyx and Bayer will each bear their own sales force and medical science liaison expenses.

Bayer will provide all product distribution and substantially all marketing services for Nexavar in the United States. With respect to distribution, Bayer will be compensated based on a fixed percent of gross sales of Nexavar in the United States. Bayer will be reimbursed for 50% of its expenses for its marketing services. Each of Onyx and Bayer will also share equally in any other out-of-pocket marketing expenses that it incurs in connection with the marketing and promotion of Nexavar in the United States. Bayer will continue to manufacture all Nexavar sold in the United States and will be reimbursed at an agreed transfer price for such manufactured product.

Note 14. Quarterly Financial Data (Unaudited)

The following table presents unaudited quarterly financial data of the Company. The Company's quarterly results of operations for these periods are not necessarily indicative of future results of operations.

	2005 Quarter Ended			
	December 31	September 30	June 30	March 31
	(In thousands, except per share data)			
Total revenues	$ —	$ —	$ —	$ 1,000
Net loss	(38,352)	(22,581)	(18,141)	(16,100)
Basic and diluted net loss per share	(1.00)	(0.64)	(0.51)	(0.46)

	2004 Quarter Ended			
	December 31	September 30	June 30	March 31
	(In thousands, except per share data)			
Total revenues	$ 500	$ —	$ —	$ —
Net loss	(14,205)	(11,264)	(13,106)	(8,181)
Basic and diluted net loss per share	(0.40)	(0.32)	(0.38)	(0.25)

Onyx employees come to work every day

with energy and commitment

to change the landscape in the treatment of cancer,

to provide hope for cancer patients.

Each person arrives

with his or her own personal reason why this

mission is so vitally important.

Here are a few words we'd like to share:

We are fighting cancer because...

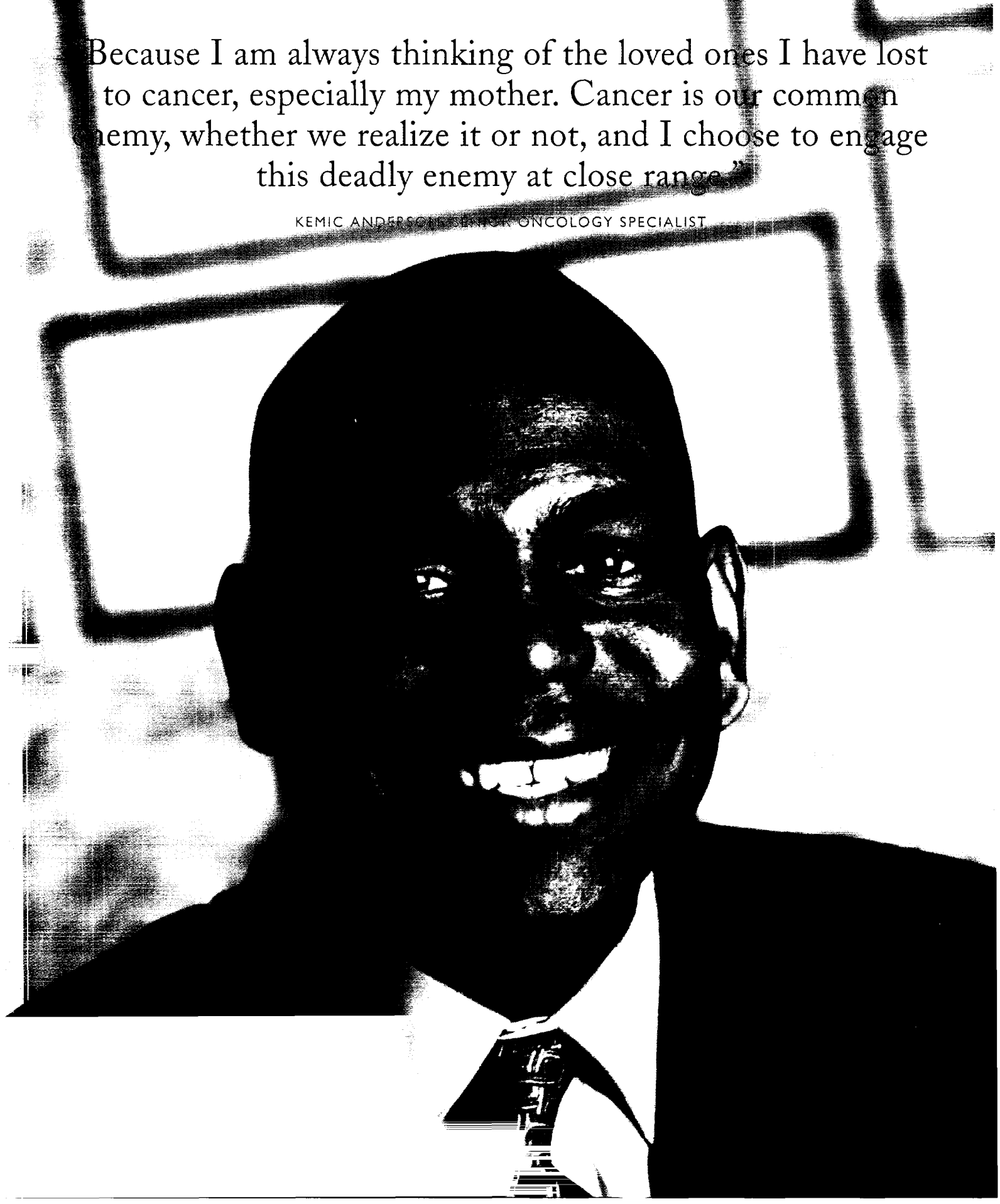
be part of an effort to make cancer
Our goal is to help people live longer
romising their quality of life."

