PROGRESS REVEALED

Onyx Pharmaceuticals Inc., 2010 Annual Report

ABOUT THE COVER We are pleased to feature the new Onyx brand in this annual report. Designed to depict the innovation, energy and dedication that drives everything we do, the brand represents our vision, our mission and our strategy for continued growth in 2011 and beyond. With its two interlocking swirls, our new logo reflects a theme of convergence — of passionate commitment combined with powerful momentum, of dedication to science combined with compassion for patients, of business disciplines combined with scientific innovation. Guided by these qualities, we look forward to our next phase of growth as we continue to build a leading biopharmaceutical company.

"With a strong foundational product in Nexavar, a second near-term commercial opportunity in carfilzomib that could provide a new treatment option for patients with multiple myeloma, and a diversified and promising pipeline, Onyx is accelerating its transformation into a multi-product, innovation-driven company."

2010

WE MADE SUBSTANTIAL PROGRESS IN 2010, POSITIONING ONYX FOR THE NEXT PHASE OF CORPORATE GROWTH and defining a clear path toward our goal of becoming a leading biopharmaceutical company with multiple products and multiple revenue streams. We reached this new inflection point by executing on a value-building strategy with four key business objectives: enhancing Nexavar's commercial contributions to increase cash flow for business expansion; advancing the clinical development program for carfilzomib; advancing current Nexavar trials and reporting important data; and building a diversified pipeline with both near- and long-term growth potential.

Our success in achieving these objectives over the past two years has enabled us to generate the revenues and create the opportunities needed to drive our business forward and enter a new phase of growth. Prime among our accomplishments was our acquisition of Proteolix in late 2009, a transformative event that brought us the global rights to carfilzomib and other earlier-stage proteasome inhibitors, catapulting Onyx into a company with multiple product candidates that offer the potential of treating patients with multiple myeloma and other serious diseases.

As a result, Onyx today has three major platforms for growth: our core asset Nexavar, our emerging proteasome inhibitor franchise, and our early stage pipeline.

We have established a set of new priorities reflecting our expansion and diversification:

- → Maintain a strong financial profile
- → Build a proteasome inhibitor franchise
- → Sustain and increase Nexavar growth
- → Leverage pipeline assets

FUNDING OUR GROWTH

Nexavar is foundational to our business and fundamental to our success. In its five years on the market, Nexavar has generated nearly $3 billon in cumulative sales, enabling us to benefit patients around the world and to invest strategically in our business. In 2010, Onyx and our collaborator Bayer HealthCare Pharmaceuticals reported global net sales of $934 million, representing an

"Onyx has reached a pivotal point in its history as it evolves into a pipeline-driven company with even more ways to potentially help people with cancer and other serious diseases."

A YEAR OF GROWTH AND TRANSFORMATION

2010

11 percent year-over-year increase despite the ongoing global recession. These revenues are recorded by Bayer, and we share equally in development costs and any profit or loss, with the exception of sales in Japan, where we receive a royalty.

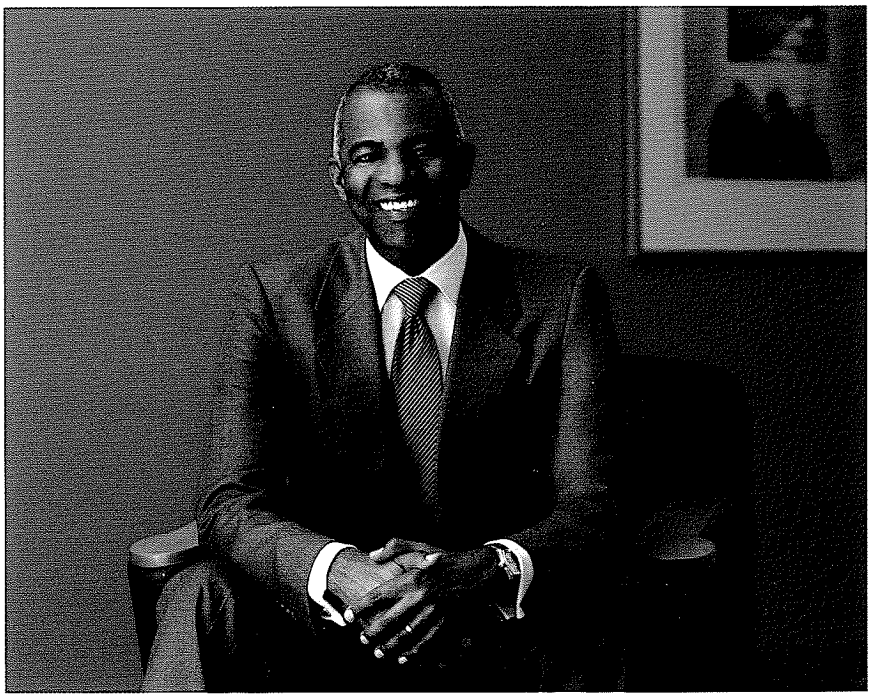
Our cash position remains strong, including approximately $578 million in cash, cash equivalents and marketable securities as of December 31, 2010. Through our continued disciplined management of both commercial and development spending, we were able to deliver yet another year of non-GAAP profitability. Nexavar, our core asset, sets Onyx apart as an emerging oncology leader, providing us not only with a commercially successful business, but also with the means to invest and expand into new areas.

BUILDING A FRANCHISE IN PROTEASOME INHIBITION

Supported by a growing body of clinical data across a range of treatment settings, carfilzomib is positioned to be a potentially meaningful advance for patients as well as our second commercial product. With a highly differentiated product profile, carfilzomib provides us with an opportunity to move into the growing $4 billion multiple myeloma market. The second most common hematologic cancer worldwide, multiple myeloma affects more than 215,000 patients worldwide, many of whom ultimately exhaust available treatment options and consequently face a very poor prognosis, underscoring the need for new treatment options.

We believe we are just beginning to uncover the potential of carfilzomib, a selective next generation proteasome inhibitor. For that reason, we are investing in the development of carfilzomib across multiple lines of therapy and in multiple treatment settings with the goal of establishing the compound as a cornerstone of treatment for patients with multiple myeloma. Additionally, we believe the drug has the potential to treat other hematological malignancies, such as lymphoma, as well as solid tumors.

