Onyx Pharmaceuticals 2006 Annual Report

Launching Our Fight Against Cancer

I am

GRATEFUL FOR EVERY DAY

Nexavar® (sorafenib) Tablets: In our first year of commercializing Nexavar, we have established a global brand and the basis for a powerful oncology franchise. With our collaborator, Bayer Pharmaceuticals Corporation, we have shown that Nexavar is a highly active drug with confirmed therapeutic benefits in patients with advanced kidney cancer. We and Bayer have also demonstrated our ability to successfully execute commercially, achieving rapid sales growth and market penetration in the United States and Europe, with $165 million in worldwide net sales in 2006. In addition, we are now preparing regulatory filings in a second indication, advanced liver cancer.

Clinically Proven, Well-tolerated Oral Drug Active in a Challenging Indication

In 2006, Onyx became a commercial company as we cont nued our collaboration with Bayer on the successful worldwide launch of Nexavar for patients with advanced kidney cancer. Working with Bayer in the United States and through Bayer in the rest of the world, we established the commercial infrastructure needed to introduce Nexavar and build a global oncology franchise. Through the dedicated teamwork of our collective clinical and commercial groups, we were able to achieve rapid sales growth and market penetration in the United States and Europe.

In the United States, more than 10,000 patients and approximately 4,500 physicians have had experience with Nexavar since its approval by the U.S. Food & Drug Administration in December 2005 – an event that established Nexavar as the first new drug for patients with advanced kidney cancer in more than a decade. Outside of the United States, Bayer has made excellent progress, securing approvals in nearly 50 countries to date, including those belonging to the European Union. Consequently, Nexavar has been launched in Germany, Italy, France, Spain and the United Kingdom, and many more product launches are either planned or underway. These combined efforts produced total worldwide net sales of $165 million in 2006.

Nexavar is a targeted anticancer therapy that impedes tumor growth in two important ways: by inhibiting the proliferation of tumor cells and by cutting off the tumor's blood supply, an effect known as anti-angiogenesis. Because Nexavar is a clinically proven, well-tolerated oral drug with activity in a challenging indication, it has generated a high degree of interest in the oncology community in testing the drug against a range of different cancers, using it in combination with a variety of different treatment regimens and treatment settings. As a result, there are over 100 company-, cooperative group-, government- or investigator-sponsored studies of Nexavar that have either been completed or are underway. We are building on this strong clinical foundation to establish Nexavar's position within the international oncology market as a valuable and important drug across multiple tumor types.

Building a Global Oncology Franchise. Kidney cancer is our first step in realizing the potential of Nexavar. With Bayer, we continue our global commercialization efforts, and are also investing in a comprehensive clinical development program to leverage Nexavar's unique attributes with the goal of establishing it as a mainstay of cancer therapy in a range of different tumor types and treatment settings.

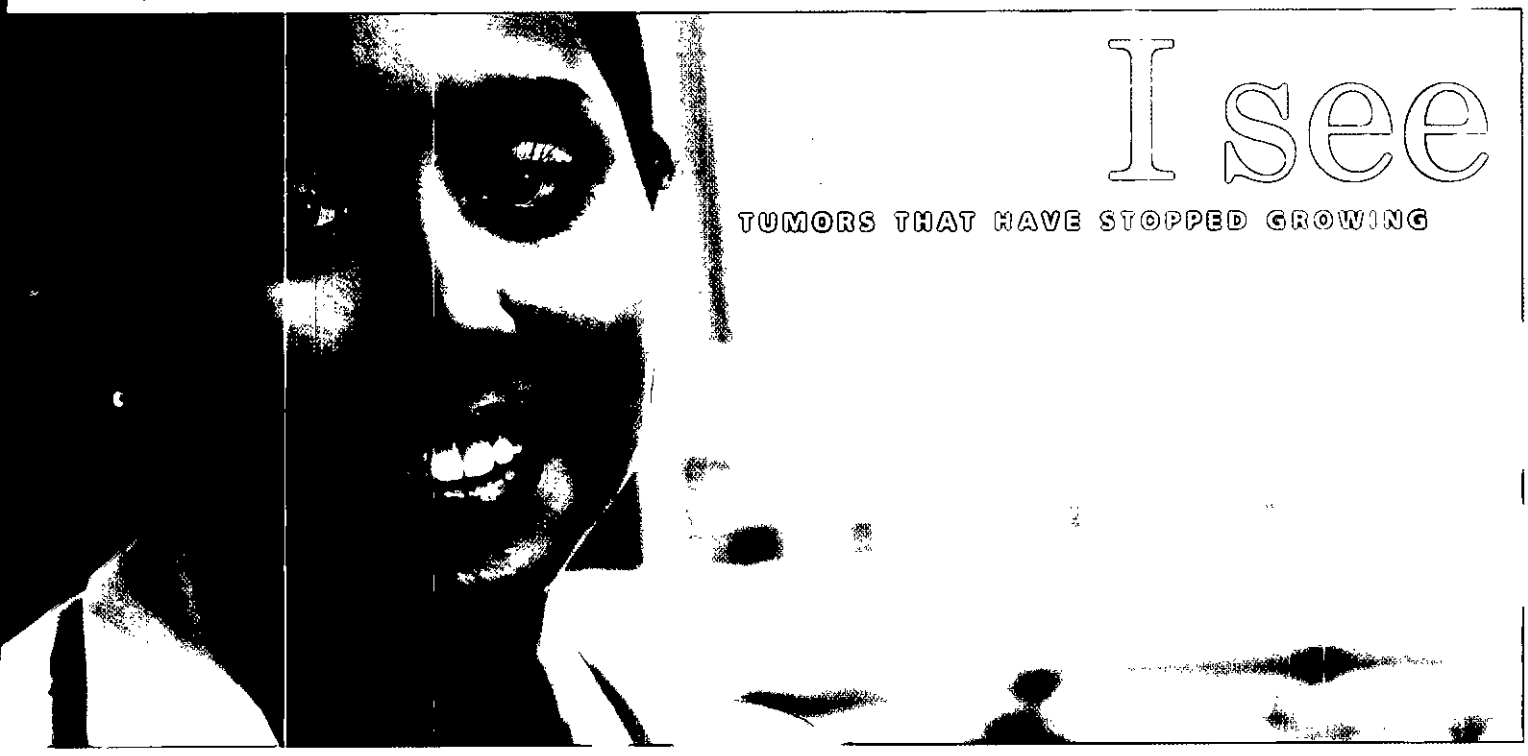
Realizing Nexavar's Full Clinical and Commercial Value

With Bayer, we have a clear two-part strategy for realizing the full clinical and commercial potential of Nexavar. First, we are addressing underserved tumors as a rapid way of getting to the market to benefit patients and establish a global oncology presence. Our success in commercializing Nexavar in its first indication just five years after beginning clinical trials validates this part of our strategy. In addition, due to positive interim results, we recently halted a Phase 3 clinical trial early in advanced liver cancer – a devastating disease for which there are limited treatment options. A pivotal trial in another tumor with limited treatment options, melanoma, is also underway.

The second part of our strategy is to leverage Nexavar's unique attributes, particularly its oral availability and combinability, to establish its efficacy in the most prevalent tumor types in combination with approved, often standard-of-care, therapies. We are focusing this program on common cancers in which targeted agents, both antiproliferatives and antiangiogenics, have demonstrated efficacy.

We have differentiated Nexavar in the marketplace to fuel both global sales and future development. One of the first multi-kinase inhibitors, Nexavar has dual mechanisms of action against two common characteristics of tumors – uncontrolled cell growth, or proliferation, and dependency on blood vessel growth for nutrients and oxygen, or angiogenesis. In kidney cancer, we have established Nexavar's activity when used as a single agent, delivered in a convenient tablet form. We have also shown Nexavar to be well tolerated, with manageable side effects. Nexavar's tolerability, along with its oral delivery, suggest that it may be used in the earlier stages of disease or as a maintenance therapy, supporting our goal of allowing patients to live longer with a higher quality of life.

Importantly, unlike most standard regimens used in cancer, Nexavar generally did not demonstrate significant bone marrow suppression in pivotal clinical studies, increasing the potential for combinability with a range of existing anticancer treatments. In fact, we have demonstrated Nexavar's combinability in early stage clinical trials involving more than a dozen leading cancer agents and believe that the full value of Nexavar may be realized in combination settings with existing therapies or other novel therapies. Because of these many differentiating characteristics, there is significant investigator enthusiasm in exploring the agent in a range of combinations and tumor types. As we execute our development strategy, we plan to leverage this interest to extend the breadth and impact of our clinical trial program.



Addressing Underserved Tumors. Our rapid commercialization of Nexavar in advanced kidney cancer, a disease without an established therapy, provided patients with a new therapeutic option while giving us broad exposure in the clinical community. We are building on this important clinical foundation by working to maximize the value of Nexavar for patients with kidney cancer. In addition, we have recently demonstrated efficacy in a Phase 3 trial in liver cancer, and we are also conducting a pivotal trial in melanoma, another cancer with limited treatment options.

Broadening Nexavar's Clinical Utility

In our program addressing underserved tumors, we are focused on expanding the utility of Nexavar in its first indication, advanced kidney cancer, and in advanced liver cancer and melanoma – cancers that remain difficult to treat and where limited progress has been made. In kidney cancer, our pivotal Phase 3 clinical trial showed Nexavar doubles the time that patients can live without disease progression. In addition, we have multiple combination treatment studies in progress. Two long-term Phase 3 studies, one in the United States and one in Europe, will assess the efficacy of Nexavar when administered to kidney cancer patients at an earlier stage of their disease.

Our studies in advanced liver cancer and melanoma, like those in kidney cancer, are very broadly focused in terms of exploring Nexavar in patients at various stages of their disease and in different treatment settings, including in combination with other agents. In this way, we expect to identify the clinical settings where Nexavar can add the most value. In liver cancer, an interim analysis of Phase 3 clinical trial data in February 2007 showed that Nexavar was able to significantly extend survival when given as a single agent to patients with advanced disease. As a result, Onyx and Bayer halted the trial early and plan to file for regulatory approval in the U.S. and Europe in this indication as rapidly as possible. In melanoma, while we were disappointed that our Phase 3 trial combining Nexavar with carboplatin and paclitaxel did not meet its primary endpoint, we are encouraged by preliminary data from a Phase 2 trial combining Nexavar with dacarbazine (DTIC). We will look to the final results of this study to guide our next steps in developing this potential combination regimen.

	PHASE 1	PHASE 2	PHASE 3	REGULATORY FILING	APPROVED
Kidney Cancer					
dvanced kidney cancer					○
djuvant, vs sunitinib vs placebo (US)			○		
djuvant, vs placebo (EU)			○		
irst line, IFN		○			
econd line, bevacizumab	○				
Liver Cancer					
irst line, single agent			○		
irst line, doxorubicin +/-		○			
Melanoma					
irst line, carboplatin/paclitaxel +/-			○		
irst line, DTIC +/-		○			
Multiple lines, temozolomide		○			

Expanding Trials in Common Tumors. We are exploring the potential of adding Nexavar to standard-of-care treatments in common tumors through an expanding clinical program in lung and breast cancer. This program seeks to leverage Nexavar's tolerability, convenient oral administration, and combinability to address the significant unmet medical needs of the hundreds of thousands of patients affected by these tumors worldwide.

Targeting Devastating Diseases with Large Patient Populations

We are beginning to explore the utility of adding Nexavar to existing drug regimens in common tumors with significant unmet medical needs and where proof of concept exists that antiangiogenics or antiproliferatives are effective. In this program, we are focusing initially on lung and breast cancer – two devastating diseases with very large patient populations that could potentially benefit from Nexavar's tolerability, oral administration, and combinability. We are partnering with key opinion leaders to explore many therapeutic options simultaneously.

In non-small cell lung cancer, a 900-patient pivotal Phase 3 trial is underway. In this study, previously untreated lung cancer patients are receiving Nexavar or a placebo in combination with carboplatin and paclitaxel, standard chemotherapeutic agents for lung cancer. We are also enrolling patients in or planning randomized Phase 2 lung cancer studies, including a large study in third-line patients sponsored by one of the largest clinical cancer research organizations in the United States.

In breast cancer, we are capitalizing on the clinical community's strong desire to explore the efficacy of Nexavar in a broad range of disease and treatment settings, including in combination with chemotherapy, hormonal therapy and targeted agents. A comprehensive Phase 2 program of multiple international, randomized studies is now being planned with leading breast cancer experts providing extensive input on trial design and collaborating on execution. We look forward to the initiation of some of these trials in the coming year.

PHASE 1 | PHASE 2 | PHASE 3 | REGULATORY FILING | APPROVED

Lung Cancer

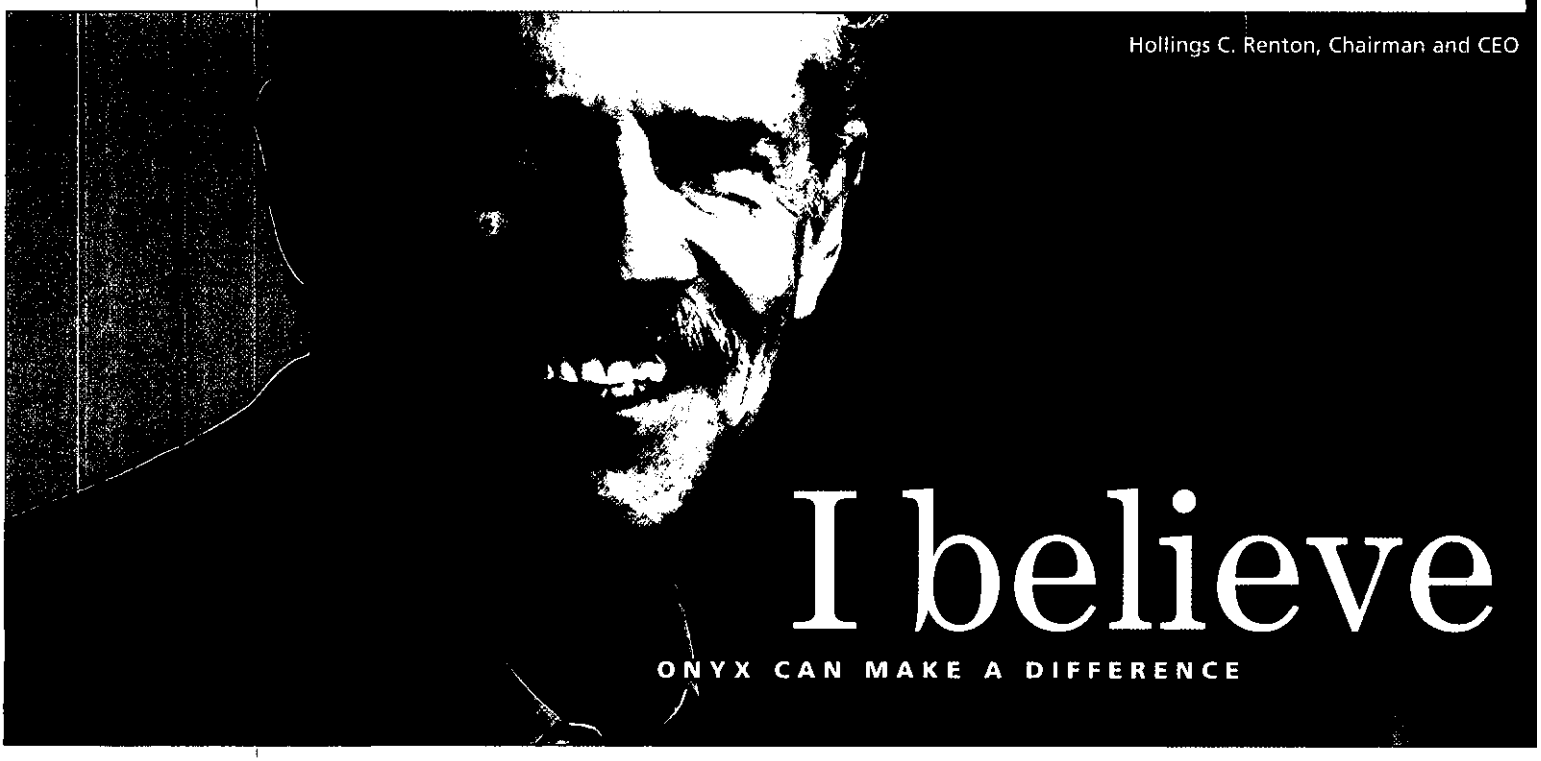
- First line, carboplatin/paclitaxel +/-
- First line, cisplatin/gemcitabine +/-
- Multiple lines, single agent
- Combination with chemotherapy*
- Combination with targeted therapy*

Breast Cancer

- Combination with chemotherapy*
- Combination with hormonal therapy*
- Combination with, or following, targeted therapies*

Finalizing protocols

Dear Fellow Stockholders: 2006 was a year of major achievement for Onyx, as we and our collaborator, Bayer, demonstrated our ability to successfully commercialize Nexavar in its first indication, the treatment of patients with advanced kidney cancer. Our launch programs in the United States and a growing number of countries internationally yielded $165 million in net sales for Nexavar in its first year of commercialization. At the same time, we are aggressively investing in and executing a comprehensive development program to fully realize Nexavar's clinical and commercial potential. As part of this effort, we have recently demonstrated efficacy in a pivotal clinical trial in a second tumor type, advanced liver cancer.