ARPE, REGIONAL BUSINESS MANAGER

Nexavar was the first new drug approved in over a decade for the treatment of people with advanced kidney cancer.

"Because I am always thinking of the loved ones I have lost to cancer, especially my mother. Cancer is our common enemy, whether we realize it or not, and I choose to engage this deadly enemy at close range."

KEMIC ANDERSON, SENIOR ONCOLOGY SPECIALIST



Approximately 13,000 individuals die from kidney cancer in the U.S. each year.

"Because I've had far too ma[illegible]mily members suffer from cancer, and worki[illegible]yx is one way I can help make some headway against this terrible disease."

SANDRA LaVAY, MANAGER, FINANCIAL PLANNING AND ANALYSIS

Nexavar doubled progression-free survival in a Phase III study in advanced kidney cancer patients.

"Because understanding cancer and devising ways to beat it is the ultimate challenge to me as a researcher. Discovering how genetic changes can lead to cancer gives us new insights into how cells grow and provides us with new targets in cancer."

FRANK McCORMICK, Ph.D., FOUNDER

Pivotal Phase III trials are underway in three indications – metastatic melanoma, advanced liver cancer and lung cancer.

"Because in developing Nexavar, we have the chance to benefit patients with many types of cancers and truly *change the way cancer is treated*™."

HOLLINGS C. RENTON, CHAIRMAN AND CEO

Nearly 8,000 patients worldwide have been treated with Nexavar in clinical trials.

DEAR FELLOW STOCKHOLDERS:

In December 2005, Onyx realized the most important milestone in the company's history – the approval of Nexavar® (sorafenib) tablets by the U.S. Food & Drug Administration (U.S. FDA) for the treatment of patients with advanced kidney cancer (renal cell carcinoma). This landmark achievement represented more than 12 years of hard work by many dedicated individuals at Onyx and at our collaborator, Bayer Pharmaceuticals Corporation, supported by the participation of numerous committed clinicians and patients in our clinical trials. The result was the first approved drug for advanced kidney cancer patients in over a decade – an event that establishes Onyx and Bayer as emerging leaders in targeted cancer therapy.

While Nexavar's initial indication is in advanced kidney cancer, Bayer and Onyx currently have pivotal trials underway in metastatic melanoma and advanced liver cancer, with another pivotal trial just beginning in non-small cell lung cancer. As we continue to expand the clinical development of this exciting new anticancer agent, our commercial organization is fully engaged in the U.S. launch of Nexavar. At the same time, regulatory filings have been completed in Europe and other territories, laying the groundwork for additional approvals of Nexavar around the world.