Carfilzomib has demonstrated encouraging efficacy and safety in a range of clinical trials, either administered alone or in combination with current multiple myeloma therapies. In December, we reported exciting complete results from a pivotal single-agent Phase 2b trial showing an overall response rate of 24.1 percent and a median duration of response (DOR) of 8.3 months in patients who entered



N. Anthony Coles, M.D.

the study after receiving a median of five prior lines of therapy (corresponding to a median of 13 anti-myeloma agents). In addition, patients enrolled in the study had progressive disease upon entering the trial and their disease was refractory to their last therapeutic regimen. Median overall survival was 15.5 months, based on current data. By comparison, patients, such as those enrolled in the 003-A1 study, can expect to respond to therapy only 11 percent of the time and survive for only six to 10 months, highlighting the need for new treatment options. In addition, carfilzomib's favorable side effect profile with low rates of neurotoxicity and neutropenia may suggest that patients can safely remain on treatment without experiencing cumulative toxicities. Based on these and other promising Phase 2 results, we plan to submit a New Drug Application (NDA) filing as early as mid-2011 for the potential accelerated approval of carfilzomib in the United States. To support registration in Europe, late in 2010, we initiated a Phase 3 clinical trial, called the FOCUS study, evaluating single-agent carfilzomib in the relapsed and refractory setting. We expect to report top-line data from this study in 2012.

In addition, as part of our global, full approval strategy, we are evaluating carfilzomib in combination with Revlimid® (lenalidomide) and low-dose dexamethasone in patients with earlier-stage disease. Clinical results to date – in both previously treated patients as well as newly diagnosed patients – demonstrate that this combination produces durable responses. As a result, we have initiated a pivotal international Phase 3 trial, known as the ASPIRE study, focused on assessing this combination in patients with relapsed disease. The study is being conducted under a Special Protocol Assessment (SPA) from the FDA and Scientific Advice from the European Medicines Agency (EMA).

While we believe that carfilzomib holds the promise of transforming the treatment of multiple myeloma, we are also excited about the potential of a second compound to expand our proteasome inhibitor franchise. Currently in Phase 1 clinical testing, ONX 0912 has the potential to be the first oral proteasome inhibitor, providing the convenience and flexibility of oral dosing as well as the possibility of treating not only myeloma, but also other hematologic malignancies and solid tumors.

A YEAR OF CLINICAL AND COMMERCIAL PROGRESS

2010

FEBRUARY

→ **ONYX ANNOUNCES AGREEMENT WITH THE FDA** ON A SPECIAL PROTOCOL ASSESSMENT (SPA) FOR PLANNED PHASE 3 CARFILZOMIB ASPIRE TRIAL FOR PATIENTS WITH RELAPSED MULTIPLE MYELOMA.

JUNE

→ **ONYX INITIATES A PHASE 1B/2 STUDY** OF ITS ORAL PROTEASOME INHIBITOR, ONX 0912, IN PATIENTS WITH ADVANCED SOLID TUMORS.

→ **INTERIM PHASE 1/2 TRIAL RESULTS** SHOW THAT CARFILZOMIB IN COMBINATION WITH LENALIDOMIDE (REVLIMID®) AND LOW-DOSE DEXAMETHASONE PROVIDES 75 PERCENT OVERALL RESPONSE IN PREVIOUSLY TREATED MYELOMA PATIENTS.

JULY

→ **ONYX BEGINS ENROLLMENT IN PHASE 3 ASPIRE TRIAL,** EVALUATING CARFILZOMIB IN COMBINATION WITH LENALIDOMIDE (REVLIMID®) AND LOW-DOSE DEXAMETHASONE IN PATIENTS WITH RELAPSED MULTIPLE MYELOMA.

SEPTEMBER

→ **ONYX ENTERS INTO AN EXCLUSIVE LICENSING AGREEMENT** POTENTIALLY VALUED IN EXCESS OF $300 MILLION WITH ONO PHARMACEUTICAL, GIVING ONO THE RIGHTS TO DEVELOP AND COMMERCIALIZE CARFILZOMIB AND ONX 0912 FOR ALL ONCOLOGY INDICATIONS IN JAPAN.

→ **TO SUPPORT REGISTRATION IN EUROPE, ONYX BEGINS THE FOCUS STUDY – A PHASE 3 CLINICAL TRIAL** OF SINGLE-AGENT CARFILZOMIB IN PATIENTS WITH RELAPSED/ REFRACTORY SETTING MULTIPLE MYELOMA.

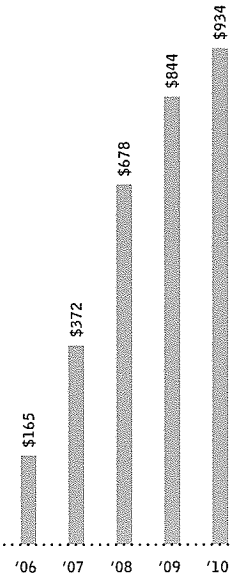
DECEMBER

→ **ONYX REPORTS POSITIVE COMPLETE RESULTS FROM PHASE 2B STUDY** OF SINGLE-AGENT CARFILZOMIB IN PATIENTS WITH RELAPSED AND REFRACTORY MULTIPLE MYELOMA, SHOWING AN OVERALL RESPONSE RATE OF 24 PERCENT, DURATION OF RESPONSE EXCEEDING EIGHT MONTHS, AND A MEDIAN OVERALL SURVIVAL OF 15.5 MONTHS.

→ **NEXAVAR RECEIVES REIMBURSEMENT APPROVAL IN SOUTH KOREA,** ONE OF THE LARGEST ASIA-PACIFIC MARKETS.

→ **NEXAVAR ANNUAL NET GLOBAL SALES INCREASE** 11 PERCENT OVER 2009, AND ONYX'S CASH POSITION REMAINS STRONG AT $578 MILLION, PROVIDING FOR ONGOING INVESTMENTS IN BUSINESS GROWTH.

NEXAVAR GLOBAL NET SALES
IN MILLIONS



"In its five years on the market, Nexavar has generated nearly $3 billon in cumulative sales, enabling us to benefit more than 100,000 patients around the world and to invest strategically in our business."

Carfilzomib and ONX 0912 are also proving to be important assets that we can leverage through corporate development transactions. In September 2010, we were pleased to announce a licensing agreement with Ono Pharmaceutical Co., Ltd., granting Ono the exclusive rights to develop and commercialize our two lead proteasome inhibitors for all oncology indications in Japan. The total potential value of the transaction is estimated to exceed $300 million, plus royalties, representing one of the largest Japan-only deals ever. Covering just one country in a single region of the world, this strategic, high-value deal demonstrates how we can accelerate development of these agents through a partner's expertise in one region while we remain focused on execution in other key countries and markets.