Commercial Success

We are proud of what we have accomplished and anticipate that this is just the beginning of building a global oncology franchise. At the core of this franchise is Nexavar – a targeted oral drug that acts against cancer by inhibiting proliferation and angiogenesis, two fundamental mechanisms associated with the growth of tumors. We have proven Nexavar's efficacy in what had historically been one of the most difficult-to-treat cancers, and we are competing successfully in that marketplace. We also completed enrollment in two pivotal clinical trials in liver cancer and melanoma, and have initiated our first large randomized Phase 3 clinical trial in lung cancer. This broad clinical development program reflects our two-part business strategy. First – establish an initial oncology presence with Nexavar in underserved indications, and second – maximize Nexavar's potential by adding it to the standard-of-care agents in common tumors.

In the United States, where Bayer and we are co-promoting Nexavar as a treatment for advanced kidney cancer, we saw very rapid sales growth and market penetration. To date, in the U.S. more than 10,000 patients have been treated by approximately 4,500 prescribing physicians. This positive response has been duplicated outside of the United States, where Bayer has made substantial progress in rapidly securing registrations, building commercial infrastructure and obtaining consistent pricing approvals at or near parity with U.S. levels. Nexavar is now available in approximately 50 countries worldwide, including Germany, France, Spain, the United Kingdom and Italy, fueling overall sales growth. Bayer's well-established presence and marketing leadership further strengthen Nexavar's market potential internationally.

Expanding Market Opportunity

Clearly, Nexavar and other new targeted agents are greatly expanding the kidney cancer market. Given the recent availability of multiple effective treatment options, physicians are able to select the most appropriate therapy based on an individual patient's profile. We believe that many patients are likely to be treated with multiple agents, either sequentially or – as new data emerges – in combination with other anticancer drugs. As an effective and well-tolerated drug that offers the convenience of oral administration, Nexavar is well positioned to play a leading role in this increasingly hopeful treatment scenario for advanced kidney cancer patients and their families.

To maximize Nexavar's potential to help patients with kidney cancer, we have multiple ongoing clinical trials exploring the agent's use in different treatment settings and in different combinations with other cancer agents. This is in addition to our pivotal Phase 3 kidney cancer trial, which showed that Nexavar doubled progression-free survival in a previously treated patient population. We also have two Phase 3 adjuvant trials to assess Nexavar's efficacy in earlier-stage patients and several Phase 2 combination treatment studies underway.

"When I was diagnosed, I made a list of all the things I wanted to do before I died. Thanks to Nexavar, I have checked almost all of them off. Most importantly, I have learned to live each day with joy and hope, and I can feel God working in the midst of my cancer."

This patient's outcome should not be considered indicative of outcomes that other patients may experience with Nexavar.

[redacted] was diagnosed with kidney cancer in February 2005. Her disease had spread from her kidneys to her lungs, and her prognosis was grim. Thinking she might have six months to one year left, the prosecutor-turned-minister rejected treatment with then-approved drugs. Following unsuccessful treatment with an experimental combination therapy, she welcomed the opportunity in September 2005 to enter the Nexavar® clinical study. In November, scans showed that her tumors had shrunk 25 percent – a result that was repeated two months later in January. Now her tumors are quite small, and her disease appears stable.

Since beginning treatment with Nexavar, Susan has traveled to Hawaii several times, enjoyed a Mediterranean cruise, and recently was feted at a "Miracle 60th Birthday Party."

"Although I have had to slow down while fighting this disease, every day is an amazing gift," stated Susan. "I am so grateful that due to the advent of drugs like Nexavar, physicians are now able to provide hope along with the diagnosis of cancer."

Broad Clinical Programs in Underserved Tumors

In addition to kidney cancer, we are seeking to develop Nexavar for two other underserved tumor types – advanced liver cancer and melanoma. In advanced liver cancer, we decided to halt our large, pivotal Phase 3 clinical trial evaluating Nexavar as a single agent in patients with advanced disease due to positive data from a planned interim analysis conducted early in 2007. These data showed that the trial met its primary endpoint resulting in superior overall survival in Nexavar-treated patients as compared to placebo-treated patients, with no demonstrated difference in the rate of serious adverse events between the two patient groups. This is a major clinical milestone for Bayer and Onyx, and most importantly, for patients with advanced liver cancer who have limited treatment options. Based on these results, we are planning to file for regulatory approval in the U.S. and Europe in this indication as soon as possible.

In advanced melanoma, we were disappointed to learn at the end of 2006 that our Phase 3 clinical trial of Nexavar in combination with the chemotherapeutics carboplatin and paclitaxel in previously treated patients did not meet its primary endpoint of improving progression-free survival. However, there is another Phase 3 trial ongoing in melanoma, in combination with the same chemotherapeutic agents in patients that have not been previously treated.

We are encouraged by the preliminary results of a Phase 2 study of Nexavar given in combination with dacarbazine (DTIC) to previously untreated patients. These results show that there was a 50 percent overall improvement in progression-free survival in patients receiving the combination therapy versus patients treated with DTIC alone. Based on the final results of this study, expected later in 2007, we will decide whether to proceed with a Phase 3 trial of this combination in this very difficult-to-treat cancer.

Large Growth Opportunities

The major growth opportunity for Nexavar – and the second part of our business strategy – focuses on adding it to the standard-of-care agents for common tumors. We are seeking to leverage Nexavar's tolerability, oral administration, and combinability to address unmet patient needs in major indications where targeted agents have been shown to be active. Our first major initiative is in lung cancer, which remains the number one cause of cancer deaths worldwide despite recent therapeutic advances. In early 2006, we and Bayer initiated a pivotal Phase 3 trial in previously untreated patients with non-small cell lung cancer who are receiving either Nexavar or placebo in combination with carboplatin and paclitaxel. We expect to complete enrollment in this large 900-patient study in 2007. In addition, to mitigate development risk and extend our reach in lung cancer, we also have multiple randomized Phase 2 studies now enrolling or being planned.

Our next major development initiative is in metastatic breast cancer, a devastating disease with an average survival period of one to three years. In breast cancer, we are working with a leading group of breast cancer

"Without Nexavar, I doubt that I would be alive today...I want to thank all the people who have worked to make this drug possible. They have given me back to my children and grandchildren. Thanks to them, I can sing again."

This patient's outcome should not be considered indicative of outcomes that other patients may experience with Nexavar.

BRENDA, a gospel and country singer, never suspected that she had kidney cancer. She only found out while undergoing routine tests prior to surgery for a ruptured disk in the fall of 2005. The scans told an ominous story: her entire left kidney was involved, and there was evidence the disease had spread to her lungs. Suffering also from severe asthma, Brenda faced a difficult challenge – an initial operation for her disk problem followed by the surgical removal of her kidney just one month later. In addition, she had come to a critical decision about her post-operative care, declining any treatment with chemotherapy or radiation due to her concern about their side effects.

Brenda's refusal of traditional cancer therapies led her physician to turn to Nexavar®, one of the first of a new generation of oral, targeted treatments for cancer. In May 2006, Brenda began taking Nexavar tablets. In October, her test results revealed that the metastasized tumor masses were shrinking. With her side effects limited to hair loss, Brenda is extremely grateful for the availability of Nexavar.

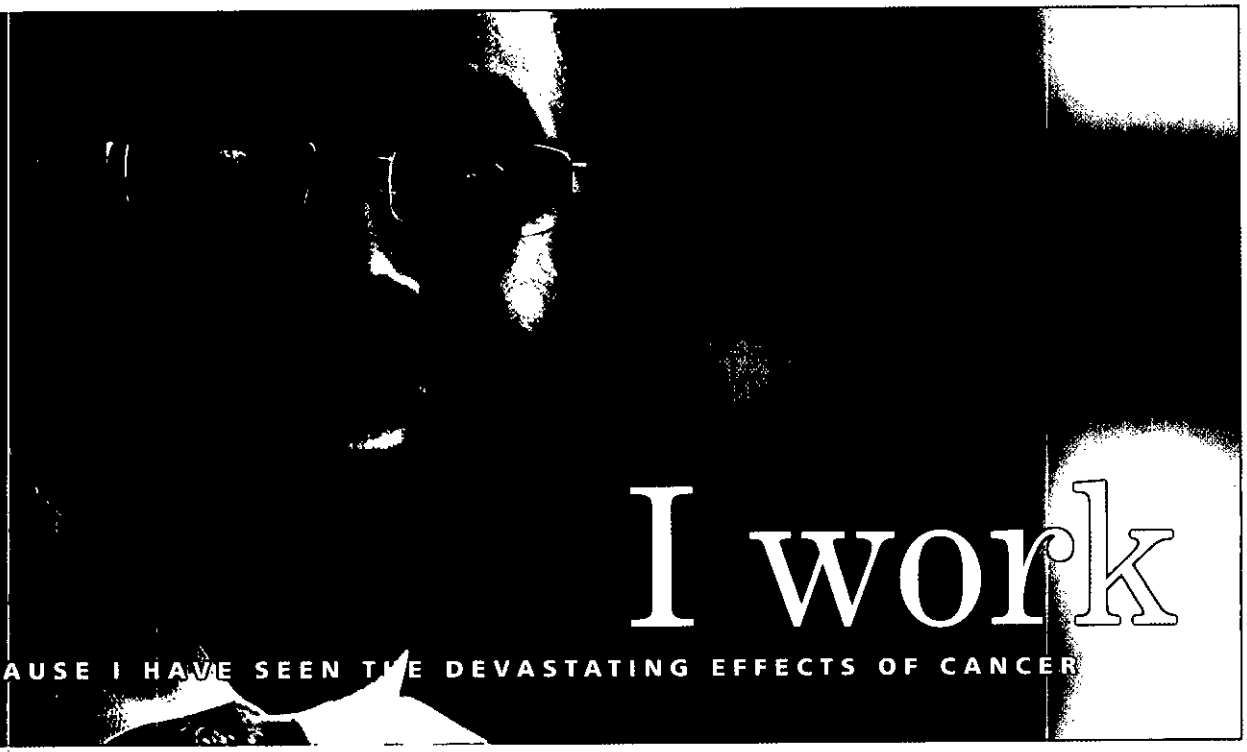
experts to design multiple randomized Phase 2 clinical trials and expect that these experts will also lead some of these studies worldwide. These trials are focused on combining Nexavar with a broad range of agents administered at various stages of the disease, including different forms of chemotherapy, hormonal therapy, and other targeted agents. We look forward to sharing more details of this comprehensive program as it advances through the coming year.

Investing in the Future

We are absolutely committed to capitalizing on Nexavar's promise as an oral antiangiogenic, antiproliferative agent, and its first-to-market status in kidney cancer. To lead the execution of our growing clinical and commercial programs, we continue to make key management appointments. In June, Laura Brege joined Onyx as Executive Vice President and Chief Business Officer. Laura was previously Senior Vice President and Chief Financial Officer at COR Therapeutics. Her strong track record of commercial operations, corporate development, and strategic finance expertise will enhance our ability to establish a major oncology franchise in Nexavar. In addition, Greg Schafer joined Laura's team as our Chief Financial Officer.

Financially, we are in a strong position to pursue comprehensive development of Nexavar. With Bayer, our success in commercializing the agent in its first indication is reflected in 2006 worldwide net sales of $165 million; these revenues are recorded by Bayer, and we share equally in the profit, with the exception of sales in Japan. As of December 31, 2006, we had cash, cash equivalents, and marketable securities of approximately $270 million. Our strong balance sheet will enable us to continue to invest in Nexavar's development, advance programs into later-stage studies, and to move into additional tumor types and more combination settings. As Nexavar sales continue to grow, we will also increase our commercial activities as needed to ensure successful launches and to maximize sales of the drug worldwide.

Our progress in the past year sets us on a clear path toward accomplishing our goal of establishing Nexavar as a global standard of care for patients living with cancer. With Bayer, we have successfully developed and commercialized a targeted oral agent in our first indication. We are also looking forward to launching Nexavar in its second indication, advanced liver cancer, assuming a favorable review by regulatory agencies. As a result, we are increasingly confident that Nexavar will benefit patients with a wide variety of cancers. We want to thank the employees, physicians, patients, partners, and stockholders who have helped to make Nexavar the success that it is today and for their continued support as we continue to work to fully capitalize on the Nexavar opportunity.



Hollings C. Renton
Chairman, President and
Chief Executive Officer
March 23, 2007

Corporate Information

Management

Hollings C. Renton
Chairman, President and Chief Executive Officer

Laura A. Brege
Executive Vice President and Chief Business Officer

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

Edward F. Kenney
Executive Vice President and Chief Commercial Officer

Jeffrey D. Bloss, 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, Sales

Patricia A. Oto, R.Ph.
Vice President, Regulatory Affairs

Gregory W. Schafer
Vice President and Chief Financial Officer

Kathleen Stafford
Vice President, Human Resources

Julianna Wood
Vice President, Corporate Communications and Investor Relations

Todd J. Yancey, M.D.
Vice President, Medical Affairs

Board of Directors

Paul Goddard, Ph.D.
Chairman and Chief Executive Officer, ARYx Therapeutics, Inc.; Chairman, AP Pharma; Director, Adolor Corporation

Antonio J. Grillo-López, M.D.
Chairman, Neoplastic and Autoimmune Diseases Research Institute

Magnus Lundberg
Chief Executive Officer, Phadia AB

Corinne H. Lyle
President, Global Operations, Edwards Lifesciences Corporation

Hollings C. Renton
Chairman, President and Chief Executive Officer, Onyx Pharmaceuticals, Inc.

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

Thomas G. Wiggans
Consultant, Stiefel Laboratories, Inc.

Advisor and Founder

Frank McCormick, Ph.D., F.R.S.
Director, UCSF Comprehensive Cancer Center and Cancer Research Institute; David A. Wood Distinguished Professor of Tumor Biology and Cancer Research; 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 Kronish LLP

Corporate Counsel

Cooley Godward Kronish 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.
Wells Fargo Shareowner Services

For telephone inquiries:
(800) 468-9716

For overnight delivery:
161 North Concord Exchange
South St. Paul, MN 55075-1139

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

Stockholder Inquiries

Inquiries and requests for information should be directed to:

Investor Relations
Onyx Pharmaceuticals, Inc.
2100 Powell Street
Emeryville, CA 94608
(510) 597-6500
email: ir@onyx-pharm.com
www.onyx-pharm.com

Dividends

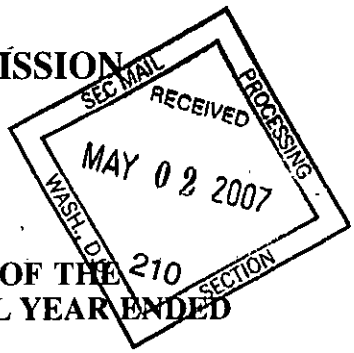
Onyx has not paid cash dividends on its common stock and does not plan to pay any cash dividends in the foreseeable future.

Annual Meeting

The annual meeting of stockholders will be held at 10:00 a.m. on May 25, 2007, at Onyx Pharmaceuticals, Inc., 2100 Powell Street, Emeryville, California.

Forward-looking Statements:
This annual report contains forward-looking statements that involve risks and uncertainties including statements about our business and the development and commercialization of Nexavar. 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.

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, 2006.**

☐ **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:

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

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

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 Global Market on June 30, 2006 was approximately $507,225,721.*

The number of shares of common stock outstanding as of February 28, 2007 was 46,585,480.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's Definitive Proxy Statement for its 2007 Annual Meeting of Shareholders (which will be filed with the Commission within 120 days of December 31, 2006), are incorporated herein by reference into Part III of this Annual Report on Form 10-K.