Powerful Targeted Cancer Therapy in a Pill Nexavar is one of a new class of anticancer therapies. It uniquely combines two important anticancer activities: inhibiting the proliferation of tumor cells, as well as cutting off the tumor's blood supply, an effect known as antiangiogenesis. Nexavar, an oral anticancer agent, is a convenient and easy-to-administer alternative to existing injectable drugs. As a result of the U.S. FDA's decision, Nexavar is now available to patients through specialty pharmacies. For more information about Nexavar, please visit www.nexavar.com.

Recognizing its clinical benefit, general tolerability, predictable safety profile, and ease of administration compared to current therapies, the U.S. FDA approved Nexavar for all patients with advanced kidney cancer. This broad label allows Nexavar to be used as a patient's first systemic therapy, as well as in patients who have failed a prior therapy.

Compelling Clinical Data Nexavar's efficacy was established in the largest randomized, placebo-controlled Phase III clinical trial ever conducted in patients with advanced kidney cancer. Data from the trial showed that Nexavar doubled progression-free survival – the length of time that a patient lives without evident tumor growth. In the trial, Nexavar-treated patients had a median progression-free survival of six months, as compared to a median of three months for those patients receiving placebo ($p<0.000001$, HR = 0.44). Nexavar is the only approved drug shown to prolong progression-free survival in this patient population in a controlled setting.

According to the results of a planned interim survival analysis, patients treated with Nexavar lived longer. These data, reported in November, based on 220 deaths, showed that patients receiving Nexavar had a 28 percent lower risk of dying compared to patients receiving placebo at the time the analysis was conducted (HR = 0.72). However, this encouraging data did not reach the prespecified criterion for statistical significance. The interim analysis was conducted while the study was ongoing and prior to the effect of allowing placebo patients to "cross over" to treatment with Nexavar. As the data mature, survival analyses will be released at the appropriate scientific meetings.

In 2005, Onyx realized the most important milestone in the company's history – the approval of Nexavar by the U.S. FDA.

These pivotal data formed the basis of our New Drug Application (NDA) with the U.S. FDA. This evidence also led Bayer and Onyx, in consultation with regulators and clinicians, to decide in April 2005 to allow patients who were receiving placebo in the clinical trial to "cross over" to treatment with Nexavar. In addition, based on this persuasive dataset, we initiated an expanded access program in the U.S. for patients with metastatic or advanced kidney cancer who were not enrolled in the Phase III trial. This program, started in May 2005, subsequently treated over 2,000 patients at approximately 300 different sites, giving many physicians direct experience with Nexavar prior to its approval.

Generally Well Tolerated In addition to its proven efficacy, Nexavar was generally well tolerated in the Phase III study. More serious adverse events – grades 3 and 4 – were observed in 38 percent of Nexavar patients, as compared to 28 percent of placebo patients. In all, 10 percent of Nexavar patients discontinued treatment due to adverse events, compared to eight percent of placebo-treated patients. This safety profile sets Nexavar apart from current treatments for advanced kidney cancer.

We are conducting further clinical evaluations of patients with advanced kidney cancer, including ongoing studies comparing treatment with Nexavar to treatment with interferon in first-line patients. Bayer and Onyx are also planning long-term adjuvant studies, expected to begin in 2006, to assess the efficacy of Nexavar when administered to patients at high risk of recurrence after the surgical removal of their primary tumor.

Full Potential of Nexavar Being Explored Bayer and Onyx believe that Nexavar's initial indication in advanced kidney cancer is just the first step in tapping the full potential of this new anticancer agent. In advanced liver cancer, we are conducting an international placebo-controlled Phase III trial evaluating Nexavar as a single agent in patients with advanced disease. In metastatic melanoma, our Phase III trial is evaluating Nexavar administered in combination with two chemotherapeutic agents. We expect to complete enrollment in these studies this year. In addition, we recently began a pivotal Phase III study of Nexavar in non-small cell lung cancer in combination with chemotherapy. The theme for future development is to explore Nexavar in combination with other anticancer agents in the more common malignancies.