SUPPORTING NEXAVAR GROWTH

As the first and only oral systemic therapy for unresectable liver cancer and an important treatment for advanced kidney cancer, Nexavar is a key platform for Onyx's current and future growth. Based on its proven efficacy, tolerability and convenient oral dosing, we believe that Nexavar presents a significant opportunity for further value creation. Accordingly, we and our partner Bayer are conducting a clinical development program to unlock Nexavar's potential in a range of cancer indications. Based on our progress in this program, we believe that Nexavar is poised to enter the most profitable and productive years of its lifecycle.

We are generating more data in liver cancer with the goal of extending the benefits of Nexavar across the full range of patients. To that end, we are conducting three large clinical trials – the STORM trial, evaluating the use of Nexavar as an adjuvant therapy in early stage patients; the SEARCH trial, exploring Nexavar's use in combination with Tarceva® (erlotinib) in advanced-stage patients; and the SPACE trial, assessing Nexavar in combination with the local-regional therapies such as transarterial chemoembolization (also known as TACE) in intermediate-stage patients. This emerging data has the potential to establish Nexavar as the standard of care across the entire liver cancer treatment spectrum.

We are also advancing a Phase 3 clinical development program in three potential new indications – lung cancer, thyroid cancer and breast cancer – devastating diseases characterized by large unmet patient

LEFT TO RIGHT: (Back row) Kaye Foster-Cheek, Juergen Lasowski, Ph.D., Julianna Wood, Suzanne M. Shema, J.D., and Matthew K. Fust (Front row) N. Anthony Coles, M.D., Ted W. Love, M.D., and Laura A. Brege

2010

needs. In non-squamous, non-small cell lung cancer, we recently completed enrollment in our pivotal MISSION trial comparing single-agent Nexavar to best supportive care in heavily pretreated patients with advanced disease. In thyroid cancer, our ongoing international DECISION trial is designed to validate the encouraging efficacy demonstrated by single-agent Nexavar in multiple earlier studies. With one of the highest reported response rates and the longest progression-free survival in Phase 2 studies, Nexavar is positioned to be the first to market for differentiated thyroid cancer, which comprises more than 90 percent of all thyroid cancer cases. We expect to complete enrollment in the DECISION trial in 2011.

Finally, in breast cancer, we have begun a pivotal Phase 3 clinical trial designed to confirm compelling Phase 2 data suggesting a potential role for Nexavar in combination with Xeloda® (capecitabine) in women with locally advanced or metastatic HER2-negative breast cancer. Known as the RESILIENCE trial, this international, randomized, placebo-controlled study will evaluate the all-oral Nexavar-capecitabine combination in 520 patients with the endpoint of progression-free survival. At the same time, we are continuing to advance our broad and integrated Phase 2b clinical trial program investigating Nexavar in combination with standard breast cancer therapies. As part of this program, we plan to share data later this year from a Phase 2 trial evaluating Nexavar in combination with gemcitabine and capecitabine as a treatment for patients whose disease has progressed on Avastin® (bevacizumab). In addition, we plan to report results from the first-line Phase 2 trial evaluating Nexavar in combination with docetaxel and/or letrozole in patients with locally recurrent or metastatic breast cancer.

INVESTING IN OUR FUTURE

Over the past two years, we have worked strategically and proactively to create a diversified pipeline for Onyx that will sustain the company's growth over time. As a result, we now have a robust pipeline of both near- and longer-term product candidates selected for their unique and compelling characteristics to help people with life-threatening diseases.

Our 2009 acquisition of Proteolix was a signature event, bringing us

A YEAR OF STRATEGIC VALUE CREATION

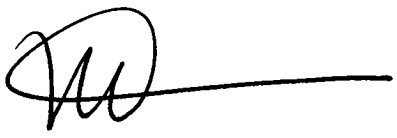
not only carfilzomib, which offers the possibility of an accelerated approval in relapsed/refractory multiple myeloma, but two other novel agents – ONX 0912, an oral proteasome inhibitor currently in the final stages of a Phase 1 clinical trial in solid tumors, and ONX 0914, an immunoproteasome inhibitor that could be the first agent in its class to find application in autoimmune disease as well as cancer.

We are also developing ONX 0801, an alpha-folate receptor targeted inhibitor of the thymidylate synthase – a commercially validated target in cancer. Currently in Phase 1 clinical testing in solid tumors, ONX 0801 is being assessed as a potential treatment for a variety of cancers. In addition, we have options to license the rights to two Janus Kinase (JAK) inhibitors – ONX 0803, currently in Phase 2 studies to potentially treat primary myelofibrosis, and ONX 0805, now in Phase 1 development. JAK inhibitors represent an exciting emerging class of therapeutics in an area of intense clinical and scientific interest, since the JAK signaling pathway is known to play a role in cancer, inflammatory conditions and other diseases.