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* Excludes 11,347,009 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 and commercializing 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 first commercially available 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 and our subsequent launch of Nexavar marked the availability of 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. We and Bayer are jointly marketing Nexavar in the U.S. under our collaboration agreement.

In July 2006, Nexavar was approved by the European Commission for the treatment of patients with advanced renal cell carcinoma who have failed prior therapy or are considered unsuitable for such therapy. Bayer is commercializing Nexavar in Europe, as well as in all other territories outside the U.S. where Nexavar is approved. As of the end of 2006, Nexavar had been approved in approximately 50 countries worldwide with multiple additional applications pending.

The approvals of Nexavar were based on data from our pivotal Phase 3 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 3 kidney cancer trial. As a result, patients who were previously administered placebo in the trial could elect to receive Nexavar.

We and Bayer are also conducting several 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. In February 2007, we and Bayer announced that an independent data monitoring committee, or DMC, had reviewed the safety and efficacy data from the pivotal liver cancer trial and concluded that the trial met its primary endpoint resulting in superior overall survival in those patients receiving Nexavar compared to patients receiving placebo. The DMC also noted that there was no indication of imbalances between the treatment arms with regards to serious adverse events. Subsequently, we and Bayer made the decision to stop the trial early and allowed all patients in the Phase 3 liver cancer trial to be offered access to Nexavar, enabling them to "crossover" to Nexavar treatment. In December 2006, we and Bayer announced that we did not meet our primary endpoint in our pivotal metastatic melanoma clinical trial. Also, in December, we announced results from a randomized phase 2 trial evaluating Nexavar in combination with dacarbazine, or DTIC. The study showed a trend toward improved progression-free survival (PFS) in patients in the Nexavar arm versus patients in the placebo arm. Based on 80 progression events, median PFS was 21.1 weeks and 11.7 weeks respectively for Nexavar in combination with DTIC as compared to DTIC plus placebo. Overall survival data are maturing. We and Bayer may decide to initiate additional clinical trials in metastatic melanoma based on the final results from this trial. 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 worldwide to patients with advanced kidney cancer. We also intend 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 thereby improving 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 1 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-1, VEGFR-2, VEGFR-3, PDGFR-ß, KIT, FLT-3, and RET.	Advanced kidney cancer	Approved in U.S., EU and other territories worldwide
		Single-agent trial for liver cancer	Phase 3
		Combination trial for metastatic melanoma	Phase 3
		Combination trial for non-small cell lung cancer	Phase 3
		Various single-agent trials for kidney and liver cancer	Phase 2
		Combination trials for kidney and liver cancer, as well as metastatic melanoma	Phase 2
		Single-agent trials for breast, non-small cell lung and other cancers	Phase 2
		Combination trials with standard chemotherapies for melanoma, colorectal, non-small cell lung, ovarian and other cancers	Phase 2 and 1b Extension
		Additional combination trials with other anticancer agents	Phase 1b
PD 332991 (licensed to Pfizer)	Small molecule inhibitor of cyclin-dependent kinase 4	Multiple cancer types	Phase 1

Nexavar

Nexavar is an orally active agent 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-1, VEGFR-2, VEGFR-3 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, Nexavar also inhibits RAF kinase, an enzyme in the RAS signaling pathway that has been shown in preclinical models to be important 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 such as liver cancer, melanoma and lung cancer, and we believe that inhibiting this pathway could have an effect on tumor growth. 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, and by December 2006 we estimated that approximately 10,000 patients in the U.S. had been treated with Nexavar. In July 2006, Nexavar was approved by the European Commission for the treatment of patients with advanced renal cell carcinoma who have failed prior therapy or are considered unsuitable for such therapy. At the end of 2006, Nexavar had been approved in approximately 50 territories worldwide.

Development Strategy

With Bayer, we have a two-part development strategy for Nexavar. We successfully achieved the first part of that strategy by commercializing Nexavar in its first tumor type — advanced kidney cancer. This approval allowed us to establish the Nexavar brand and a commercial oncology presence. The liver cancer and metastatic melanoma trials further expand on this part of our strategy to evaluate Nexavar for the treatment of cancers for which there are significant unmet medical needs. The next phase of our strategy is to establish Nexavar's efficacy in the most prevalent tumor types in combination with already approved anti-cancer therapies such as lung cancer and breast cancer. We believe Nexavar's unique features, including its oral availability and combinability profile, may be important attributes that could differentiate it from other anti-cancer agents and enable it to be used broadly in the treatment of cancer. As we move forward, in addition to company-sponsored studies, we plan to expand our collaborations with government agencies, cooperative groups, and individual investigators. Our goal is to maximize Nexavar's commercial and clinical prospects by simultaneously running multiple studies to produce the clinical evidence necessary to demonstrate Nexavar can benefit patients with many different types of cancers.

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 3 Trial. In October 2003, we and Bayer announced the initiation of an international, placebo-controlled, multicenter Phase 3 clinical trial to evaluate the safety and efficacy of Nexavar in the treatment of advanced kidney cancer. More than 900 people participated in the Phase 3 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 3 kidney cancer trial to be offered access to Nexavar, enabling them to "crossover" to Nexavar treatment. Results from the Phase 3 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 or PFS was significantly prolonged by Nexavar. As assessed by independent radiologic review, PFS 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). 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. For example, the p-value listed above (p-value$<$0.000001) indicates that there is less than one chance in a million that the difference in PFS obtained with Nexavar compared to placebo was the result of chance rather than due to Nexavar.

In addition, an interim analysis of overall survival of patients in the Phase 3 trial was presented at ASCO in June 2006. This analysis, conducted six months following crossover, showed a continued improvement in overall survival of 19.3 months for Nexavar patients versus 15.9 months for placebo patients (p-value=0.015) despite the fact that 48 percent of placebo patients crossed over to Nexavar. Overall survival of 19.3 months for Nexavar as compared to 14.3 months for placebo (p-value=0.010) after censoring the placebo patients was also reported. These data, while not reaching the pre-specified result required to stop the study early, suggest a favorable survival trend for patients who received Nexavar. The final analysis of overall survival is expected to be presented in 2007.

Based on the current approved U.S. package insert for the treatment of patients with advanced kidney cancer, 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. The incidence of bleeding regardless of causality was 15 percent for Nexavar versus 8 percent for placebo, and the incidence of treatment-emergent cardiac ischemia/infarction was 2.9 percent for Nexavar versus 0.4 percent for placebo. Gastrointestinal perforation was an uncommon event and

has been reported in less than 1 percent of patients taking Nexavar. The 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 versus 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 2 Trial. In December 2006, we announced the results of the Phase 2 clinical trial that compares Nexavar to Interferon (IFN), which is commonly used as a first-line therapy in patients with advanced kidney cancer. Progression-free survival was comparable for patients who received either Nexavar or IFN. Based on 121 progression events, median progression-free survival was 5.6 months and 5.7 months, respectively, for IFN- and Nexavar-treated patients. Products that have shown efficacy as compared to IFN or interleukin-2, or IL-2, or in treatment naïve-patients may be preferred by the medical community.

Liver Cancer Program

Phase 3 Trial. In March 2005, we and Bayer initiated a randomized, double-blind, placebo-controlled Phase 3 clinical trial of Nexavar administered as a single agent in patients with advanced hepatocellular carcinoma, also known as liver cancer. The Phase 3 study was designed to measure differences in overall survival, time to symptom progression, and time to tumor progression of Nexavar versus placebo in patients with advanced liver cancer. Over 600 patients with advanced liver cancer, who had not received previous systemic treatment for their disease, were randomized to receive Nexavar or matching placebo. This study enrolled patients in the Americas, Europe, Australia and New Zealand and enrollment in this study was completed in 2006. In February 2007, we and Bayer announced that an independent DMC had reviewed the safety and efficacy data from the trial and concluded that the trial met its primary endpoint resulting in superior overall survival in those patients receiving Nexavar. The DMC also noted no demonstrated difference in the serious adverse event rates between Nexavar and placebo. Subsequently, we and Bayer made the decision to stop the trial early and allowed all patients in the Phase 3 liver cancer trial to be offered access to Nexavar, enabling them to "crossover" to Nexavar treatment.

Phase 2 Trial. The decision to begin the Phase 3 liver cancer trial was based upon data from a Phase 2 clinical trial. In September 2004, the data from this Phase 2 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 trial, 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 trial, 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. In 2005, we and Bayer announced a randomized Phase 2 trial evaluating Nexavar in this disease in combination with doxorubicin, a chemotherapeutic agent commonly used to treat liver cancer.

Metastatic Melanoma Program

Phase 3 Trials. In May 2005, we and Bayer commenced a randomized, double-blind Phase 3 trial administering Nexavar in combination with the chemotherapeutic agents carboplatin and paclitaxel in patients with advanced metastatic melanoma who had failed one prior treatment. The trial, which enrolled 270 patients, had progression-free survival as its primary endpoint. Participating patients failed one previous systemic chemotherapeutic treatment with either dacarbazine, also known as DTIC, or temozolomide. Patients were randomized to receive Nexavar or matching placebo, in addition to a standard dosing schedule of carboplatin and paclitaxel. In December 2006, Bayer and Onyx announced that this study did not meet its primary endpoint of improving PFS,

noting that the treatment effect was comparable in each arm. Data from the study is expected to be presented at an upcoming scientific congress in 2007.

In 2005, a second Phase 3 study administering Nexavar in combination with carboplatin and paclitaxel was initiated under the sponsorship of the Eastern Cooperative Oncology Group, or ECOG. Patients are being randomized to receive Nexavar plus the chemotherapeutic agents paclitaxel and carboplatin, or placebo in addition to the chemotherapeutic agents at the doses described above. 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. This study is continuing to enroll patients.

Phase 2 Trial. In addition, we are conducting a randomized, double-blind, placebo-controlled, multicenter, Phase 2 study underway administering Nexavar in combination with DTIC with PFS as its primary endpoint. Approximately 100 patients with advanced melanoma who had not received prior chemotherapy were randomized to receive Nexavar in combination with DTIC or placebo in combination with DTIC. In December 2006, we reported that there was a trend toward improved PFS in patients in the Nexavar arm versus patients in the placebo arm. Based on 80 progression events, median PFS was 21.1 weeks and 11.7 weeks respectively for Nexavar in combination with DTIC as compared to DTIC plus placebo (Hazard Ratio=0.67). We are continuing to analyze data from this trial as it becomes available and will use this data to determine what potential additional clinical studies we may undertake, if any.

Phase 1/2 Trial. The decision to conduct the above Phase 3 trials in patients with metastatic melanoma was based upon single-arm data from a Phase 1b combination trial evaluating Nexavar in combination with these agents. By the fall of 2006, investigators had reported on a total of 105 melanoma patients enrolled in the trial at two different sites. At the time of the report, PFS was more than eight 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 3 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 is comparing 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 PFS, 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 is being conducted at over 100 sites in North America, South America, Europe and the Asia Pacific region. We expect to complete accrual in 2007. A data monitoring committee is overseeing the conduct of the trial.

Phase 1/Phase 2 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 PFS 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 1 study administering the combination of carboplatin, paclitaxel and Nexavar. For the lung cancer patients on the combination therapy, the investigator reported an overall median PFS of approximately 245 days, or approximately eight months. As this

investigator-initiated analysis was not reviewed by the sponsors, the results are subject to change until the database is finalized.

Breast Cancer Program

With Bayer, we have identified advanced breast cancer as the next major development initiative for Nexavar. In 2007, Onyx and Bayer intend to launch a broad, multinational Phase 2 program in advanced breast cancer. The program is being designed and led by an international group of experts in the field of breast cancer and includes multiple randomized Phase 2 trials. These Phase 2 trials are screening studies intended to provide information that will be used to design a Phase 3 program. The program involves a number of different drug combinations with Nexavar and encompasses various treatment settings. The advisors are particularly interested in studying Nexavar in breast cancer where the product's features, such as its oral administration and favorable hematologic toxicity profile, may translate into benefits for patients over other existing and experimental treatments. We expect to begin enrolling patients in these planned breast cancer studies in 2007.

Earlier Stage Clinical Development

Phase 2 in Multiple Tumor Types. With Bayer we have multiple ongoing Phase 2 studies evaluating Nexavar as a single agent in tumors such as prostatic, 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 1b in Combination with Anticancer Agents in Multiple Tumor Types. Together with Bayer, we are conducting multiple Phase 1b 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 2 trials are pending.

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 1 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 a payment of $1.0 million in 2005 and may receive additional milestone payments upon the achievement of clinical, regulatory and commercial events. We are entitled to 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.

In March 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. 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.

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 2 clinical studies and $15.0 million in the fourth quarter of 2003 based upon the initiation of a Phase 3 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.

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 2006, 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 2007, 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, has been approved by the FDA, and because we have retained U.S. co-promotion rights, in 2005 we 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

Under our collaboration agreement with Bayer, Bayer has the manufacturing responsibility to supply Nexavar for commercial requirements and to support any clinical trials. To date, Bayer has manufactured sufficient drug supply to support the current needs of commercial activity and clinical trials in progress. We believe that Bayer has the capability to meet all future drug supply needs and meet the FDA and other regulatory agency requirements. 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.

At this time, we do not have any internal manufacturing capability. 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.

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, 2006, we owned or had licensed rights to 58 United States patents and 37 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 1 clinical trials is to establish initial data about safety and tolerability of the product candidate in humans. The goal of Phase 2 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 3 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 4 clinical trials are carried out. If these Phase 4 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, Amgen, AstraZeneca PLC, OSI Pharmaceuticals, Inc., Wyeth, and Genentech, 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.

For example, Sutent, a multi-kinase inhibitor marketed by Pfizer, was approved by the FDA and the European Union for treating patients with kidney cancer and Gleevec-resistant gastrointestinal stromal tumors, or GIST. In January 2007, Pfizer reported that European regulators approved Sutent as an initial, or first-line, treatment for advanced kidney cancer patients and granted the product full marketing authorization. Previously, Sutent only had conditional approval for second-line use after the failure of alternative treatments. In June 2006, results of a randomized Phase 3 trial comparing Sutent to IFN in treatment-naive patients with advanced kidney cancer were reported. The primary endpoint of the study was PFS with a median PFS of 11 months for patients receiving Sutent compared to five months for patients receiving IFN. 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. In June 2006, results from a randomized Phase 2 trial comparing Avastin with or without erlotinib in treatment-naive advanced renal cancer patients were reported. The median PFS for the Avastin-treated patients was 8.5 months. A Phase 3 randomized trial in treatment-naïve advanced kidney cancer patients is underway comparing Avastin and IFN that may produce superior PFS or overall survival data than Nexavar. In December, Genentech announced that an interim analysis showed that a randomized Phase 3 clinical study of Avastin in combination with IFN in patients with first-line metastatic renal cell carcinoma significantly improved PFS compared to IFN therapy alone.

In addition, Wyeth is conducting a Phase 3 study of temsirolimus, an mTOR inhibitor, in poor-risk patients with advanced kidney cancer. In June 2006, results of a randomized Phase 3 trial comparing temsirolimus to interferon to both agents combined in treatment-naïve, poor-risk advanced kidney cancer patients were reported. The primary endpoint of the study was overall survival. The reported median overall survival was 10.9 months for temsirolimus alone as compared to 7.3 months for interferon. Wyeth filed a new drug application for this compound in October 2006.

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.

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 Amgen and ImClone Systems, Inc. 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 and non-small cell lung cancer and is in clinical development for kidney cancer, among other indications. In addition, many other pharmaceutical companies are developing novel cancer therapies that, if successful, would also provide competition for 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, 2006, we had 125 full-time employees of whom 16 hold Ph.D., M.D. or Pharm.D. degrees. Of our employees, 18 are in research and development, 74 are in sales and marketing and 33 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 our SEC filings available free of charge on or through our website, 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*

You should carefully consider the risks described below, together with all of the other information included in this report, in considering our business and prospects. The risks and uncertainties described below contain forward-looking statements, and our actual results may differ materially from those discussed here. Additional risks and uncertainties not presently known to us or that we currently deem immaterial also may impair our business operations. Each of these risk factors could adversely affect our business, operating results and financial condition, as well as adversely affect the value of an investment in our common stock and/or contingent value rights.

Risks Related to Our Business

Nexavar® (sorafenib) tablets is our only product, and we do not have any other product candidates in Phase 2 or Phase 3 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 the development and commercialization of Nexavar and managing our relationship with Bayer, 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.