Worldwide Economic Participation in Nexavar Our codevelopment and profit-sharing agreement with Bayer is worldwide except for Japan, where Bayer will fund all development costs for Nexavar, and Onyx will earn a high single-digit royalty on sales. In the U.S., the companies will share sales and marketing responsibilities and split equally any profits that are generated. This arrangement has enabled Onyx to establish a commercial presence in the U.S. oncology market. Outside of the U.S., Bayer will be responsible for all promotional activities. As a result, the profit split will be somewhat less than 50/50.

In preparation for the U.S. approval, Bayer and Onyx established a team of sales and marketing personnel, as well as medical liaisons. This experienced group of oncology professionals

2005 MILESTONES

March

Endpoint met in Phase III study, according to Data Monitoring Committee

Enrollment of largest randomized Phase III clinical trial in advanced kidney cancer completed

Phase III clinical study initiated in advanced liver cancer patients

April

Placebo-treated patients in Phase III renal trial offered access to Nexavar treatment

May

Nexavar accepted into U.S. FDA's Pilot 1 program

Phase III clinical trial started in metastatic melanoma patients

Nexavar shown to double progression-free survival in advanced kidney cancer patients

is focused on educating the medical community about the benefits of our exciting new anticancer agent. As the first approved targeted therapy for advanced kidney cancer patients, Nexavar provided us with an important first-mover advantage in the competitive oncology marketplace. We expect that the clinical experience gained by physicians through the expanded access program will facilitate Nexavar's entry into the marketplace.

To ensure that we have the resources in place to develop the full value of Nexavar, we strengthened our management team and board in the past year. We expanded our executive team by adding Hank Fuchs, M.D., as Executive Vice President and Chief Medical Officer. Hank brings to Onyx extensive experience from Genentech and Intrabiotics, where he served most recently as Chief Executive Officer. Hank leads an integrated medical and clinical affairs team in supporting and extending the use of Nexavar. We also added two new directors – Corinne Lyle, President, Global Operations of Edwards Lifesciences Corporation, and Thomas Wiggans, Chairman and Chief Executive Officer of Connetics Corporation, both of whom bring additional commercial perspectives to the board.

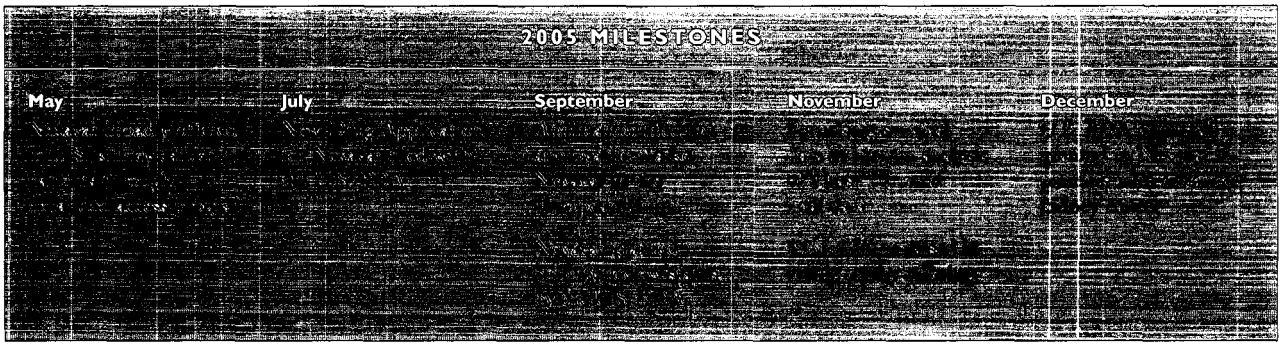
Investing in the Future As of December 31, 2005, we had cash, cash equivalents and marketable securities of approximately $285 million; in addition, we received a final $10 million creditable milestone payment from Bayer in the first quarter of 2006. These cash reserves will enable us to invest substantially in the continued development and commercialization of Nexavar.