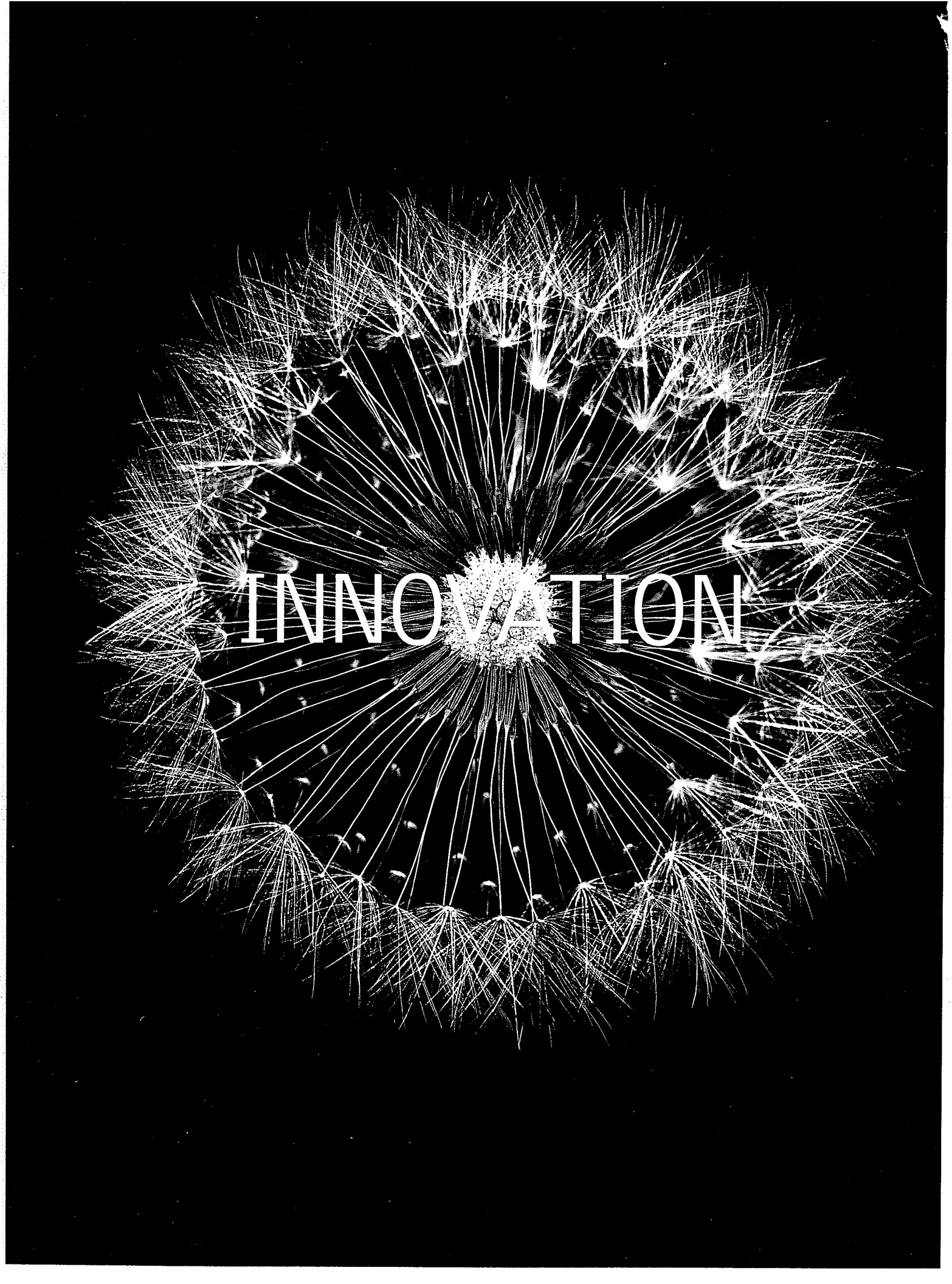
THE NEW ONYX

We enter 2011 with the recognition that Onyx is a very different company than it was just one year ago. Through a series of strategic decisions and actions, we believe Onyx has reached the next significant value-inflection point in our evolution from a single-product company to a portfolio-based, pipeline-driven organization. Our story is multi-faceted and unique in our industry – not only do we have a commercially successful business in Nexavar to fuel our growth, but we have a near-term opportunity in carfilzomib that is poised to be a second breakthrough drug as well as our first wholly owned product.

This is an exciting and energizing time, as we move closer to realizing the future we envision for Onyx, and transforming the treatment of cancer and other serious diseases while building sustainable value for investors. We would like to thank our employees, collaborators, stockholders, physicians, patients and their families for their continued support in this important effort.



N. Anthony (Tony) Coles, M.D.
President and Chief Executive Officer
March 7, 2011


INNOVATION

ACTION: PREPARING NDA FOR POTENTIAL ACCELERATED APPROVAL IN U.S.

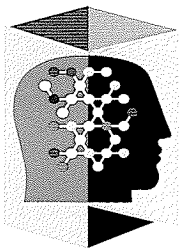
→ MULTIPLE MYELOMA IS THE SECOND MOST COMMON HEMATOLOGIC CANCER AND RESULTS FROM AN ABNORMALITY OF BLOOD PLASMA CELLS.

→ DESPITE TREATMENT ADVANCES OVER THE PAST DECADE, MULTIPLE MYELOMA IS NOT CURABLE AND MOST PATIENTS EXHAUST CURRENT TREATMENT OPTIONS, UNDERSCORING THE NEED FOR NEW THERAPIES.

→ WORLDWIDE, MORE THAN 215,000 PEOPLE ARE LIVING WITH MULTIPLE MYELOMA, AND APPROXIMATELY 86,000 NEW CASES ARE DIAGNOSED ANNUALLY.

→ IN THE U.S., MORE THAN 50,000 INDIVIDUALS ARE ESTIMATED TO HAVE MULTIPLE MYELOMA, AND ABOUT 20,000 NEW CASES ARE DI AGNOSED EACH YEAR.

→ CURRENTLY VALUED AT $4 BILLION, THE WORLDWIDE MULTIPLE MYELOMA MARKET IS EXPECTED TO EXCEED $7 BILLION OVER THE NEXT FIVE YEARS.