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 1 single-agent clinical trials of Nexavar. We are currently conducting a number of Phase 1b clinical trials of Nexavar in combination with other anticancer agents. Phase 1 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 2 clinical trials of Nexavar in kidney and liver cancer and are conducting Phase 2 clinical trials in non-small cell lung, melanoma and other cancers. Phase 2 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, we and Bayer are conducting a number of Phase 3 trials of Nexavar. Phase 3 trials are designed to more rigorously test the efficacy of a product candidate and are normally randomized and double-blinded. In February 2006, we and Bayer initiated a Phase 3 clinical trial of Nexavar in combination with carboplatin and paclitaxel in patients with non-small cell lung cancer, or NSCLC. In May 2006, we and Bayer completed enrollment of both a Phase 3 clinical trial of Nexavar in patients with liver cancer and a separate Phase 3 clinical trial of Nexavar in combination with the chemotherapeutic agents carboplatin and paclitaxel in patients with malignant melanoma. In December 2006, we and Bayer announced that a Phase III trial administering Nexavar® (sorafenib) or placebo tablets in combination with the chemotherapeutic agents carboplatin and paclitaxel in patients with advanced melanoma did not meet its primary endpoint of improving progression-free survival (PFS). The treatment effect was comparable in each arm.

Although we have received approvals 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. While we and Bayer have stopped the Phase 3 liver cancer trial based on the recommendation of the DMC, the data has not yet been filed or reviewed by

regulatory authorities, and may not result in marketing approval in this indication. Historically, many companies have failed to demonstrate the effectiveness of pharmaceutical product candidates in Phase 3 clinical trials notwithstanding favorable results in Phase 1 or Phase 2 clinical trials. Even though we have obtained fast track designation for Nexavar in metastatic liver and skin cancer, we and Bayer may not obtain marketing approval for the use of Nexavar in these indications from the FDA or other regulatory authorities. 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.

Even though we have stopped the Phase 3 liver cancer trial, Nexavar may never be approved for use in this indication, or its approval may be significantly delayed.

In February 2007, we and Bayer announced that an independent DMC had reviewed the safety and efficacy data from our Phase 3 clinical trial of Nexavar administered as a single agent in patients with advanced liver cancer. The DMC concluded that the trial met its primary endpoint resulting in superior overall survival in those patients receiving Nexavar. Subsequently, we and Bayer made the decision to stop the Phase 3 liver cancer trial early and offer all patients in the trial access to Nexavar, enabling them to "crossover" to Nexavar treatment. While we and Bayer have stopped the Phase 3 liver cancer trial based on the recommendation of the DMC, the data has not yet been filed with or reviewed by regulatory authorities, and may not result in marketing approval in this indication.

Based on the results of this trial, and together with Bayer, we intend to file an application with the FDA and foreign regulatory authorities for marketing approval of Nexavar for use in patients with advanced liver cancer. The regulatory authorities may be unsatisfied with the safety and efficacy data submitted in support of these applications, which could result in either non-approval or a requirement of additional clinical trials or further analysis of existing data. In addition to the question of whether Nexavar has demonstrated sufficient efficacy in the treatment of liver cancer, the FDA may have questions about the safety of the drug. For these or other reasons, there is no assurance that Nexavar will be approved for the treatment of advanced liver cancer, or that any such approval, if granted, will occur quickly.

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

Many companies are marketing and developing products to treat patients with advanced kidney cancer. The market is highly competitive and we expect the competition to increase as additional products are approved to treat advanced kidney cancer.

For example, Sutent, a multi-kinase inhibitor marketed by Pfizer, is available in the U.S. and the European Union for treating patients with kidney cancer and Gleevec-resistant gastrointestinal stromal tumors, or GIST. In January 2007, Pfizer reported that European regulators approved Sutent as an initial, or first-line, treatment for advanced kidney cancer patients and granted the product full marketing authorization. Prior to this approval, Sutent had only conditional approval for second-line use after the failure of alternative treatments. In June 2006, results of a randomized Phase 3 trial comparing Sutent to IFN in treatment-naive patients with advanced kidney cancer were reported. The primary endpoint of the study was progression-free survival with a median progression-free survival of 11 months for patients receiving Sutent compared to five months for patients receiving IFN. 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 A Phase 3 randomized trial in treatment-naïve advanced kidney cancer patients is underway comparing Avastin and IFN that may produce superior progression-free survival or overall survival data than Nexavar. In December, Genentech announced that an interim

analysis showed that a randomized Phase 3 clinical study of Avastin in combination with IFN in patients with first-line metastatic renal cell carcinoma significantly improved PFS compared to IFN therapy alone.

In addition, Wyeth is conducting a Phase 3 study of temsirolimus (CCI-779), an mTOR inhibitor, in patients with advanced kidney cancer. In June 2006, results of a randomized Phase 3 trial comparing temsirolimus to interferon to both agents combined in treatment-naïve, poor-risk advanced kidney cancer patients were reported. The primary endpoint of the study was overall survival. The reported median overall survival was 10.9 months for temsirolimus alone as compared to 7.3 months for interferon. Wyeth filed a new drug application with the FDA for this compound in October 2006.

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.

In April 2005, as a result of a recommendation by us and Bayer, all patients in our ongoing randomized Phase 3 kidney cancer trial who were previously administered placebo in the trial were given the opportunity to receive Nexavar. This action reduced the number of patients in the trial receiving placebo. In November 2005 and June 2006, investigators presented interim analyses on overall survival of patients in this Phase 3 kidney cancer trial. In both cases, the data presented were not sufficient to be considered statistically significant according to the predefined specifications for the interim analyses. The final analysis of overall survival is expected to be presented in 2007. Crossover of patients from placebo to Nexavar is likely to negatively impact our ability to obtain statistically significant overall survival data. Competitors with statistically significant overall survival data could be preferred in the marketplace, impairing our ability to successfully market Nexavar.

In December 2006, we announced the results of the Phase 2 clinical trial that compares Nexavar to Interferon (IFN), which is commonly used as a first-line therapy in patients with advanced kidney cancer. Progression-free survival was comparable for patients who received either Nexavar or IFN. Based on 121 progression events, median progression-free survival was 5.6 months and 5.7 months, respectively, for IFN- and Nexavar-treated patients. Products that have shown efficacy as compared to IFN or interleukin-2, or IL-2, or in treatment naïve-patients may be preferred by the medical community. Further, survival may become the single most important element in determining standard of care. We expect that our ability to obtain statistically significant overall survival data has been impaired by the cross over of patients from placebo to Nexavar beginning in April 2005, and we have not demonstrated a measurable difference in Nexavar's efficacy as compared to IFN or IL-2. The use of any particular therapy may limit the use of a competing therapy with a similar mechanism of action. The FDA approval of Nexavar permits Nexavar to be used as an initial, or first-line, therapy for the treatment of advanced kidney cancer, but some other approvals do not. For example, the European Union approval indicates Nexavar only for advanced kidney cancer patients that have failed prior therapy, or whose physicians deem alternate therapies inappropriate. The successful introduction of other 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.

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.

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, cooperative oncology organizations 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 2 and Phase 3 clinical trials of Nexavar for the treatment of malignant melanoma. In 2007, Onyx and Bayer intend to launch a broad, multinational Phase 2 program in advanced breast cancer. The program is being designed and led by an international group of experts in the field of breast cancer and includes multiple randomized Phase 2 trials. 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 indications other than kidney cancer, and thus seriously harm our business.

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 includes the following warnings relating to 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.
- Gastrointestinal perforation has been reported in less than one percent of patients taking Nexavar.
- 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.

As Nexavar becomes more widely available worldwide, we and Bayer anticipate we will routinely update side effects and adverse events listed on the package insert to reflect current information. For example, subsequent to FDA approval, we and Bayer updated the package insert to include additional information on types of internal bleeding observed and new adverse events reported by physicians using Nexavar, including gastrointestinal perforations, congestive heart failure, keratoacanthomas/squamous cell cancer of the skin, which is a form of a skin lesion, and reversible posterior leukoencephalopathy syndrome, or RPLS, a rare but reversible neurological phenomenon associated with severe hypertension. 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 or other international regulatory agencies could modify or revoke 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.

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. Due to a highly competitive environment with existing and emerging products, Nexavar sales will be difficult to predict from period to period. 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, Bayer and our investments in the research and development and commercialization of Nexavar, and expenditures we may incur to acquire additional products.

In addition, as a result of our adoption of FAS 123(R), we must measure compensation cost for stock-based awards made to employees at the grant date of the award, based on the fair value of the award, and recognize the cost

as an expense over the employee's requisite service period. As the variables that we use as a basis for valuing these awards change over time, the magnitude of the expense that we must recognize may vary significantly. Any such variance from one period to the next could cause a significant fluctuation in our operating results.

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

Our net loss for the year ended December 31, 2004 was $46.8 million, for the year ended December 31, 2005 was $95.2 million and for the year ended December 31, 2006 was $92.7 million. As of December 31, 2006, we had an accumulated deficit of approximately $438.5 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 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 received regulatory approval only for the use of Nexavar in the treatment of advanced kidney cancer in the United States and a number of foreign markets.

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.

While Nexavar has received approvals for sale in several countries outside of the United States, it has not received pricing approval in all of these foreign countries, and may not receive marketing approval in additional countries.

In July 2005, we and Bayer filed for approval of Nexavar based on the progression-free survival data. The FDA granted full approval in December 2005 for patients with advanced kidney cancer. In March 2006, the Swiss Agency for Therapeutic Products approved Nexavar as a treatment for patients with advanced kidney cancer, after nepherectomy and prior palliative or adjuvant therapy with cytokines. In April 2006 the Mexican Ministry of Health granted approval of Nexavar as a treatment for advanced kidney cancer. In July 2006, the European Commission granted marketing authorization for Nexavar for the treatment of patients with advanced kidney cancer who have failed prior interferon-alpha or interleukin-2 based therapy or are considered unsuitable for such therapy. Nexavar has also received approvals in more than 50 territories worldwide. Other foreign regulatory authorities may not, however, be satisfied with the safety and efficacy data submitted in support of the foreign applications, which could result in non-approval, a requirement of additional clinical trials, further analysis of existing data or a restricted use of Nexavar. Lack of marketing approval in a particular country would prevent us from selling Nexavar in that country, which could harm our business. In addition, we and Bayer will be required to negotiate the price of Nexavar with European governmental authorities in order for Nexavar to be eligible for government reimbursement. In many European countries, patients will not use prescription drugs that are not reimbursable by their governments. European price negotiations could delay commercialization in a particular country by twelve months or more.

Nexavar was approved by the FDA for the treatment of advanced kidney cancer on the basis of the progression-free survival endpoint. The final analysis of overall survival is expected to be presented later in the year. 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. 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 in some countries, or will receive more limited approval than that granted by the FDA. For example, neither the European Union nor the Swiss Agency for Therapeutic Products approved Nexavar as an initial or first-line therapy, and it is possible that other foreign regulatory agencies will take a similar approach. In addition to the question of whether Nexavar has demonstrated sufficient efficacy in the treatment of kidney cancer, 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 Phase 3 trial, and physicians have reported some incidents of additional adverse events in patients receiving Nexavar. 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 any additional foreign approvals on the basis of the current application without amendment, if it is approved at all.

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

We are engaged in a rapidly changing and highly competitive field. We are seeking to develop and market Nexavar to 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 at various stages of clinical development include Pfizer, Wyeth, Novartis International AG, Amgen, AstraZeneca PLC, OSI Pharmaceuticals, Inc. and Genentech, 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 non-small cell lung cancer, or NSCLC and pancreatic cancer in combination with gemcitabine. Companies working on developing antibody approaches include Amgen 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 NSCLC and is in clinical development for kidney cancer, among other indications. 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.

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;
- repayment of our of milestone-based advances;
- 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 capital 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.

In September 2006, in connection with our committed equity financing facility, we entered into a stock purchase agreement with Azimuth Opportunity Ltd., or Azimuth. The committed equity financing facility entitles us to sell and obligates Azimuth to purchase, from time to time over a period of two years, shares of our common stock for cash consideration up to an aggregate of $150.0 million, subject to certain conditions and restrictions. Capital will not be available to us under the committed equity financing facility if our stock price is below $8.00 per share or if we are unable to meet other conditions specified in the stock purchase agreement. In addition, when we draw down under the committed equity financing facility, we will sell shares to Azimuth at a discount of up to 5.05 percent from the volume weighted average price of our common stock. If we draw down amounts under the committed equity financing facility when our share price is decreasing, we will need to issue more shares to raise the same amount than if our share price was higher.

We believe that our existing capital resources and interest thereon will be sufficient to fund our current development plans into 2009. However, if we change our development plans or if Nexavar is not broadly accepted in the marketplace, we may need additional funds sooner than we expect. Moreover, once a development program has been initiated, under our collaboration with Bayer we may have limited ability to control the expenditures made under that program, which we share equally with Bayer. 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 2009. 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.

We are dependent on the efforts of Bayer to market and promote Nexavar in countries outside the United States where Nexavar has received 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 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. 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 Bayer's business strategy changes, it may adversely affect our collaborative relationship.

Bayer may change its business strategy. Bayer recently completed a public takeover of Schering AG and the integration of the two companies will consume management resources at Bayer that may negatively impact our collaboration. 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.

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.

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; and
- cease operations.

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

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, Laura A. Brege, our Executive Vice President and Chief Business Officer, Edward F. Kenney, our Executive Vice President and Chief Commercial 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. 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 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.

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. Changes in government legislation or regulation, such as the Medicare Act, including Medicare Part D, or changes in private third-party payers' policies towards reimbursement for our products may reduce reimbursement of our products costs to physicians. 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.

Nexavar's success in Europe 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 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. While an application is pending, a United States patent has not been issued 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. Patent applications for Nexavar are also pending throughout the world. As of December 31, 2006, we owned or had licensed rights to 58 United States patents and 37 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 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 face product liability risks and may not be able to obtain adequate insurance.

The sale of Nexavar and its ongoing use in clinical trials 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.

If we do not receive timely and accurate financial and market information from Bayer regarding the development and sale of Nexavar, we may be unable to accurately report our results of operations.

As a result of our arrangements with Bayer, we are highly dependent on Bayer for timely and accurate information regarding the costs incurred in developing and selling Nexavar, and any revenues realized from its sale, in order to accurately report our results of operations. If we do not receive timely and accurate information, or underestimate activity levels associated with the co-promotion and development of Nexavar at a given point in time, we could record significant additional expense in future periods, and may be required to restate our results for prior periods. Such inaccuracies or restatements could cause a loss of investor confidence in our financial reporting or lead to claims against us, resulting in a decrease in the trading price of shares of our common stock.

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, 2006, 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:

- reported sales of Nexavar by Bayer;
- interim or final results of, or speculation about, clinical trials from Nexavar;
- decisions by regulatory agencies;
- 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;
- changes in healthcare reimbursement policies;
- sales of our common stock by existing holders, or sales of shares issuable upon exercise of outstanding options and warrants; and

- sales by us of our common stock, including sales under our committed equity financing facility arrangement with Azimuth.

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 2 clinical trial data in patients with advanced kidney cancer, our stock price declined significantly. In December 2006, following our announcement that a Phase 3 trial administering Nexavar or placebo tablets in combination with the chemotherapeutic agents carboplatin and paclitaxel in patients with advanced melanoma did not meet its primary endpoint, our stock price declined significantly. 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.

Existing stockholders have significant influence over us.

Our executive officers, directors and five-percent stockholders own, in the aggregate, approximately 25 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.

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.

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 requires 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 adopted FAS 123(R) using the modified prospective basis on January 1, 2006. The adoption of FAS 123(R) had a material adverse impact on our results of operations and our net loss per share. For example, as a result of our adoption of FAS 123(R), for the year ended December 31, 2006, our net loss increased by $14.0 million, or $0.33 per share, as compared to the year ended December 31, 2005 net loss. We expect that our future results will continue to be adversely affected by FAS 123(R) and that the FASB could issue new accounting pronouncements that could affect our future financial position and results of operations.

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. In December 2006, we amended the existing lease to occupy an additional 14,000 square feet of office space. The lease expires in March 2013.

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, 2006.