We are very proud of what we accomplished in 2005. Nexavar was approved by the U.S. FDA as we established its effectiveness in a disease that historically has been very difficult to treat. We launched Nexavar ahead of the competition and with the advantage of a very successful expanded access program that put the drug in the hands of physicians and patients alike. At the same time, we are actively investigating a range of other tumor types as a way to create a platform for sustainable corporate growth.

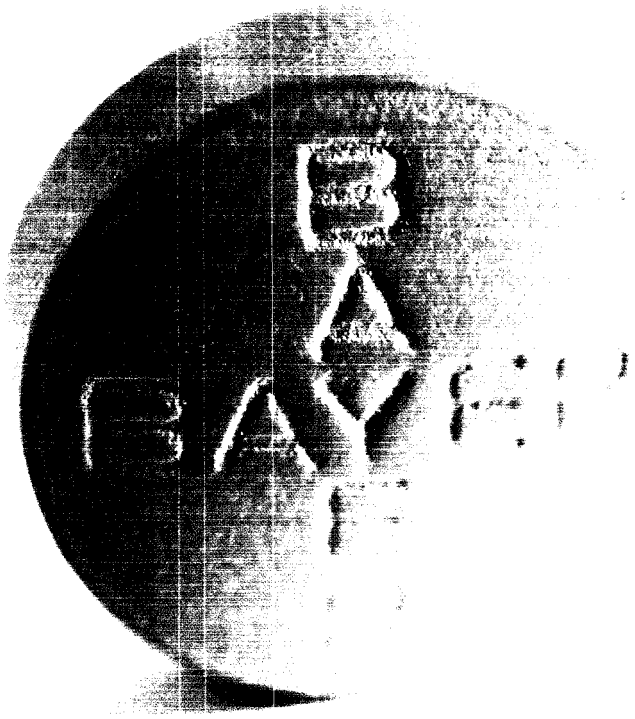
Most importantly, we made historic progress toward our goal of *changing the way cancer is treated*™, providing a much-needed option to patients with limited treatment alternatives. We would like to thank everyone – employees, collaborators, stockholders, physicians, and patients – who helped to bring Nexavar from the laboratory to the marketplace, where it can benefit countless patients to come.

Sincerely,

Hollings C. Renton
Chairman, President and Chief Executive Officer
March 20, 2006

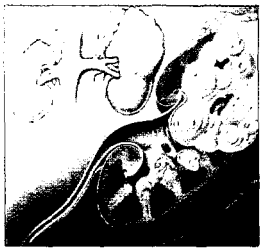


The U.S. FDA's approval of Nexavar in late 2005 was a milestone event in the treatment of patients with advanced kidney cancer.



NEXAVAR > BRINGING NEW HOPE

RENAL (kidney) CANCER



The most common type of kidney cancer, renal cell carcinoma, is estimated to strike 35,000 individuals in the U.S. each year, resulting in approximately 13,000 deaths annually. The disease is almost twice as common in men as in women. Like many cancers, successful treatment is linked to early detection; however, about 25 percent of patients have metastatic disease at diagnosis. Renal cell carcinoma is resistant to conventional chemotherapy and radiation, and the development of effective systemic therapies has been difficult.

The U.S. FDA's approval of Nexavar in late 2005 was a milestone event in the treatment of patients with advanced kidney cancer. Not only was Nexavar the first new drug approved in the U.S. in over a decade for this challenging indication, it is the first oral multi-kinase inhibitor that targets proteins involved in tumor growth (proliferation), as well as the tumor's blood supply (angiogenesis).

Based on compelling clinical efficacy and safety data, Nexavar was granted a broad label by the U.S. FDA, enabling all advanced kidney cancer patients to receive Nexavar treatment, whether or not they have been previously treated with other anticancer agents. According to Phase III clinical trial results, Nexavar doubled median progression-free survival in advanced kidney cancer patients from three months to six months, compared to placebo. In addition, Nexavar demonstrated an encouraging survival trend in a preliminary analysis of overall survival.