CARFILZOMIB

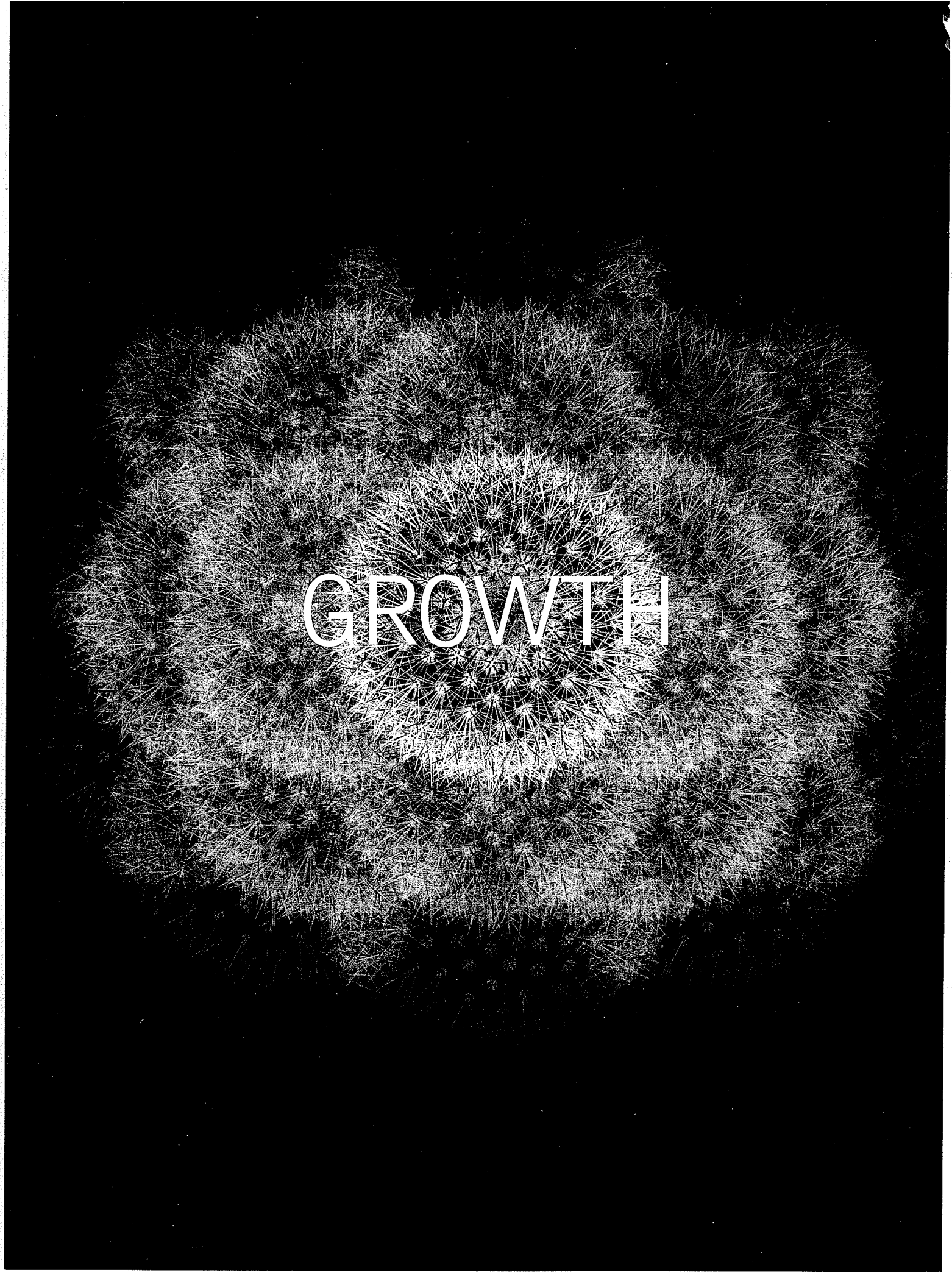
POSITIONED TO ADVANCE MULTIPLE MYELOMA TREATMENT

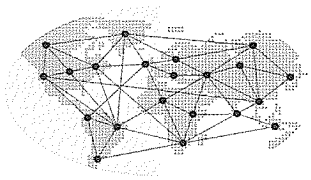
Compelling clinical data across a range of treatment settings

Carfilzomib, a selective, next-generation proteasome inhibitor, represents a near-term product opportunity in the large and growing multiple myeloma market. Carfilzomib is designed to target the proteasome with a high degree of specificity, thereby potentially increasing therapeutic efficacy and reducing off-target toxicities.

In clinical studies, carfilzomib has demonstrated encouraging activity with durable disease control and long-term tolerability across a range of treatment settings and patient populations. These results form the basis of our exploration into carfilzomib's potential as a cornerstone of care for patients at every stage of their disease. Based on positive complete results from a Phase 2b study of single-agent carfilzomib in patients with relapsed and refractory multiple myeloma, we are planning to submit an NDA filing as early as mid-2011 for potential accelerated U.S. approval. To support registration in Europe, we are currently conducting a Phase 3 trial, known as the FOCUS study, of single-agent carfilzomib in the same population of late-stage patients.

We also plan to seek full approval for the use of carfilzomib earlier in the course of the disease through a large, international Phase 3 trial, called the ASPIRE study, evaluating carfilzomib in combination with standard therapy in patients who have failed one to three previous treatment regimens. In addition, we have reported encouraging interim results from a Phase 1/2 trial showing 100 percent overall response rate and a 67 percent complete response rate in newly diagnosed patients after only eight cycles of treatment with carfilzomib in combination with standard therapy. These results support our conviction that carfilzomib has the potential to change the treatment landscape for multiple myeloma and make Onyx a key player in this rapidly growing market.


GROWTH



NEXAVAR

FOUNDATION FOR GROWTH TODAY AND TOMORROW

Unlocking Nexavar's potential in multiple cancer indications

Nexavar, our lead product and growth engine, is the first and only oral systemic therapy approved for liver cancer and an important treatment for advanced kidney cancer. A novel, multiple kinase inhibitor that targets key proteins involved in the growth and spread of cancer, Nexavar has benefited more than 100,000 patients worldwide to date and is currently being evaluated in a range of other important cancers in a late-stage clinical development program.

We believe that significant growth opportunities remain for Nexavar across the full spectrum of liver cancer patients. To that end, we have completed enrollment in three major clinical trials, including the STORM, SEARCH and SPACE studies. Despite macroeconomic pressures, demand is still increasing in the U.S., as our outreach to oncologists and to interdisciplinary healthcare specialists who treat liver cancer continues to yield results. Worldwide, we are augmenting sales in major European markets with efforts aimed at emerging, secondary markets in Europe as well as the Asia-Pacific region, where we anticipate robust growth due to a high incidence of the disease. In late 2010, Onyx and Bayer received reimbursement approval in South Korea where an estimated 13,000 people have liver cancer, a number similar to the incidence in the U.S. This approval is expected to generate additional Nexavar revenues in that region.

We and our collaborator Bayer are generating extensive clinical data in new tumor types with large unmet patient needs. Later this year, we expect to report results from our pivotal Phase 3 study of Nexavar in non-small cell lung cancer. We are also conducting large, randomized Phase 3 studies in thyroid cancer and HER2-negative metastatic breast cancer, designed to confirm compelling Phase 2 results. Success in any one of these high potential areas would provide meaningful benefits for patients and shareholders alike.

→ NEXAVAR IS APPROVED IN MORE THAN 100 COUNTRIES WORLDWIDE FOR THE TREATMENT OF PATIENTS WITH HEPATOCELLULAR CARCINOMA (HCC), THE MOST COMMON FORM OF LIVER CANCER, AND FOR PATIENTS WITH ADVANCED RENAL CELL CARCINOMA (RCC), OR KIDNEY CANCER.

→ APPROXIMATELY 750,000 NEW CASES OF LIVER CANCER OCCUR ANNUALLY WORLDWIDE.