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			
	2006		2005	
	High	Low	High	Low
First Quarter	$29.10	$25.82	$33.77	$25.30
Second Quarter	25.29	14.67	33.46	23.70
Third Quarter	17.29	12.87	27.66	19.30
Fourth Quarter	19.60	10.44	30.14	22.45

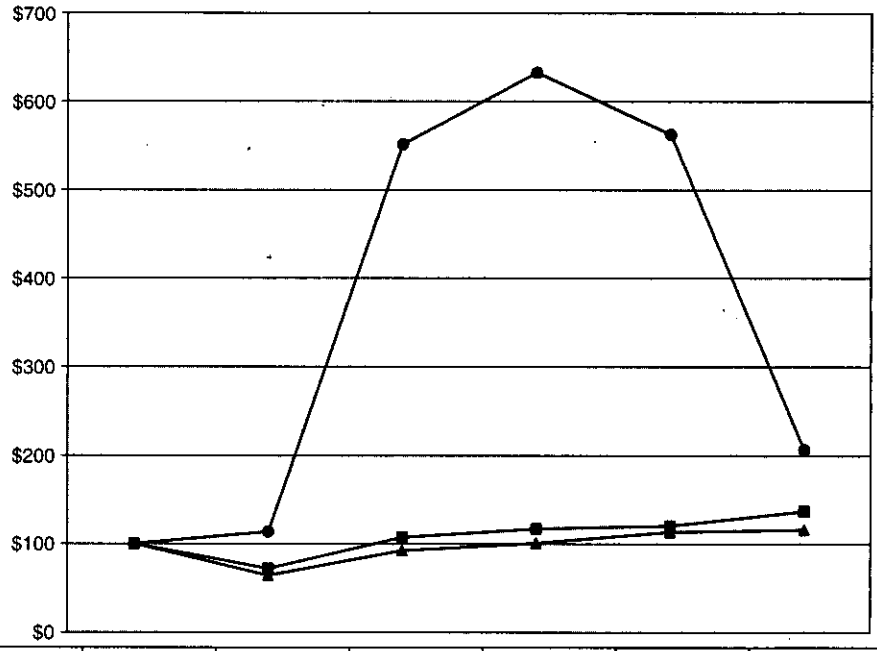
On February 28, 2007, the last reported sales price of our common stock on NASDAQ was $26.25 per share.

Stock Performance Graph

This performance graph is not "soliciting material," is not deemed filed with the SEC and is not to be incorporated by reference in any filing by us under the Securities Act of 1933, as amended (the "Securities Act"), or the Exchange Act, whether made before or after the date hereof and irrespective of any general incorporation language in any such filing. The stock price performance shown on the graph is not necessarily indicative of future price performance.

COMPARISON OF 5 YEAR CUMULATIVE TOTAL RETURN*

Among ONYX Pharmaceuticals, Inc., The NASDAQ Composite Index And The NASDAQ Pharmaceutical Index



	Dec-01	Dec-02	Dec-03	Dec-04	Dec-05	Dec-06
—●— ONYX PHARMACEUTICALS, INC.	$100.00	$113.48	$551.37	$632.62	$562.50	$206.64
—■— NASDAQ STOCK MARKET (U.S.)	$100.00	$ 71.97	$107.18	$117.07	$120.50	$137.02
—▲— NASDAQ PHARMACEUTICAL	$100.00	$ 64.40	$ 92.31	$100.78	$113.36	$115.84

Holders

There were approximately 207 holders of record of our common stock as of February 28, 2007.

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, 2006

Plan Category (1)	Number of securities to be issued upon exercise of outstanding options, warrants and rights Column a	Weighted-average exercise price of outstanding options, warrants and rights Column b	Number of securities remaining available for future issuance under equity compensation plans (excluding securities reflected in column a) Column c
Equity compensation plans approved by security holders . . .	5,334,477	$22.05	1,825,782(2)

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

(2) Of these securities, 91,004 shares remain available for purchase under our Employee Stock Purchase Plan.

Recent Sales of Unregistered Securities

None.

Issuer Purchases of Equity Securities

We did not repurchase any of our equity securities during the fiscal year ended December 31, 2006.

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, 2006, 2005, and 2004 and the Balance Sheet data as of December 31, 2006 and 2005 has been derived from our audited financial statements included elsewhere in this report. The Statement of Operations data for the years ended December 31, 2003 and 2002 and the Balance Sheet data as of December 31, 2004, 2003 and 2002 has 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,				
	2006	2005	2004	2003	2002
	(In thousands, except per share data)				
Statement of Operations Data:					
Total revenue	$ 250	$ 1,000	$ 500	$ —	$ 2,715
Operating expenses:					
Net expense from unconsolidated joint business	23,915	—	—	—	—
Research and development	30,980	63,120	35,846	32,059	43,604
Selling, general and administrative	50,019	39,671	14,316	7,939	6,192
Restructuring	—	—	258	5,530	—
Loss from operations	(104,664)	(101,791)	(49,920)	(45,528)	(47,081)
Interest and other income and expense, net	11,983	6,617	3,164	559	1,294
Net loss	$ (92,681)	$ (95,174)	$(46,756)	$(44,969)	$(45,787)
Basic and diluted net loss per share	$ (2.20)	$ (2.64)	$ (1.36)	$ (1.73)	$ (2.23)
Shares used in computing basic and diluted net loss per share	42,170	36,039	34,342	25,953	20,535

	December 31,				
	2006	2005	2004	2003	2002
	(In thousands)				
Balance Sheet Data:					
Cash, cash equivalents, and marketable securities	$ 271,403	$ 284,680	$ 209,624	$ 105,400	$ 39,833
Total assets	286,246	294,665	215,546	109,138	46,241
Working capital	256,432	241,678	197,873	92,826	28,727
Advance from collaboration partner	40,000	30,000	20,000	20,000	5,000
Accumulated deficit	(438,491)	(345,810)	(250,636)	(203,880)	(158,911)
Total stockholders' equity	222,780	223,240	179,988	73,519	28,784

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 dedicated to developing innovative therapies that target the molecular mechanisms that cause 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 product, Nexavar® (sorafenib) tablets, 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. In July 2006, Nexavar received approval to treat patients in the European Union with advanced kidney cancer who have failed prior interferon-alpha or interleukin-2 based therapy or are considered unsuitable for such therapy. Nexavar has received approvals in other territories worldwide. Nexavar is a novel, orally available multi-kinase inhibitor and is one of a new class of anticancer treatments that target growth signaling.

On March 6, 2006, we and Bayer entered into a Co-Promotion Agreement to co-promote Nexavar in the United States. This agreement amends the original 1994 Collaboration Agreement and supersedes the provisions of that agreement that relate to the co-promotion of Nexavar in the United States. 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 refer to Note 2 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. Since inception, we have relied on public and private financings, combined with milestone payments from our collaborators to fund our operations. In January 2006, we received the fourth and final $10.0 million milestone advance from Bayer as a result of the FDA approval of Nexavar. However, we expect that our losses will continue and will fluctuate from quarter to quarter and that such fluctuations may be substantial. As of December 31, 2006, our accumulated deficit was approximately $438.5 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 consider certain accounting policies related to net expense from unconsolidated joint business, stock-based compensation and research and development to be critical policies. 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 2006 included assumptions used in the determination of stock-based compensation related to 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.

Net Expense from Unconsolidated Joint Business: Net expense from unconsolidated joint business relates to our collaboration with Bayer for the development and marketing of Nexavar. It consists of our share of the net collaboration loss generated from our Collaboration Agreement with Bayer net of the reimbursement of our development and marketing expenses related to Nexavar. Under the collaboration, Bayer recognizes all revenue from the sale of Nexavar. The net expense from the unconsolidated joint business is, in effect, the net amount due to Bayer to balance the companies' economics under the Nexavar collaboration. Under the terms of the collaboration, the companies share all research and development, marketing, and non-U.S. sales expenses, excluding Japan. Some of the revenue and expenses recorded to derive the net expense from unconsolidated joint business during the period presented are estimates of both parties and are subject to further adjustment based on each party's final review should actual results differ materially from these estimates. If the Company underestimates activity levels associated with the collaboration of Nexavar at a given point in time, the Company could record significant additional expenses in future periods.

Stock Based-Compensation: Effective January 1, 2006, we adopted the Statement of Financial Accounting Standards, or FAS, No. 123(R), "Share-Based Payment", ("FAS 123(R)"), which requires the measurement and recognition of compensation expense for all stock-based payments made to our employees and directors including employee stock option awards and employee stock purchases made under our Employee Stock Purchase Plan, or ESPP, based on estimated fair value. We previously applied the provisions of Accounting Principles Board Opinion, or APB, No. 25, "Accounting for Stock Issued to Employees" ("APB 25") and related Interpretations and provided the required pro forma disclosures under FAS 123, "Accounting for Stock-Based Compensation", or FAS 123.

We adopted FAS 123(R) using the modified prospective transition method beginning January 1, 2006. Accordingly, during the year ended December 31, 2006, we recorded stock-based compensation expense for awards granted prior to but not yet vested as of January 1, 2006 as if the fair value method required for pro forma disclosure under FAS 123 were in effect for expense recognition purposes adjusted for estimated forfeitures. For these awards, the Company has continued to recognize compensation expense using the accelerated amortization method under FASB Interpretation No. 28, "Accounting for Stock Appreciation Rights and Other Variable Stock Option or Award Plans." For stock-based awards granted after January 1, 2006, we recognized compensation expense based on the estimated grant date fair value method required under FAS 123(R). The compensation expense for these awards was recognized using a straight-line amortization method. The net loss for the year ended December 31, 2006 includes stock-based compensation expense of $14.0 million, or $0.33 per share for the adoption of FAS 123(R). As of December 31, 2006, the total unrecorded stock-based compensation balance for unvested shares, net of expected forfeitures, was $23.1 million, which is expected to be amortized over a weighted-average period of 23 months.

On November 10, 2005, the Financial Accounting Standards Board (FASB) issued FASB Staff Position No. FAS 123(R)-3, "Transition Election Related to Accounting for Tax Effects of Share-Based Payment Awards." We have elected to adopt the alternative transition method provided in the FASB Staff Position for calculating the tax effects (if any) of stock-based compensation expense pursuant to SFAS 123R. The alternative transition method includes simplified methods to establish the beginning balance of the additional paid-in capital pool (APIC pool)

related to the tax effects of employee stock-based compensation, and to determine the subsequent impact to the APIC pool and the consolidated statements of operations and cash flows of the tax effects of employee stock-based compensation awards that are outstanding upon adoption of SFAS 123R.

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. Option valuation models require the input of highly subjective assumptions, including but not limited to stock price volatility and stock option exercise behavior. 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 future periods, 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, expected life 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, stock-based compensation expense, 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 and 93 percent in 2004, relates to our cost sharing arrangement with Bayer and represents our share of the research and development costs incurred by Bayer. Such amounts were 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 2006, consistent with the terms of our collaboration agreement, our share of Bayer's Nexavar product development expenses are included in Net Expense from Unconsolidated Joint Business. Thus, in 2006, only our direct research and development expenses are included in the research and development line item.

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 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 underestimate 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, 2006, 2005 and 2004

Revenue Nexavar, our only marketed product, was approved in the U.S. in December 2005. In accordance with our collaboration agreement with Bayer, Bayer recognizes all revenue from the sale of Nexavar. As such, for the year ended December 31, 2006, we reported no revenue related to Nexavar. For the year ended December 31,

2006, Nexavar net sales recorded by Bayer were $165.0 million, primarily in the United States and the European Union.

Total revenue was $250,000 in 2006, $1.0 million in 2005 and $500,000 in 2004. Total revenue in 2006 represents $100,000 recognized for selling the rights to certain viruses from our now discontinued therapeutic virus program to Shanghai Sunway Biotech Co. Ltd and $150,000 recognized for licensing rights to certain cytopathic viruses for therapy and prophylaxis of neoplasia to DNAtriX. 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 any of these agreements. Total revenue in 2004 of $500,000 represented a milestone payment from Warner-Lambert, now a subsidiary of Pfizer Inc, when they initiated Phase 1 clinical testing advancing a lead candidate from our previous cell cycle kinase discovery collaboration.

Net Expense from Unconsolidated Joint Business. Nexavar is currently marketed and sold in the United States, several countries in the European Union and other countries worldwide for the treatment of advanced kidney cancer. We co-promote Nexavar in the United States with Bayer under a collaboration agreement. Under the terms of the collaboration agreement, we 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 outside of Japan and its continued promotion of Nexavar in the United States. The collaboration was created through a contractual arrangement, not through a joint venture or other legal entity.

Bayer provides all product distribution and all marketing support services for Nexavar in the United States, including managed care, customer service, order entry and billing. Bayer is compensated for distribution expenses based on a fixed percent of gross sales of Nexavar in the United States. Bayer is reimbursed for half of its expenses for marketing services provided by Bayer for the sale of Nexavar in the United States. We and Bayer share equally in any other out-of-pocket marketing expenses (other than expenses for sales force and medical science liaisons) that we and Bayer incur in connection with the marketing and promotion of Nexavar in the United States. Bayer manufactures all Nexavar sold in the United States and is reimbursed at an agreed transfer price per unit for the cost of goods sold.

In the United States, we contribute half of the overall number of sales force personnel required to market and promote Nexavar and half of the medical science liaisons to support Nexavar. Onyx and Bayer each bears its own sales force and medical science liaison expenses. These expenses are not included in the calculation of the profits or losses of the collaboration.

Outside of the United States, except in Japan, Bayer incurs all of the sales and marketing expenditures, and we share equally in those expenditures. In addition, upon approval of Nexavar in countries outside the United States, except Japan, we will reimburse Bayer a fixed percentage of sales to reimburse them for their marketing infrastructure. Research and development expenditures on a worldwide basis, except in Japan, are equally shared by both companies regardless of whether we or Bayer incurs the expense. In Japan, Bayer is responsible for all development and marketing costs and we will receive a royalty on net sales of Nexavar.

Net expense from unconsolidated joint business consists of our share of the pretax collaboration loss generated from our collaboration with Bayer net of the reimbursement of our marketing and research and development costs related to Nexavar. Under the collaboration; Bayer recognizes all sales of Nexavar worldwide. We record our share of the collaboration pre-tax loss on a quarterly basis. Collaboration loss is derived by calculating net sales of Nexavar to third-party customers and deducting the cost of goods sold, distribution costs, marketing costs (including without limitation, advertising and education expenses, selling and promotion expenses, marketing personnel expenses, and Bayer marketing services expenses), Phase 4 clinical trial costs, allocable overhead costs and research and development costs. The net expense from the unconsolidated joint business is, in effect, the net amount due to Bayer to balance the companies' economics under the Nexavar collaboration. As noted above, United States sales force and medical science liaison expenditures incurred by both companies are borne by each company separately and are not included in the calculation. Some of the revenue and expenses recorded to derive the net expense from unconsolidated joint business during the period presented are estimates of both parties and are subject to further adjustment based on each party's final review should actual results differ from these estimates. If

we underestimate activity levels associated with the co-promotion and collaboration of Nexavar at a given point in time, we could record significant additional expense in future periods.

Net expense from unconsolidated joint business decreases with increased Nexavar net revenue and as the differential between Bayer's and our shared Nexavar expenses declines. If Nexavar net revenue is greater than the differential between Bayer's and our shared Nexavar expenses, we will report a net profit from unconsolidated joint business. Conversely, if Nexavar net revenue declines or if the differential between Bayer's and our shared Nexavar expenses increases, net expense from unconsolidated joint business will increase. Due to the uncertainty in Bayer's revenue from the sale of Nexavar and the relative expenses of Bayer's and our shared Nexavar expenses, it is not possible to predict our net expense from unconsolidated joint business for future periods. We expect Bayer's and our shared Nexavar research and development expenses to increase in future periods as the companies develop Nexavar for indications beyond advanced kidney cancer. We also expect Bayer's and our shared cost of goods sold, distribution, selling and general administrative expense to increase as Bayer continues to expand Nexavar marketing and sales activities outside of the United States.

For the year ended December 31, 2006, net expense from unconsolidated joint business was $23.9 million calculated as follows:

	Year Ended December 31, 2006
	(In thousands)
Product revenue, net	$ 164,994
Combined cost of goods sold, distribution, selling, general and administrative	123,004
Combined research and development	161,180
Combined collaboration loss	$(119,190)
Onyx's share of collaboration loss	$ (59,595)
Reimbursement of Onyx's direct development and marketing expenses	35,680
Onyx's net expense from unconsolidated joint business	$ (23,915)

Research and Development Expenses. Research and development expenses were $31.0 million, including stock-based compensation expense of $2.5 million in 2006, a net decrease of $32.1 million, or 51 percent, from $63.1 million in 2005. We did not expense employee stock-based compensation prior to our adoption of FAS 123(R) on January 1, 2006. The decrease was primarily due to the change in presentation of our Statement of Operations to reflect the co-promotion agreement by including the net expense from unconsolidated joint business line item. Our share of Bayer's Nexavar product development expenses is included in net expense from unconsolidated joint business for the year ended December 31, 2006. In years prior to 2006, Bayer's Nexavar product development expense was included in research and development expense. In the new presentation beginning in 2006, only our direct research and development expenses are included in the research and development line item. Onyx and Bayer are continuing to expand their investment in the development of Nexavar for additional indications including Phase 3 trials for Nexavar in melanoma, liver cancer and lung cancer.