Nexavar was also shown to be generally well tolerated with predictable side effects. The incidence of serious adverse events (grade 3 or 4) only exceeded five percent in one category (hand-foot skin reaction – six percent), and the rate of drug discontinuation for adverse events was similar between Nexavar and placebo (10 percent versus eight percent, respectively). This encouraging safety profile supports the long-term administration of Nexavar.

Building on these strong results, we intend to establish Nexavar as a new, broadly effective approach to kidney cancer treatment. Consequently, we are conducting a study in first-line advanced kidney cancer patients to evaluate the efficacy of Nexavar compared to interferon. We are also planning adjuvant studies focused on the long-term use of Nexavar to prevent cancer recurrence in high-risk patients following surgery to remove their primary tumor.

We believe that Nexavar's approval in advanced kidney cancer is just the first step in tapping the full potential of this new anticancer agent.

LIVER CANCER

Phase III

The most common form of primary liver cancer, hepatocellular carcinoma, is estimated to affect about 15,000 new patients in the U.S. each year and results in about 15,000 annual deaths. It is the fifth most common cancer in the world. Only a very small number of liver tumors are found in the early stages and are suitable for surgical removal. The overall five-year survival rate for liver cancer is about seven percent, and there is currently no approved first-line therapy for advanced liver cancer.

In 2004, investigators reported results from a single-arm Phase II study of Nexavar in 137 patients who had not received prior systemic therapy. The reported median time-to-tumor progression was 4.2 months. We are now conducting an international placebo-controlled Phase III study evaluating Nexavar as a single agent in advanced liver cancer patients who have not had previous local treatment. Expected to enroll 550 individuals, the trial will assess overall survival and time-to-symptom progression as primary endpoints.

METASTATIC MELANOMA

Phase III

Melanoma is the most serious type of skin cancer, affecting approximately 60,000 new U.S. patients in 2005 and resulting in about 8,000 deaths. Melanoma is becoming more common each year. If the disease is detected early, it can be successfully treated; however, once the cancer has spread to other parts of the body, five-year survival rates drop to roughly 10 percent. To date, systemic therapy has proved to be less than satisfactory.