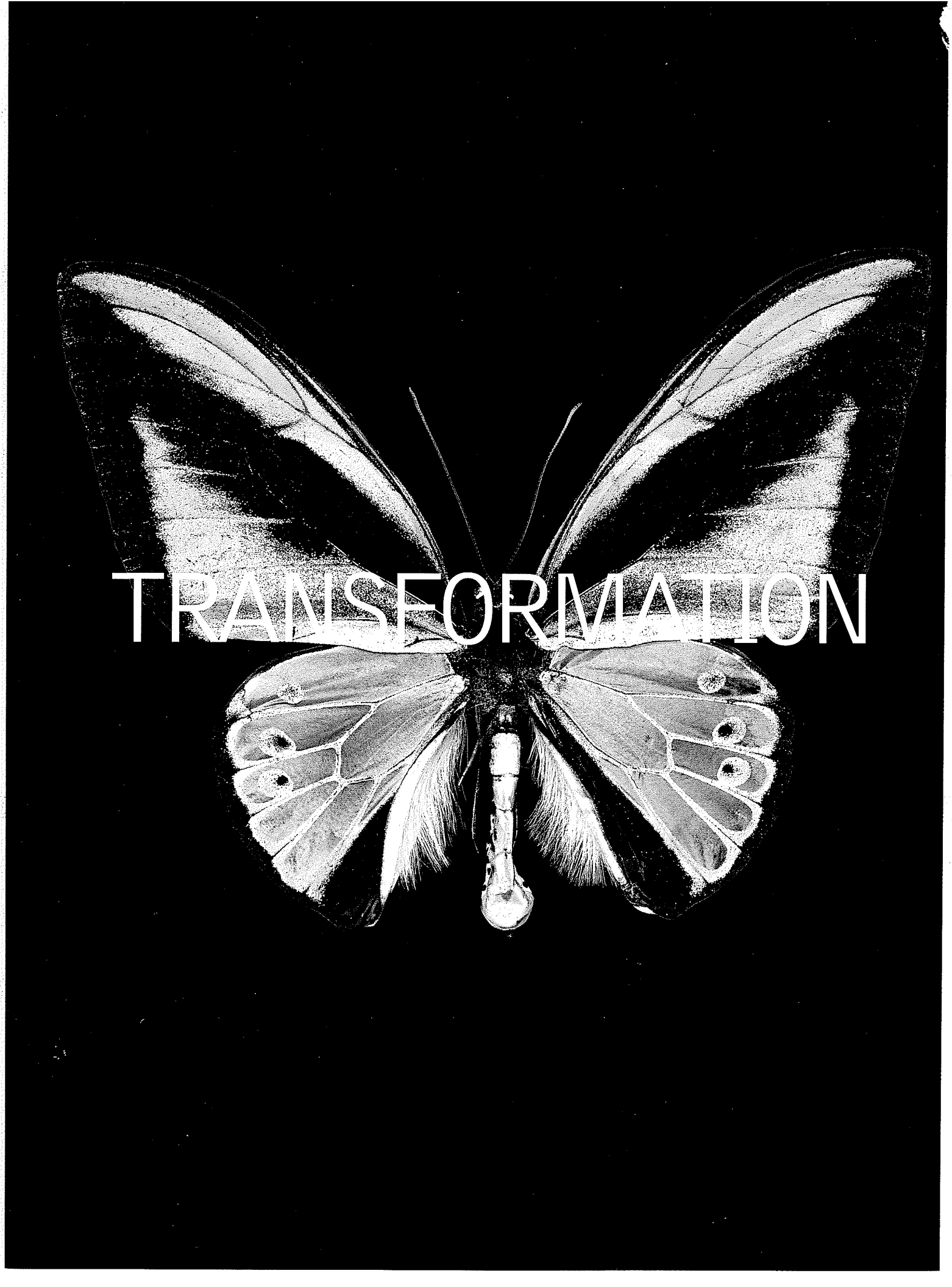
→ LUNG CANCER STRIKES MORE THAN 1.5 MILLION INDIVIDUALS WORLDWIDE EACH YEAR AND IS RESPONSIBLE FOR MORE THAN 1.4 MILLION ANNUAL DEATHS.

→ THE GLOBAL LUNG CANCER MARKET IS APPROXIMATELY $6 BILLION.

→ HER2-NEGATIVE METASTATIC BREAST CANCER ACCOUNTS FOR NEARLY 460,000 ANNUAL DEATHS WORLDWIDE, 40,000 OF WHICH OCCUR IN THE U.S.

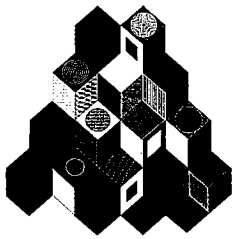
→ THE GLOBAL MARKET FOR METASTATIC BREAST CANCER IS ESTIMATED AT $5 BILLION.

→ THE WORLDWIDE INCIDENCE FOR THYROID CANCER EXCEEDS 200,000 PATIENTS ANNUALLY.


TRANSFORMATION

→ THROUGH A SERIES OF STRATEGIC TRANSACTIONS, ONYX HAS BUILT A DEEP AND DIVERSFIED PIPELINE OF COMPELLING COMPOUNDS THAT PROVIDE MULTIPLE PATHWAYS FOR GROWTH AND MULTIPLE POTENTIAL REVENUE STREAMS.

→ ONYX'S EXCLUSIVE DEVELOPMENT AND COMMERCIALIZATION AGREEMENT WITH ONO PHARMACEUTICAL FOR CARFILZOMIB AND ONX 0912 IS POTENTIALLY VALUED IN EXCESS OF $300 MILLION, PLUS DOUBLE-DIGIT ROYALTIES COMMENSURATE WITH A LATE-STAGE ASSET.