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 co-development costs for the Nexavar program, principally for the clinical trial program which included the expanded access program in the Phase 3 kidney cancer trial initiated in the second quarter of 2005. In addition, 2005 Nexavar development costs reflect the ongoing pivotal Phase 3 kidney cancer trial, a Phase 3 trial in liver cancer initiated in the first quarter of 2005 and a Phase 3 trial in metastatic melanoma initiated in May 2005, as well as several Phase 1b and 2 clinical trials. This increase was partially offset by a decrease of $1.4 million from the therapeutic virus program, which was terminated in 2003.

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, stock-based compensation expense, 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 1, 2 and 3 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, 2006	2005	2004
					(In millions)	
Nexavar (sorafenib) Tablets (1)	Small molecule inhibitor of tumor cell proliferation and angiogenesis, targeting RAF, VEGFR-2, PDGFR- β, KIT, FLT-3, and RET.	Bayer	Phase 1 – 2004 Phase 2 – Unknown Phase 3 – Unknown	$84.2(2)	$62.1	$33.4
Therapeutic Virus Programs (3)	Programs discontinued during the second quarter of 2003.	—	—	—	1.0	2.4
			Total Research and Development Expenses	$84.2	$63.1	$35.8

(1) Aggregate research and development costs-to-date through December 31, 2006 incurred by Onyx since fiscal year 2000 for the Nexavar project is $219.0 million.

(2) Costs reflected in this table represent our share of Bayer's product development costs included in net expenses from unconsolidated joint business and our direct research and development costs.

(3) Costs in 2005 were comprised of:

a. stock-based compensation for consultants;

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 $50.0 million, including stock-based compensation expense of $11.5 million, in 2006, a net increase of $10.3 million, or 26 percent, from $39.7 million in 2005. We did not expense employee stock-based compensation prior to our adoption of FAS 123(R) on January 1, 2006. In addition to the stock-based compensation expense, the increase was primarily due to the establishment of our U.S. Nexavar sales force in the second half of 2005 and our marketing expenses relating to the Nexavar launch. Offsetting this increase is a change in accounting presentation of our Statement of Operations to reflect the co-promotion agreement by including the net expense from unconsolidated joint business line item. Our share of Bayer's Nexavar-related marketing expenses is included in the net expense from unconsolidated joint business line item. In years prior to 2006, our share of Nexavar-related marketing expenses was included in the Company's selling, general and administrative line item. Under the new presentation

only our direct selling, general and administrative expenses are included in the selling, general and administrative expenses line item. Our direct selling, general and administrative expenses increased in 2006 due to the adoption of FAS 123(R), as well as the payroll-related costs of our sales force and medical science liaisons who were hired in the second half of 2005. Additionally, general and administrative costs, excluding stock-based compensation, increased $3.2 million primarily due to employee-related costs as a result of headcount increases to support commercialization of Nexavar.

Selling, general and administrative expenses were $39.7 million in 2005, an increase of $25.4 million, or 177 percent, from 2004. The increase primarily related to increased selling and marketing costs of $24.1 million due to employee related costs for hiring our sales and marketing personnel as we established 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.

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.

Restructuring. In 2004, we recorded a 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 had been fully paid.

Interest Income, Net. We had net interest income of $12.0 million in 2006, an increase of $5.7 million from 2005, primarily due to higher interest rates in 2006 compared to 2005. In addition, our average cash balances in 2006 benefited from our October and November 2006 sale of equity securities from which we received approximately $74.3 million in net cash proceeds. 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. Interest expense was immaterial for the periods presented.

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 other fiscal years presented.

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, 2006, our net operating loss carryforwards for federal income tax purposes were approximately $385.9 million and for state income tax purposes were approximately $321.2 million. We also had federal research and development tax credit carryforwards of approximately $22.3 million and state research and development tax credit carryforwards of approximately $10.5 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 13 of the Notes to Financial Statements included in Item 8 of this Form 10-K for further information.

Related Party Transactions

The Company has a loan receivable from a non-officer employee of which approximately $228,000 is outstanding at December 31, 2006. This loan bears interest at 4.82% per annum and is due in three annual payments, beginning in 2007.

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, we have incurred losses, and we have relied primarily on public and private financing, combined with milestone payments we have received from our collaborators to fund our operations

At December 31, 2006, we had cash, cash equivalents, and short and long-term marketable securities of $271.4 million, compared to $284.7 million at December 31, 2005 and $209.6 million at December 31, 2004. The decrease in cash, cash equivalents, and marketable securities in 2006 of $13.3 million is primarily due to net cash used in operating activities of $100.2 million. This use of cash was partially offset by net cash proceeds of $74.3 from our October and November sales of equity securities under our committed equity financing, $2.5 million from stock option exercises and the $10.0 million milestone-based advance received from Bayer in January 2006. This $10.0 million payment, in addition to $30.0 million of milestones received in previous years, 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.

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. These sources of cash were partially offset by net cash used in operating activities of $72.6 million and capital expenditures of $624,000.

Our cash used in operations was $100.2 million in 2006, $72.6 million in 2005 and $46.9 million in 2004. In 2006, the cash used primarily related to the net loss and payments of the 2005 year-end and 2006 first, second and third quarter payables to Bayer, our collaboration partner. 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. Expenditures for capital equipment amounted to $619,000 in 2006, $624,000 in 2005 and $1.6 million in 2004. Capital expenditures in 2006 and 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 $2.7 million in 2007 primarily for leasehold improvements, furniture and equipment and information technology software.

In September 2006, we secured a commitment for up to $150 million in a common stock purchase agreement with Azimuth Opportunity Ltd. or Azimuth. During the two-year term of the commitment, Onyx may sell at its discretion registered shares of its common stock to Azimuth at a discount to the market price ranging from 3.30% to 5.05%. Onyx will determine, at its sole discretion, the timing and amount of any sales of stock, subject to certain conditions. In October and November 2006, Azimuth purchased an aggregate of 4,326,098 shares of our common stock under the purchase agreement for an aggregate purchase price of $75.0 million. We received $74.4 million in net proceeds from the sale of these shares after deducting our offering expenses.

We believe that our existing capital resources and interest thereon will be sufficient to fund our current and planned operations into 2009. 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 throughout the world. While these costs are unknown at the current time, we may need to raise additional capital to continue the co-funding of the program in future periods through and beyond 2009. We intend to seek any required 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 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	$6,520	$1,036	$3,130	$2,092	$262

(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 $40.0 million creditable milestone-based payments that we received from Bayer as of December 31, 2006 because the repayment of this amount 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 2006, we amended our existing operating lease to occupy 14,000 square feet of office space in addition to the 23,000 square feet already occupied in Emeryville, California, which serves as our corporate headquarters. The lease expires on March 31, 2013. 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 which we are currently subleasing through September 2010.

Recently Issued Accounting Standards

In July 2006, the FASB issued FASB Interpretation No. 48, "Accounting for Uncertainty in Income Taxes — an interpretation of FASB Statement No. 109" ("FIN 48"). FIN 48 defines the threshold for recognizing the benefits of tax return positions in the financial statements as "more-likely-than-not" to be sustained by the taxing authority and provides guidance on the derecognition, measurement and classification of income tax uncertainties, along with any related interest and penalties. FIN 48 also includes guidance concerning accounting for income tax uncertainties in interim periods and increases the level of disclosures associated with any recorded income tax uncertainties. FIN 48 is effective for fiscal years beginning after December 15, 2006. The differences between the amounts recognized in the statements of financial position prior to the adoption of FIN 48 and the amounts reported after adoption will be accounted for as a cumulative-effect adjustment recorded to the beginning balance of retained earnings. We are currently evaluating the impact of FIN 48 on our financial statements.

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, 2006, the fair value of our portfolio would decline by approximately $716,000.

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

	2006			2005		
	Maturity	Fair Value ($ in millions)	Average Interest Rate	Maturity	Fair Value ($ in millions)	Average Interest Rate
Cash equivalents, fixed rate	0 – 2 months	$ 94.1	5.34%	0 – 2 months	$ 45.4	3.97%
Marketable securities, fixed rate	0 – 13 months	$177.0	4.91%	0 – 23 months	$238.6	4.66%

We did not hold any derivative instruments as of December 31, 2006, 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 52 to 75 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, 2006 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, 2006. 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, 2006, 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, 2006 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, 2006 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, 2006, 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, 2006, 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, 2006, 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, 2006 and 2005, and the related statements of operations, stockholders' equity and cash flows for each of the three years in the period ended December 31, 2006 of Onyx Pharmaceuticals, Inc. and our report dated February 28, 2007 expressed an unqualified opinion thereon.

/s/ ERNST & YOUNG LLP

Palo Alto, California
February 28, 2007

Item 9B. ***Other information***

On November 3, 2006, we entered into a First Amendment to Sublease, dated August 5, 2004, with Oracle USA, Inc. (successor in interest to Siebel Systems, Inc.), with respect to our office space located at 2100 Powell Street, Emeryville, California. The amendment increased the leased space from approximately 23,000 square feet to approximately 37,000 square feet and extended the lease by approximately three years. Rent for the additional space will be $33,722.80 per month for the first year and will increase annually thereafter by a predetermined amount until the new term of the sublease expires on March 31, 2013.

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 2007 Definitive Proxy Statement filed not later than 120 days following the close of the fiscal year ended December 31, 2006.

Item 11. ***Executive Compensation***

The information required under this item is hereby incorporated by reference from our 2007 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 2007 Definitive Proxy Statement.

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

The information required under this item is hereby incorporated by reference from our 2007 Definitive Proxy Statement.

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

The information required under this item is hereby incorporated by reference from our 2007 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 52 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(3)	Certificate of Amendment to Amended and Restated Certificate of Incorporation.
3.4(18)	Certificate of Amendment to Amended and Restated Certificate of Incorporation.
4.1(1)	Reference is made to Exhibits 3.1, 3.2, 3.3 and 3.4.
4.2(1)	Specimen Stock Certificate.
10.1(15)*	Collaboration Agreement between Bayer Corporation (formerly Miles, Inc.) and the Company dated April 22, 1994.
10.1(i)(15)*	Amendment to Collaboration Agreement between Bayer Corporation and the Company dated April 24, 1996.
10.1(ii)(15)*	Amendment to Collaboration Agreement between Bayer Corporation and the Company dated February 1, 1999.
10.2(8)*	Amended and restated Research, Development and Marketing Collaboration Agreement dated May 2, 1995 between the Company and Warner-Lambert Company.
10.2(i)(8)*	Research, Development and Marketing Collaboration Agreement dated July 31, 1997 between the Company and Warner-Lambert Company.
10.2(ii)(8)*	Amendment to the Amended and Restated Research, Development and Marketing Collaboration Agreement, dated December 15, 1997, between the Company and Warner-Lambert Company.
10.2(iii)(8)*	Second Amendment to the Amended and Restated Research, Development and Marketing Agreement between Warner-Lambert and the Company dated May 2, 1995.
10.2(iv)(8)*	Second Amendment to Research, Development and Marketing Collaboration Agreement between Warner-Lambert and the Company dated July 31, 1997.
10.2(v)(23)*	Amendment #3 to the Research, Development and Marketing Collaboration Agreement between the Company and Warner-Lambert dated August 6, 2001.
10.2(vi)(4)*	Amendment #3 to the Amended and Restated Research, Development and Marketing Collaboration Agreement between the Company and Warner-Lambert dated August 6, 2001.
10.3(5)*	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(11)+	Form of Executive Change in Control Severance Benefits Agreement.
10.10(2)*	Collaboration Agreement between the Company and Warner-Lambert Company dated October 13, 1999.

Exhibit Number	Description of Document
10.10(i)(4)*	Amendment #1 to the Collaboration Agreement between the Company and Warner-Lambert dated August 6, 2001.
10.10(ii)(7)*	Second Amendment to the Collaboration Agreement between the Company and Warner-Lambert Company dated September 16, 2002.
10.11(6)	Stock and Warrant Purchase Agreement between the Company and the investors dated May 6, 2002.
10.12(9)	Sublease between the Company and Siebel Systems dated August 5, 2004.
10.12(i)	First Amendment to Sublease between the Company and Oracle USA Inc., dated November 3, 2006.
10.13(10)+	Onyx Pharmaceuticals, Inc. 2005 Equity Incentive Plan.
10.13(i)+	Form of Stock Option Agreement pursuant to the 2005 Equity Incentive Plan.
10.13(ii)+	Form of Stock Option Agreement pursuant to the 2005 Equity Incentive Plan and the Non-Discretionary Grant Program for Directors.
10.14(12)+	Separation Agreement between Onyx Pharmaceuticals, Inc. and Leonard E. Post, Ph.D., dated December 5, 2005.
10.15(13)+	2006 Base Salaries and Bonuses for Fiscal Year 2005 for Named Executive Officers.
10.16(14)**	U.S. Co-Promotion Agreement by and between the Company and Bayer Pharmaceuticals Corporation, dated March 6, 2006.
10.17(16)+	Letter Agreement between Gregory W. Schafer and the Company, dated April 12, 2006.
10.18(17)+	Separation Agreement between the Company and Scott M. Freeman, M.D., dated May 3, 2006.
10.19(19)+	Letter Agreement between Laura A. Brege and the Company, dated May 19, 2006.
10.20(20)+	Letter Agreement between Gregory W. Schafer and the Company, dated July 7, 2006.
10.21(20)+	Form of Stock Bonus Award Grant Notice and Agreement between the Company and certain award recipients.
10.22(21) +	Separation Agreement between Fabio M. Benedetti, M.D. and the Company, dated September 6, 2006.
10.23(22)	Common Stock Purchase Agreement between Onyx Pharmaceuticals, Inc. and Azimuth Opportunity Ltd., dated September 29, 2006.
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.

** Confidential treatment has been requested 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 Current Report on Form 8-K filed on March 1, 2000.

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

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

(5) Filed as an exhibit to Onyx's Annual Report on Form 10-K for the year ended December 31, 2001. The redactions to this agreement have been amended since its original filing in accordance with a request for extension of confidential treatment filed separately by the Company with the Securities and Exchange Commission.

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

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

(8) Filed as an exhibit to Onyx's Annual Report on Form 10-K for the year ended December 31, 2002. The redactions to this agreement have been amended since its original filing in accordance with a request for extension of confidential treatment filed separately by the Company with the Securities and Exchange Commission.

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

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

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

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

(13) Filed as an exhibit to the registrant's Current Report on Form 8-K filed on March 7, 2006.

(14) Filed as an exhibit to Onyx's Quarterly Report on Form 10-Q for the quarter ended March 31, 2006.

(15) Filed as an exhibit to Onyx's Quarterly Report on Form 10-Q for the quarter ended March 31, 2006. The redactions to this agreement have been amended since its original filing in accordance with a request for extension of confidential treatment filed separately by the Company with the Securities and Exchange Commission.

(16) Filed as an exhibit to the registrant's Current Report on Form 8-K filed on April 18, 2006.

(17) Filed as an exhibit to the registrant's Current Report on Form 8-K filed on May 12, 2006.

(18) Filed as an exhibit to Onyx's Registration Statement on Form S-3 (No. 333-134565) filed on May 30, 2006.

(19) Filed as an exhibit to the registrant's Current Report on Form 8-K filed on June 12, 2006.

(20) Filed as an exhibit to the registrant's Current Report on Form 8-K filed on July 12, 2006.

(21) Filed as an exhibit to the registrant's Current Report on Form 8-K filed on September 7, 2006.

(22) Filed as an exhibit to Onyx's Current Report on Form 8-K filed on September 29, 2006.

(23) Filed as an exhibit to Onyx's Quarterly Report on Form 10-Q for the quarter ended September 30, 2006. The redactions to this agreement have been amended since its original filing in accordance with a request for extension of confidential treatment filed separately by the Company with the Securities and Exchange Commission.

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 5th day of March, 2007.