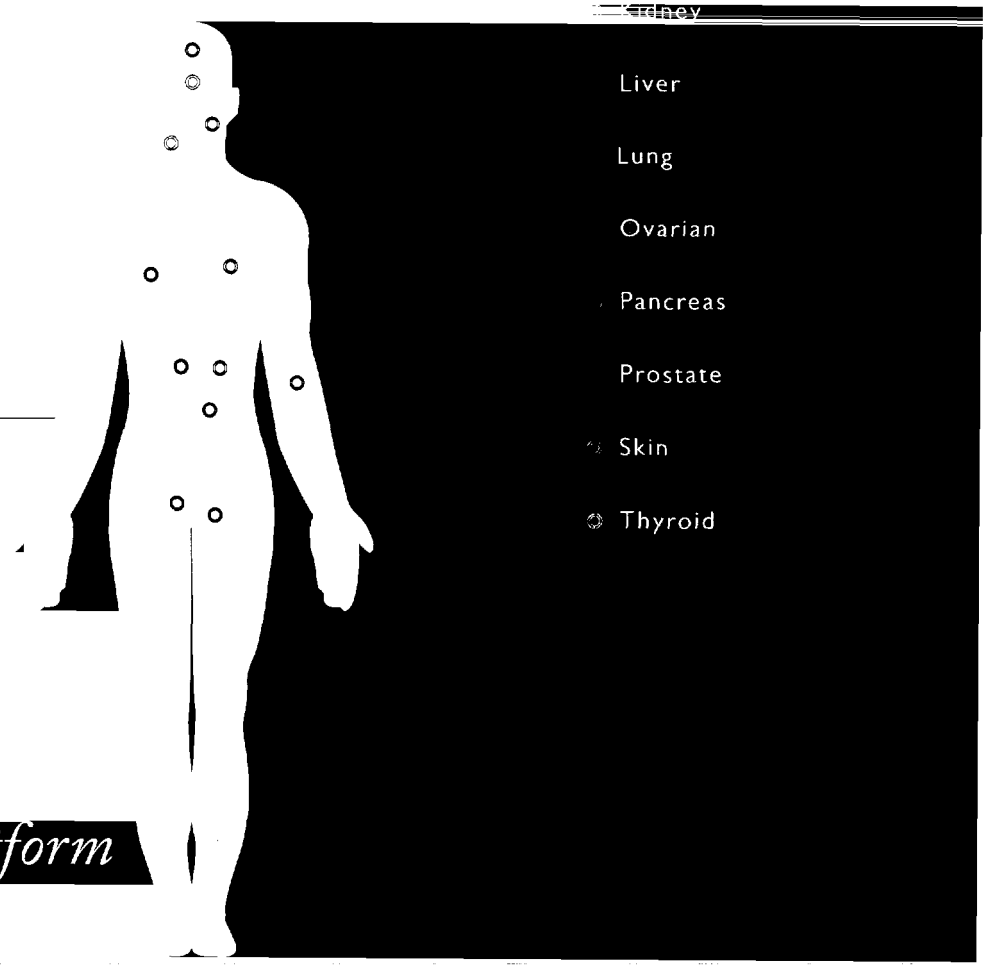
In 2006, investigators reported encouraging interim clinical results from a study of Nexavar administered in combination with the chemotherapeutics carboplatin and paclitaxel in metastatic melanoma patients. The single-arm study enrolled approximately 100 patients at two sites. The progression-free survival for these patients was 8.8 months. Currently there are two Phase III clinical trials comparing treatment with Nexavar in combination with these two chemotherapeutics to administration of the two agents alone. One is a company-sponsored trial in previously treated patients that will assess progression-free survival as the primary endpoint. The other, sponsored by the Eastern Cooperative Oncology Group (ECOG), will enroll patients not previously treated for metastatic disease and assess overall survival.

LUNG CANCER

Phase III

Lung cancer is the leading cause of cancer death for both men and women – claiming more lives than colon, breast, and prostate cancers combined. In 2005, there were nearly 175,000 new cases of lung cancer in the U.S.; approximately 75 percent of these were due to non-small cell lung cancer. Annual deaths in the U.S. are estimated at 160,000. Despite recent advances, non-small cell lung cancer remains a devastating disease.

Bayer and Onyx recently initiated a Phase III clinical trial in patients with non-small cell lung cancer. This study will administer Nexavar in combination with standard chemotherapeutics to lung cancer patients. Our decision to study Nexavar in this indication was based on preliminary results in a small number of patients (n=14) showing that the administration of Nexavar along with carboplatin and paclitaxel provided disease stabilization in 59 percent of patients and median progression-free survival of approximately eight months. In another study (n=52) administering Nexavar as a single agent, we observed a median PFS of approximately three months in patients who had already failed chemotherapy.



a broad-based platform

Nexavar's dual mechanism of action – targeting both the tumor and its blood supply – extends the potential of this new anticancer drug to a range of tumor types. In clinical trials in nearly 8,000 patients, we have observed that Nexavar is generally well tolerated.

The mechanism of action and the product features make us optimistic that Nexavar may be broadly active. Along with our current Phase III clinical trials in metastatic melanoma, liver cancer, and non-small cell lung cancer, there are dozens of other earlier-stage trials in which Onyx and Bayer are amassing an important body of data to guide further clinical development decisions. These include company-sponsored, single-agent Phase II clinical trials for the treatment of breast, non-small cell lung and other cancers, as well as a range of Phase Ib clinical trials evaluating Nexavar's use in combination with a variety of agents.

Cooperative groups and investigators around the world are also conducting a number of single-agent and combination clinical trials of Nexavar for the treatment of breast, ovarian, head and neck, prostate, thyroid and other cancers. Through this active program of clinical investigation, we intend to realize the full potential of Nexavar as a new anticancer therapy.