OUR COMPANY

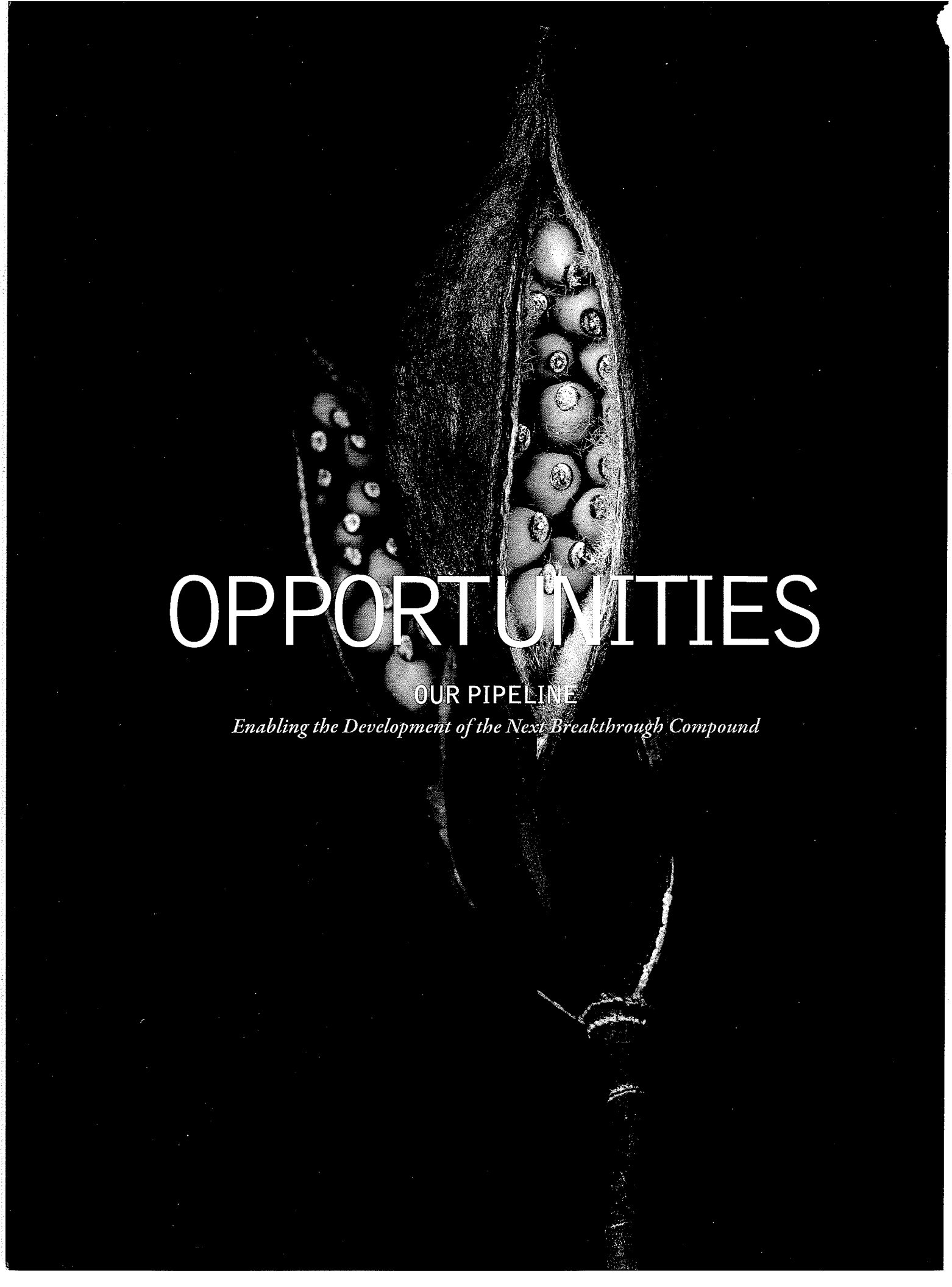
BECOMING A PORTFOLIO-BASED, PIPELINE-DRIVEN COMPANY

Anticipating launch of second oncology drug, first wholly owned product

In 2008, Onyx embarked on a new strategy for corporate growth and transformation focused on leveraging our core asset, Nexavar – a proven drug and growing global brand – to create a world-class biopharmaceutical company driven by innovation and offering multiple products for improving the lives of patients with cancer and other serious diseases. Our strategic plan centered around growing Nexavar revenues and margins in order to generate cash for investment in the further development of Nexavar and the creation of a pipeline capable of delivering both near- and long-term product opportunities. We have achieved these objectives through a series of strategic decisions and actions that now position us for the next phase of corporate growth – including the opportunity to help additional patients by introducing our second oncology drug, carfilzomib.

As we plan and execute pre-launch activities for carfilzomib, we are leveraging our proven strengths in clinical development and commercialization and building on the preclinical work of Proteolix, which developed carfilzomib and other next-generation proteasome inhibitors prior to its acquisition by Onyx in 2009. Anticipated to be our first wholly owned, approved product, carfilzomib could bring Onyx to a new inflection point along our growth trajectory. Based on this opportunity, we are growing our operations and capabilities, expanding our global footprint, and strengthening our corporate identity and leadership.

As we move ahead, a key strategy for our continued growth will be to leverage our pipeline assets to address global market opportunities through strategic corporate development transactions. For example, our exclusive development and commercialization agreement with Ono Pharmaceutical, signed in the fall of 2010, will accelerate the availability of carfilzomib in Japan, while allowing us to focus on execution in the U.S. and Europe. In this way, we intend to build on our strengths to create an even more valuable company with robust growth opportunities.