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 Gregory W. Schafer 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 Officer)	March 5, 2007
/s/ GREGORY W. SCHAFER Gregory W. Schafer	Vice President and Chief Financial Officer (Principal Financial and Accounting Officer)	March 5, 2007
/s/ PAUL GODDARD Paul Goddard, Ph.D.	Director	March 5, 2007
/s/ ANTONIO GRILLO-LÓPEZ Antonio Grillo-López, M.D.	Director	March 5, 2007
/s/ MAGNUS LUNDBERG Magnus Lundberg	Director	March 5, 2007
/s/ CORINNE LYLE Corinne Lyle	Director	March 5, 2007
/s/ WENDELL WIERENGA Wendell Wierenga, Ph.D.	Director	March 5, 2007
/s/ THOMAS G. WIGGANS Thomas G. Wiggans	Director	March 5, 2007

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, 2006 and 2005, and the related statements of operations, stockholders' equity and cash flows for each of the three years in the period ended December 31, 2006. 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, 2006 and 2005, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2006, in conformity with U.S. generally accepted accounting principles.

As discussed in Note 1 to the financial statements, in 2006 Onyx Pharmaceuticals, Inc. changed its method of accounting for stock-based compensation in accordance with guidance provided in Statement of Financial Accounting Standards No. 123(R), "Share-Based Payment".

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, 2006, based on criteria established in Internal Control — Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission and our report dated February 28, 2007 expressed an unqualified opinion thereon.

/s/ ERNST & YOUNG LLP

Palo Alto, California
February 28, 2007

ONYX PHARMACEUTICALS, INC.

BALANCE SHEETS

	December 31, 2006	December 31, 2005
	(In thousands, except share and per share amounts)	
ASSETS		
Current assets:		
Cash and cash equivalents	$ 94,413	$ 46,064
Short-term marketable securities	172,545	228,754
Receivable from collaboration partner	9,281	4,350
Other current assets	3,659	3,935
Total current assets	279,898	283,103
Long-term marketable securities	4,445	9,862
Property and equipment, net	1,478	1,617
Other assets	425	83
Total assets	$ 286,246	$ 294,665
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 297	$ 581
Payable to collaboration partner	8,391	30,823
Accrued liabilities	3,194	1,343
Accrued clinical trials and related expenses	8,263	5,567
Accrued compensation	3,321	3,111
Total current liabilities	23,466	41,425
Advance from collaboration partner	40,000	30,000
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; 100,000,000 shares authorized; 45,913,370 and 41,210,734 shares issued and outstanding as of December 31, 2006 and 2005, respectively	46	41
Additional paid-in capital	661,402	569,800
Receivable from stock option exercises	—	(24)
Accumulated other comprehensive loss	(177)	(767)
Accumulated deficit	(438,491)	(345,810)
Total stockholders' equity	222,780	223,240
Total liabilities and stockholders' equity	$ 286,246	$ 294,665

See accompanying notes.

ONYX PHARMACEUTICALS, INC.

STATEMENTS OF OPERATIONS

	Year Ended December 31,		
	2006	2005	2004
	(In thousands, except per share amounts)		
License fee revenue	$ 250	$ 1,000	$ 500
Operating expenses:			
Net expense from unconsolidated joint business	23,915	—	—
Research and development	30,980	63,120	35,846
Selling, general and administrative	50,019	39,671	14,316
Restructuring	—	—	258
Total operating expenses	104,914	102,791	50,420
Loss from operations	(104,664)	(101,791)	(49,920)
Interest income, net	11,983	6,242	3,164
Other income	—	375	—
Net loss	$ (92,681)	$ (95,174)	$(46,756)
Basic and diluted net loss per share	$ (2.20)	$ (2.64)	$ (1.36)
Shares used in computing basic and diluted net loss per share	42,170	36,039	34,342

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, 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
Exercise of stock options at prices ranging from $4.00 to $25.30 per share	347,287	—	2,520	24	—	—	2,544
Issuance of common stock in connection with Azimuth common stock purchase agreement	4,326,098	5	74,353	—	—	—	74,358
Stock-based compensation, related to stock option grants	—	—	13,957	—	—	—	13,957
Issuance of common stock pursuant to employee stock purchase plan	22,584	—	602	—	—	—	602
Issuance of restricted stock awards	6,667	—	170	—	—	—	170
Comprehensive loss:							
Change in unrealized loss on investments	—	—	—	—	590	—	590
Net loss	—	—	—	—	—	(92,681)	(92,681)
Comprehensive loss	—	—	—	—	—	—	(92,091)
Balances at December 31, 2006	45,913,370	$46	$661,402	$ —	$(177)	$(438,491)	$222,780

See accompanying notes.

ONYX PHARMACEUTICALS, INC.

STATEMENTS OF CASH FLOWS

	Year Ended December 31		
	2006	2005	2004
		(In thousands)	
Cash flows from operating activities:			
Net loss	$ (92,681)	$ (95,174)	$ (46,756)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	758	630	194
Gain on investment	—	(375)	—
Noncash restructuring charges	—	—	280
Gain on sale of fixed assets	—	(7)	(18)
Forgiveness of note receivable	—	—	11
Stock-based compensation	14,406	906	1,353
Changes in operating assets and liabilities:			
Receivable from collaboration partner	(4,931)	(3,321)	(445)
Prepaid expenses and other current assets	352	(1,157)	(1,139)
Other assets	(190)	34	(84)
Accounts payable	(284)	(457)	739
Accrued liabilities	1,851	(552)	1,121
Accrued clinical trials and related expenses	2,696	5,567	(147)
Payable to collaboration partner	(22,432)	19,303	(2,112)
Accrued compensation	210	2,201	188
Accrued restructuring	—	(195)	(130)
Net cash used in operating activities	(100,245)	(72,597)	(46,945)
Cash flows from investing activities:			
Purchases of marketable securities	(360,272)	(336,645)	(201,304)
Maturities of marketable securities	422,488	233,020	115,607
Proceeds from sale of Syrxx Investment	—	750	—
Capital expenditures	(619)	(624)	(1,573)
Notes receivable from related parties	(228)	—	—
Proceeds from sale of fixed assets	—	7	595
Proceeds from repayment of note receivable	—	—	275
Net cash provided by (used in) investing activities	61,369	(103,492)	(86,400)
Cash flows from financing activities:			
Advance from collaboration partner	10,000	10,000	—
Net proceeds from issuances of common stock	77,225	137,910	152,276
Net cash provided by financing activities	87,225	147,910	152,276
Net increase (decrease) in cash and cash equivalents	48,349	(28,179)	18,931
Cash and cash equivalents at beginning of period	46,064	74,243	55,312
Cash and cash equivalents at end of period	$ 94,413	$ 46,064	$ 74,243

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. 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 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.

Net Expense from Unconsolidated Joint Business

Net expense from unconsolidated joint business relates to our collaboration with Bayer for the development and marketing of Nexavar. It consists of our share of the net collaboration loss generated from our Collaboration Agreement with Bayer net of the reimbursement of our development and marketing expenses related to Nexavar. Under the collaboration, Bayer recognizes all revenue from the sale of Nexavar. The net expense from the unconsolidated joint business is, in effect, the net amount due to Bayer to balance the companies' economics under the Nexavar collaboration. Under the terms of the collaboration, the companies share all research and development, marketing, and non-U.S. sales expenses, excluding Japan. Some of the revenue and expenses recorded to derive the net expense from unconsolidated joint business during the period presented are estimates of both parties and are

subject to further adjustment based on each party's final review should actual results differ materially from these estimates. If the Company underestimates activity levels associated with the collaboration of Nexavar at a given point in time, the Company could record significant additional expenses in future periods.

Research and Development

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, stock-based compensation expense, 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 and 93 percent in 2004, 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 2006, consistent with the terms of our collaboration agreement, our share of Bayer's Nexavar product development expenses are included in Net Expense from Unconsolidated Joint Business. Thus, in 2006, only our direct research and development expenses are included in the research and development line item in the accompanying statement of operations.

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.

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 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.

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, 2006 and 2005, 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 (loss). 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, 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, 2006, 2005 and 2004. Interest and dividends on securities classified as available-for-sale are included in interest income, 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 five to six years.

Impairment of Long-Lived Assets

Impairment of long-lived assets is measured or assessed 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 2006 and 2005 and $40,000 in 2004. The write-down in 2004 was related to property and equipment abandoned as a result of the Company's facility move. See Note 5 for additional discussion.

Stock-Based Compensation

Effective January 1, 2006, the Company adopted Statement of Financial Accounting Standards, or FAS, No. 123(R), "Share-Based Payment", ("FAS 123(R)"), which requires the measurement and recognition of compensation expense for all stock-based payments made to employees and directors including employee stock option awards and employee stock purchases made under the Employee Stock Purchase Plan, or ESPP, based on estimated fair value. The Company previously applied the provisions of Accounting Principles Board Opinion, or APB, No. 25, "Accounting for Stock Issued to Employees" ("APB 25") and related Interpretations and provided the required pro forma disclosures under FAS 123, "Accounting for Stock-Based Compensation", or FAS 123.

We adopted FAS 123(R) using the modified prospective transition method beginning January 1, 2006. Accordingly, during the year ended December 31, 2006, we recorded stock-based compensation expense for awards granted prior to but not yet vested as of January 1, 2006 as if the fair value method required for pro forma disclosure under FAS 123 were in effect for expense recognition purposes adjusted for estimated forfeitures. For stock-based awards granted after January 1, 2006, we recognized compensation expense based on the estimated grant date fair value method required under FAS 123(R). The compensation expense for these awards was recognized using a straight-line amortization method. The net loss for the year ended December 31, 2006 includes stock-based compensation expense of $14.0 million, or $0.33 per share for the adoption of FAS 123(R). As of December 31, 2006, the total unrecorded stock-based compensation balance for unvested shares, net of expected forfeitures, was $23.1 million, which is expected to be amortized over a weighted-average period of 23 months.

On November 10, 2005, the Financial Accounting Standards Board (FASB) issued FASB Staff Position No. FAS 123(R)-3, "Transition Election Related to Accounting for Tax Effects of Share-Based Payment Awards." We have elected to adopt the alternative transition method provided in the FASB Staff Position for calculating the tax effects (if any) of stock-based compensation expense pursuant to SFAS 123R. The alternative transition method includes simplified methods to establish the beginning balance of the additional paid-in capital pool (APIC pool) related to the tax effects of employee stock-based compensation, and to determine the subsequent impact to the

APIC pool and the consolidated statements of operations and cash flows of the tax effects of employee stock-based compensation awards that are outstanding upon adoption of SFAS 123R.

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 $365,000, $906,000 and $1.4 million for the years ended December 31, 2006, 2005 and 2004, respectively.

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 for the years ended December 31, 2005 and 2004. 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
Risk-free interest rate	3.80%	2.92%
Expected life	3.8 years	3.7 years
Expected volatility	0.74	0.85
Expected dividends	None	None
Weighted average fair value of options at date of grant	$ 13.55	$ 22.93

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
	(In thousands, except per share amounts)	
Net loss — as reported	$ (95,174)	$ (46,756)
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)
Pro forma net loss	$ (108,507)	$ (52,827)
Loss per share:		
Basic and diluted net loss per share — as reported	$ (2.64)	$ (1.36)
Basic and diluted net loss per share — pro forma	$ (3.01)	$ (1.54)

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

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,		
	2006	2005	2004
	(In thousands)		
Stock options	5,335	3,806	2,296
Stock warrants	9	9	40
Restricted stock awards	33	—	—
	5,377	3,815	2,336

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 July 2006, the FASB issued FASB Interpretation No. 48, "Accounting for Uncertainty in Income Taxes — an interpretation of FASB Statement No. 109" ("FIN 48"). FIN 48 defines the threshold for recognizing the benefits of tax return positions in the financial statements as "more-likely-than-not" to be sustained by the taxing authority and provides guidance on the derecognition, measurement and classification of income tax uncertainties, along with any related interest and penalties. FIN 48 also includes guidance concerning accounting for income tax uncertainties in interim periods and increases the level of disclosures associated with any recorded income tax uncertainties. FIN 48 is effective for fiscal years beginning after December 15, 2006. The differences between the amounts recognized in the statements of financial position prior to the adoption of FIN 48 and the amounts reported after adoption will be accounted for as a cumulative-effect adjustment recorded to the beginning balance of retained earnings. We are currently evaluating the impact of FIN 48 on our financial statements.

Note 2. Collaboration Agreements

Bayer Pharmaceuticals 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 2002 upon initiation of Phase 2 clinical studies and $15.0 million in 2003 based upon the initiation of a Phase 3 study. Based on the July 2005 New Drug Application, or NDA, filing, the Company received the third milestone payment of $10.0 million in 2005. 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. 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 March 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 will continue to govern.

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 upon the achievement of clinical development and registration of any resulting products and is

entitled to 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 1 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. Net Expense from Unconsolidated Joint Business

Nexavar is currently marketed and sold primarily in the United States and the European Union for the treatment of advanced kidney cancer. Nexavar also has regulatory applications pending in other territories internationally. Onyx co-promotes Nexavar in the United States with Bayer Pharmaceuticals Corporation, (Bayer) under collaboration and co-promotion agreements. In March 2006, Onyx and Bayer entered into a Co-Promotion Agreement to co-promote Nexavar in the United States. This agreement amends the original 1994 Collaboration Agreement and supersedes the provisions of that agreement that relate to the co-promotion of Nexavar in the United States. 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, Onyx and Bayer will share equally in the profits or losses of Nexavar, if any, in the United States, subject only to the Company's continued co-funding of the development costs of Nexavar worldwide, excluding Japan. The collaboration was created through a contractual arrangement, not through a joint venture or other legal entity.

Bayer provides all product distribution and all marketing support services, including managed care, customer service, order entry and billing, for Nexavar sales in the United States. Bayer is compensated for distribution expenses based on a fixed percent of gross sales of Nexavar in the United States. Bayer is reimbursed for half of its expenses for marketing services provided by Bayer for the sale of Nexavar in the United States. The parties share equally in any other out-of-pocket marketing expenses (other than expenses for sales force and medical science liaisons) that Onyx and Bayer incur in connection with the marketing and promotion of Nexavar in the United States. Bayer manufactures all Nexavar sold in the United States and is reimbursed at an agreed transfer price per unit for the cost of goods sold.

In the United States, Onyx contributes half of the overall number of sales force personnel required to market and promote Nexavar and half of the medical science liaisons to support Nexavar. Each of Onyx and Bayer bears its own sales force and medical science liaison expenses. These expenses are not included in the calculation of the profits or losses of the collaboration.

Outside of the United States, except in Japan, Bayer incurs all of the sales and marketing expenditures, and Onyx reimburses Bayer for half of those expenditures. In addition, upon approval of Nexavar in countries other than the United States, except Japan, Onyx will reimburse Bayer a fixed percentage of net sales for their marketing infrastructure. Research and development expenditures on a worldwide basis, except in Japan, are equally shared by both companies regardless of whether Onyx or Bayer incurs the expense. In Japan, Bayer is responsible for all development and marketing costs, and Onyx will receive a royalty on any net sales of Nexavar.

Net expense from the unconsolidated joint business consists of Onyx's share of the pretax collaboration loss generated from its collaboration with Bayer net of the reimbursement of Onyx's marketing and research and development costs related to Nexavar. Under the collaboration, Bayer recognizes net product revenue of Nexavar worldwide. Onyx records its share of the collaboration pre-tax loss on a quarterly basis. Collaboration loss is derived by calculating sales of Nexavar to third-party customers and deducting the cost of goods sold, distribution costs, marketing costs (including without limitation, advertising and education expenses, selling and promotion expenses, marketing personnel expenses, and Bayer marketing services expenses), Phase 4 clinical trial costs, allocable overhead costs and research and development costs. As noted above, United States sales force and medical science liaison expenditures incurred by both companies are borne by each company separately and are not included in the calculation. Some of the revenue and expenses recorded to derive the net expense from unconsolidated joint business during the period presented are estimates of both parties and are subject to further adjustment based on each party's final review should actual results differ from these estimates.

For the year ended December 31, 2006, net expense from unconsolidated joint business was $23.9 million, calculated as follows:

	Year Ended December 31, 2006
	(In thousands)
Onyx's share of collaboration loss	$(59,595)
Reimbursement of Onyx's direct development and marketing expenses	35,680
Onyx's net expense from unconsolidated joint business	$(23,915)

As of December 31, 2006, we have invested $219.0 million in the development of Nexavar, representing our share of the costs incurred to date under the collaboration.

Note 4. Marketable Securities

Investments that are subject to concentration of credit risk are marketable securities. To mitigate this risk, the Company invests in marketable debt securities, primarily United States government securities, agency bonds 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, 2006 was five months. Realized gains (losses) on these sales were immaterial for each of the years ended December 31, 2006, 2005 and 2004.