Through our employees' energy and efforts,
we intend to change the way cancer is treated.

Thank you all for making Nexavar
a reality for thousands of patients worldwide.

ONYX PEOPLE, PEOPLE AT THEIR BEST.

CORPORATE INFORMATION

MANAGEMENT

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Chief Executive Officer

Henry J. Fuchs, M.D.
Executive Vice President and
Chief Medical Officer

Edward F. Kenney
Executive Vice President and
Chief Business Officer

Fabio M. Benedetti, M.D.
Vice President
Medical Affairs

Scott M. Freeman, M.D.
Vice President
Clinical Development

Gregory J. Giotta, Ph.D., J.D.
Vice President and
Chief Legal Counsel

Jeanne Y. Jew
Vice President
Corporate and Commercial Development

Randy A. Kelley
Vice President
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Julianna Wood
Vice President
Corporate Communications and
Investor Relations

Marilyn E. Wortzman
Vice President
Finance and Administration

BOARD OF DIRECTORS

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Chairman and Chief Executive Officer
ARYx Therapeutics, Inc.

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Chairman, Neoplastic and Autoimmune
Diseases Research Institute

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Chief Executive Officer
Phadia AB

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President, Global Operations
Edwards Lifesciences Corporation

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Onyx Pharmaceuticals, Inc.

Wendell Wierenga, Ph.D.
Executive Vice President,
Research and Development
Neurocrine Biosciences, Inc.

Thomas G. Wiggans
Chairman and Chief Executive Officer
Connetics Corporation

ADVISOR AND FOUNDER

Frank McCormick, Ph.D., F.R.S.
Director, UCSF Comprehensive Cancer
Center and Cancer Research Institute;
David A. Wood Chair of Tumor Biology
and Cancer Research, Microbiology and
Immunology; Associate Dean, School of
Medicine, University of California,
San Francisco; Founder of Onyx
Pharmaceuticals, Inc.

CORPORATE SECRETARY

Robert L. Jones, J.D.
Partner, Cooley Godward LLP

CORPORATE COUNSEL

Cooley Godward LLP
San Francisco and Palo Alto, California

INDEPENDENT AUDITORS

Ernst & Young LLP
Palo Alto, California

SEC FORM 10-K

A copy of the Company's Annual Report on Form 10-K, as filed with the Securities and Exchange Commission, is available without charge by calling or writing the Investor Relations Department as listed under Stockholder Inquiries.

TRANSFER AGENT AND REGISTRAR

Inquiries regarding change of address, lost stock certificates, changes in stock ownership, and other matters related to stock ownership should be directed to the Transfer Agent.

Wells Fargo Bank, N.A.
Shareowner Services

For telephone inquiries:
800.468.9716

For overnight delivery:
161 North Concord Exchange
South St. Paul, MN 55075-0738

For mail delivery:
P.O. Box 64854
St. Paul, MN 55164-0854

STOCKHOLDER INQUIRIES

Inquiries and requests for information should be directed to:

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510.597.6500
email: ir@onyx-pharm.com
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DIVIDENDS

Onyx has not paid cash dividends on its common stock and does not plan to pay any cash dividends in the foreseeable future.

ANNUAL MEETING

The annual meeting of stockholders will be held at 10:00 a.m. on May 25, 2006, at Onyx Pharmaceuticals, Inc., 2100 Powell Street, Emeryville, California.

Forward-looking Statements: This annual report contains forward-looking statements that involve risks and uncertainties. Our actual results could differ materially from those anticipated in these forward-looking statements as a result of certain factors, including those set forth under "Business" and "Risk Factors," and elsewhere in our Annual Report on Form 10-K.

Design:
Hane Chow, Inc., Oakland, California
www.hanechow.com

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Michael Johnson, San Francisco, California
www.friendandjohnson.com

"Because cancer is such a major disease, with far-reaching social and scientific implications. By developing a new way to treat cancer, I want to make a difference in the lives of cancer patients and their families. I want to give them hope."

SCOTT FREEMAN, M.D., VICE PRESIDENT, CLINICAL DEVELOPMENT

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