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

	2006			
	Adjusted Cost	Unrealized Gains	Unrealized Losses	Estimated Fair Value
		(In thousands)		
U.S. government investments:				
Maturing within 1 year	$ 15,195	$ —	$ (57)	$ 15,138
Maturing between 1 and 2 years	—	—	—	—
Total government investments	15,195	—	(57)	15,138
Agency bond investments:				
Maturing within 1 year	41,663	1	(22)	41,642
Maturing between 1 and 2 years	9,996	—	(8)	9,988
Total agency bond investments	51,659	1	(30)	51,630
Corporate debt investments:				
Maturing within 1 year	105,853	1	(77)	105,777
Maturing between 1 and 2 years	4,460	—	(15)	4,445
Total corporate investments	110,313	1	(92)	110,222
Total available-for-sale marketable securities	$177,167	$ 2	$(179)	$176,990

	2005			
	Adjusted Cost	Unrealized Gains	Unrealized Losses	Estimated Fair Value
	(In thousands)			
U.S. government investments:				
Maturing within 1 year	$ 7,488	$ —	$ (44)	$ 7,444
Maturing between 1 and 2 years	15,182	—	(107)	15,075
Total government investments	22,670	—	(151)	22,519
Agency bond investments:				
Maturing within 1 year	12,936	1	(21)	12,916
Maturing between 1 and 2 years	—	—	—	—
Total agency bond investments	12,936	1	(21)	12,916
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

The unrealized losses in 2006 and 2005 on the Company's investments in United States government investments, agency bond 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 $60.0 million of marketable securities, representing 33.9 percent of our total portfolio at December 31, 2006, 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 2006 and 2005, we classified $4.4 million and $9.9 million of marketable securities balances as long-term because these securities carry maturity dates greater than twelve months from the balance sheet date.

Note 5. Property and Equipment

Property and equipment consist of the following:

	December 31,	
	2006	2005
	(In thousands)	
Computers, machinery and equipment	$ 2,279	$ 1,708
Furniture and fixtures	446	413
Leasehold improvements	734	734
Construction in progress	15	—
	3,474	2,855
Less accumulated depreciation and amortization	(1,996)	(1,238)
	$ 1,478	$ 1,617

Depreciation expense was $758,000, $630,000 and $194,000 for the years ended December 31, 2006, 2005 and 2004, 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.

Note 6. Long-Term Obligations

In January 2006, the Company received the fourth and final development payment from Bayer for $10.0 million under its collaboration agreement in connection with the approval of Nexavar by the FDA. In July 2005, the Company received a $10.0 million development payment from Bayer 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 3 clinical trials of Nexavar. In August 2002, the Company received a $5.0 million development payment from Bayer for the initiation of Phase 2 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, 2006 and 2005 of $40.0 million and $30.0 million, respectively, are included in the caption "Advance from collaboration partner" in the accompanying balance sheets.

Note 7. Facility Leases

In 2004, the Company entered into an operating lease for 23,000 square feet of office space in Emeryville, California, which serves as the Company's corporate headquarters. 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.

In 2006, the Company amended its existing operating lease to occupy an additional 14,000 square feet of office space in addition to the 23,000 square feet already occupied in Emeryville, California. The lease expires on March 31, 2013. 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.

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, 2006 are as follows (in thousands):

Year ending December 31:	
2007	$1,036
2008	1,023
2009	1,049
2010	1,058
2011	1,046
Thereafter	1,308
	$6,520

Rent expense, net of sublease income and restructuring, for the years ended December 31, 2006, 2005 and 2004 was approximately $587,000, $490,000 and $343,000, respectively. Sublease income was $62,000, $102,000 and $99,000 for the years ended December 31, 2006, 2005 and 2004, respectively.

Note 8. Related Party Transactions

The Company has a loan receivable from a non-officer employee of which approximately $228,000 is outstanding at December 31, 2006. This loan bears interest at 4.82% per annum and is due in three annual payments, beginning in 2007. The payment due in 2007 is recorded in current assets at December 31, 2006. The noncurrent portion of the loan receivable is recorded in other assets at December 31, 2006.

Note 9. 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 10. Stockholders' Equity

Stock Options and Employee Stock Purchase Plan

The Company has one stock option plan from which it is able to grant new awards, the 2005 Equity Incentive Plan. Prior to adoption of the 2005 Equity Incentive Plan, the Company had two stock option plans, the 1996 Equity Incentive Plan and the 1996 Non-Employee Directors' Stock Option Plan. Following is a brief description of the plans:

1) The 1996 Equity Incentive Plan which amended and restated the 1992 Incentive Stock Plan in March 1996. The Board 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.

2) The 1996 Non-Employee Directors' Stock Option Plan (the "Directors' Plan") which was approved in March 1996 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.

The 2005 Equity Incentive Plan was approved at the Company's annual meeting of stockholders to supersede and replace both 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. Any shares subject to outstanding stock awards under the 1996 Equity Incentive Plan and the Directors' Plan that expire or terminate for any reason prior to exercise or settlement are added to the share reserve under the 2005 Equity Incentive Plan. All outstanding stock awards granted under the two prior plans remain subject to the terms of those plans.

In March 1996, the Board of Directors adopted the Employee Stock Purchase Plan (ESPP). The number of shares available for issuance over the term of the ESPP is limited to 400,000 shares. The ESPP 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 ESPP 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 ESPP were 22,584 shares in 2006, 12,424 shares in 2005 and 16,852 shares in 2004. Since inception, a total of 308,996 shares have been issued under the ESPP, leaving a total of 91,004 shares available for issuance.

In December 2005, stock options were exercised that were not settled prior to December 31, 2005. The Company recorded a receivable from stock option exercises of $24,000 as of December 31, 2005 related to these stock options. This is included in the caption "Receivable from stock option exercises" in the accompanying balance sheet and Statement of Stockholders' Equity as of December 31, 2005. There were no such amounts as of December 31, 2006 nor 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, 2006, 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 for the purchase of common stock 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. There were no warrants issued nor exercised in 2006.

As of December 31, 2006 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 11. Stock-Based Compensation

Effective January 1, 2006, the Company adopted Statement of Financial Accounting Standards, or FAS, No. 123(R), "Share-Based Payment", ("FAS 123(R)"), which requires the measurement and recognition of compensation expense for all stock-based payments made to employees and directors including employee stock option awards and employee stock purchases made under the Employee Stock Purchase Plan, or ESPP, based on estimated fair value. The Company previously applied the provisions of Accounting Principles Board Opinion, or APB, No. 25, "Accounting for Stock Issued to Employees" ("APB 25") and related Interpretations and provided the required pro forma disclosures under FAS 123, "Accounting for Stock-Based Compensation", or FAS 123.

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(R) 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.

Pro forma Information for Periods prior to the Adoption of FAS 123(R)

Prior to the adoption of FAS 123(R), the Company elected to follow APB 25 to account for employee stock options and complied with the disclosure provisions of FAS 123 and FAS 148, "Accounting for Stock-Based Compensation-Transition and Disclosure." No employee stock-based compensation expense was reflected in the Company's results of operations for the year ended December 31, 2005, for employee stock option awards as all options were granted with an exercise price equal to the market value of the underlying common stock on the date of grant. Our ESPP was deemed non-compensatory under the provisions of APB 25. Previously reported amounts have not been restated.

The pro forma information for the years ended December 31, 2005 and 2004 was as follows:

	Year Ended December 31, 2005	Year Ended December 31, 2004
	(In thousands except per share data)	
Net loss, as reported	$ (95,174)	$(46,756)
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)
Net loss — pro forma	$(108,507)	$(52,827)
Loss per share:		
Basic and diluted net loss per share — as reported	$ (2.64)	$ (1.36)
Basic and diluted net loss per share — pro forma	$ (3.01)	$ (1.54)

Impact of the Adoption of FAS 123(R)

The Company adopted FAS 123(R) using the modified prospective transition method beginning January 1, 2006. Accordingly, during the year ended December 31, 2006, the Company recorded stock-based compensation expense for awards granted prior to but not yet vested as of January 1, 2006, as if the fair value method required for pro forma disclosure under FAS 123 has been followed for expense recognition purposes adjusted for estimated forfeitures. For these awards, the Company has continued to recognize compensation expense using the accelerated amortization method under FASB Interpretation No. 28, "Accounting for Stock Appreciation Rights and Other Variable Stock Option or Award Plans." For stock-based awards granted after January 1, 2006, the Company recognized compensation expense based on the estimated grant date fair value method required under FAS 123(R). The compensation expense for these awards was recognized using a straight-line amortization method. As FAS 123(R) requires that stock-based compensation expense be based on awards that are ultimately expected to vest, estimated stock-based compensation for the year ended December 31, 2006, has been reduced for estimated forfeitures. Compensation expense for stock bonus awards is based on the market price of our stock on the date of grant. In the Company's pro forma information required under FAS 123 for periods prior to January 1, 2006, the Company accounted for forfeitures as they occurred. FAS 123(R) requires forfeitures to be estimated at the time of grant and revised, if necessary, in subsequent periods if actual forfeitures differ from those estimates. The impact on

the results of operations of recording stock-based compensation for the year ended December 31, 2006, was as follows:

	Year Ended December 31, 2006 (In thousands except per share data)
Research and development	$ 2,545
Selling, general and administrative	11,496
Total share-based compensation expense	$14,041
Impact on basic and diluted net loss per share	$ (0.33)

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 $365,000 , $906,000 and $1.4 million for the years ended December 31, 2006, 2005 and 2004, respectively.

	Year Ended December 31, 2006
Stock option plans:	
Weighted average grant date fair value	$ 13.83
Total fair value vested (in thousands)	$14,460
Stock bonus awards:	
Weighted average grant date fair value	$ 21.04
Total fair value vested (in thousands)	$ 140

As of December 31, 2006, the total unrecorded stock-based compensation balance for unvested stock options shares, net of expected forfeitures, was $23.1 million which is expected to be amortized over a weighted-average period of 23 months. As of December 31, 2006, the total unrecorded stock-based compensation balance for unvested stock bonus awards, net of expected forfeitures, was $633,000 which is expected to be amortized over a weighted-average period of 2.4 years. Cash received during the year ended December 31, 2006, for stock options exercised under all stock-based compensation arrangements was $2.5 million.

Valuation Assumptions

As of December 31, 2006 and 2005, the fair value of stock-based awards for employee stock option awards, stock bonus awards and employee stock purchases made under the ESPP was estimated using the Black-Scholes option pricing model. The following weighted average assumptions were used:

	Year Ended December 31		
	2006	2005	2004
Stock Option Plans:			
Risk-free interest rate	4.68%	3.80%	2.92%
Expected life	4.2 years	3.8 years	3.7 years
Expected volatility	59%	74%	85%
Expected dividends	None	None	None
Weighted average option fair value	$ 11.00	$ 13.55	$ 22.93
Stock bonus awards:			
Expected life	3 years	—	—
Expected dividends	None	—	—
Weighted average fair value per share	$ 21.04	—	—
ESPP:			
Risk-free interest rate	4.33%	3.14%	2.52%
Expected life	6 months	6 months	2 years
Expected volatility	59%	74%	88%
Expected dividends	None	None	None
Weighted average fair value per share	$ 8.65	$ 10.79	$ 23.30

The Black-Scholes fair value model requires the use of highly subjective and complex assumptions, including the option's expected life and the price volatility of the underlying stock. Beginning January 1, 2006, the expected stock price volatility assumption was determined using a combination of historical and implied volatility for our stock. Prior to the adoption of FAS 123(R), we used the historical volatility in deriving our expected volatility assumption. We have determined that the combined method of determining volatility is more reflective of market conditions and a better indicator of expected volatility than historical volatility. We consider several factors in estimating the expected life of our options granted, including the expected lives used be a peer group of companies and the historical option exercise behavior of our employees, which we believe are representative of future behavior.

Stock-Based Payment Award Activity

The following table summarizes stock option and award activity under all option plans for the years ended December 31, 2006, 2005 and 2004:

Employee Stock Options:	Shares Available for Grant	Number of Shares Outstanding	Weighted Average Exercise Price
Balance at December 31, 2003	1,419,216	1,983,684	$ 7.65
Shares authorized	600,000	—	—
Granted	(802,925)	802,925	$38.27
Exercised	—	(424,265)	$ 7.72
Cancelled/expired/forfeited	65,902	(65,902)	$19.85
Balance at December 31, 2004	1,282,193	2,296,442	$17.99
Shares authorized	3,990,000	—	—
Granted	(1,718,000)	1,718,000	$24.52
Exercised	—	(152,093)	$ 7.73
Expired/forfeited	56,268	(56,268)	$29.85
Balance at December 31, 2005	3,610,461	3,806,081	$21.17
Granted	(1,987,950)	1,987,950	$21.60
Exercised	—	(347,287)	$ 7.26
Expired	19,058	(19,058)	$37.83
Forfeited	93,209	(93,209)	$28.73
Balance at December 31, 2006	1,734,778	5,334,477	$22.05

Stock Bonus Awards:	Shares	Weighted Average Grant Date Fair Value
Balance at December 31, 2005	—	—
Granted	40,000	$21.04
Vested	(6,667)	$21.04
Cancelled	—	—
Balance at December 31, 2006	33,333	$21.04

The options outstanding and exercisable for stock-based payment awards as of December 31, 2006 were in the following exercise price ranges:

	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 - $15.29	1,101,389	5.1	$ 7.87	927,222	$ 7.20
$15.36 - $20.29	1,111,271	9.1	$16.76	121,338	$17.98
$20.40 - $25.30	1,150,555	8.4	$23.43	436,959	$23.69
$25.44 - $29.04	1,113,330	9.0	$28.43	257,816	$28.49
$29.39 - $48.19	857,932	7.6	$36.95	532,794	$37.18
Total	5,334,477	7.9	$22.05	2,276,129	$20.37

As of December 31, 2005, 1,597,054 shares outstanding options were exercisable, at a weighted average price of $14.74. As of December 31, 2004, 1,167,759 shares outstanding options were exercisable, at a weighted average price of $9.86.

As of December 31, 2006, weighted average contractual life remaining for exercisable shares is 6.4 years. The total number of in-the-money awards exercisable as of December 31, 2006, was approximately 801,995 shares. The aggregate intrinsic values of awards exercised were $5.5 million and $3.1 million for the years ended December 31, 2006 and 2005, respectively. The aggregate intrinsic values of in-the-money outstanding and exercisable awards were $3.4 million and $3.3 million, respectively as of December 31, 2006. The aggregate intrinsic value of options represents the total pretax intrinsic value, based on the Company's closing stock price of $10.58 at December 31, 2006, which would have been received by award holders had all award holders exercised their awards that were in-the-money as of that date.

Note 12. Restructuring

In 2004, the Company recorded a 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 lease facility in Richmond, California. As of December 31, 2005, all restructuring costs had been fully paid.

Note 13. 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,	
	2006	2005
	(In thousands)	
Net operating loss carryforwards	$ 149,955	$ 122,854
Tax credit carryforwards	33,046	23,952
Capitalized research and development	3,216	4,115
Deferred revenue	15,934	11,950
Other	5,022	399
Total deferred tax assets	207,173	163,270
Valuation allowance	(207,173)	(163,270)
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 $43.9 million, $53.4 million and $28.2 million in 2006, 2005 and 2004, respectively.

The 2005 deferred tax assets have been revised to reflect the gross amounts of tax credit carryforwards with the corresponding increase in the valuation allowance.

At December 31, 2006, the Company has net operating loss carryforwards for federal and state income tax purposes of approximately $385.9 million and $321.2 million, respectively, which expire beginning in 2007 if not utilized. Approximately $3.3 million of the federal and $563,000 of the state valuation allowance for deferred tax assets related to net operating loss carry forwards represent the stock option deduction arising from activity under the Company's stock option plan, the benefit of which will increase additional paid in capital when realized. At December 31, 2006, the Company has research and development credit carryforwards for federal income tax purposes of approximately $22.3 million, which expire beginning in 2008 if not utilized. At December 31, 2006, the Company has research and development credit carryforwards for state income tax purposes of approximately $10.5 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 14. 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, 2006 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 15. 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.

	2006 Quarter Ended			
	December 31	September 30	June 30	March 31
	(In thousands, except per share data)			
Total revenues	$ —	$ 100	$ 150	$ —
Net loss	(20,707)	(20,148)	(31,474)	(20,352)
Basic and diluted net loss per share	(0.47)	(0.49)	(0.76)	(0.49)

	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)

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