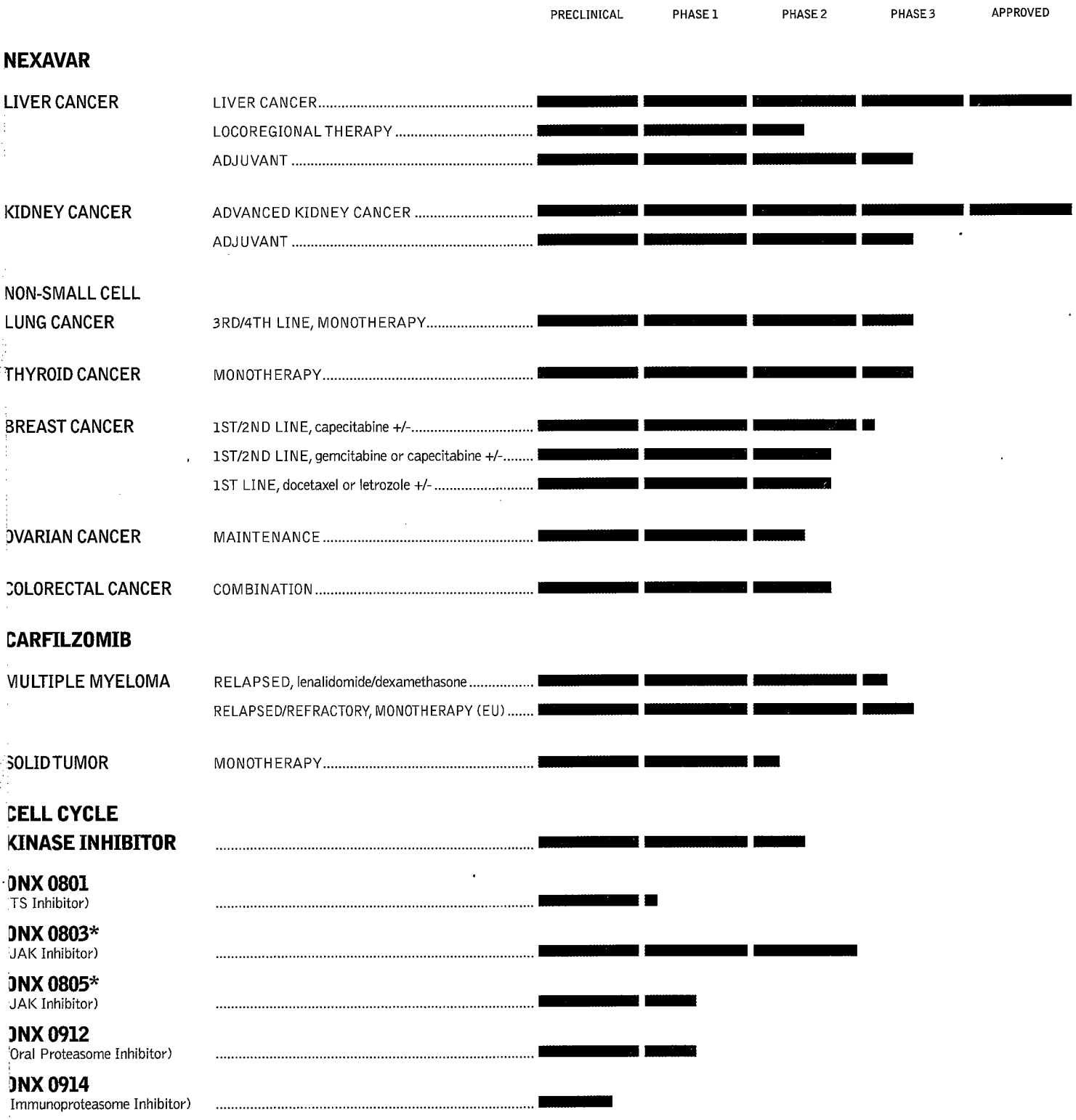


OPPORTUNITIES

OUR PIPELINE

Enabling the Development of the Next Breakthrough Compound

DIVERSIFIED PIPELINE TARGETS KEY CANCER AND PATHWAYS CREATING OPPORTUNITIES FOR GROWTH



*Subject to option exercise

CORPORATE INFORMATION

EXECUTIVE TEAM

N. Anthony Coles, M.D.
President, Chief Executive Officer and Member of the Board

Laura A. Brege
Executive Vice President, Corporate Affairs

Matthew K. Fust
Executive Vice President, Chief Financial Officer

Juergen Lasowski, Ph.D.
Executive Vice President, Corporate Development and Strategy

Ted W. Love, M.D.
Executive Vice President, Research & Development and Technical Operations

Kaye Foster-Cheek
Senior Vice President, Global Human Resources

Suzanne M. Shema, J.D.
Senior Vice President, General Counsel

Julianna Wood
Vice President, Public Affairs

BOARD OF DIRECTORS

N. Anthony Coles, M.D.
President and Chief Executive Officer, Onyx Pharmaceuticals, Inc.

Paul Goddard, Ph.D.
Lead Director, Onyx Pharmaceuticals, Inc.
Chairman and Chief Executive Officer, ARYx Therapeutics, Inc.

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

Magnus Lundberg
Chief Executive Officer, Phadia Group

Corinne H. Nevinny
General Partner, LMNVC LLC

Bill Ringo
Executive Director, Sofinnova Ventures
Senior Advisor, Barclays Capital

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

Thomas G. Wiggans
Former Chairman and Chief Executive Officer, Peplin, Inc. and Connetics Corporation

CORPORATE INFORMATION

Corporate Secretary
Robert L. Jones, J.D.
Partner, Cooley LLP

Corporate Counsel
Cooley LLP
San Francisco and Palo Alto, CA

Independent Auditors
Ernst & Young LLP
Palo Alto, CA

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 64874
St. Paul, MN 55164-0874

Stockholder Inquiries
Inquiries and requests for information should be directed to:

Investor Relations
Onyx Pharmaceuticals, Inc.
249 E. Grand Avenue
South San Francisco, CA 94080
(650) 266-1675
ir@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 meeting of stockholders will be held at 10:00 a.m. PDT on May 26, 2011, at the San Francisco Airport Marriott, 1800 Old Bayshore Highway, Burlingame, CA.

Forward-looking Statements: This report contains forward-looking statements that involve risks and uncertainties, including statements about our business, the development an commercialization of Nexavar, carfilzomib, and our other product candidates, and the potential clinical and market opportunities for our products and product candidates. Our actual result could differ materially from those anticipated in these forward-looking statements as a result of many factors, including risks and uncertainties related to: Nexavar being our only approve product; we may never receive marketing approval for carfilzomib; failures or delays in our clinical trials; our collaborative relationship with Bayer; commercially launching carfilzomib; seriou adverse side effects, if they are associated with Nexavar or carfilzomib; and other risks and uncertainties set forth under "Business" and "Risk Factors," and elsewhere in our Annual Report o Form 10-K for the year ended December 31, 2010, to which reference should be made. We undertake no obligation to update forward-looking statements except as required by law.

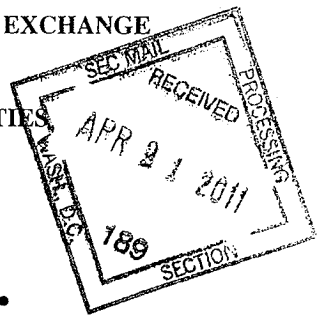
Non-GAAP Financial Measures: This report references our non-GAAP measure of profitability for the year ended December 31, 2010. Onyx management uses non-GAAP financial measure to monitor and evaluate our operating results. On a GAAP basis, we reported a net loss for the year. Our non-GAAP measure excludes the following items: contingent consideration expens related to the change in fair value of the liability for contingent consideration in connection with the acquisition of Proteolix; employee stock-based compensation expense; imputed interes related to our convertible senior notes due 2016; and milestone payments and acquisition related transaction costs.

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, 2010

☐ **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 whether the registrant has submitted electronically and posted on its corporate Website, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§ 232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). 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, a non-accelerated filer, or a smaller reporting company. See the definitions of "large accelerated filer," "accelerated filer" and "smaller reporting company" in Rule 12b-2 of the Exchange Act. (Check one):

Large accelerated filer ☑ Accelerated filer ☐ Non-accelerated filer ☐ Smaller reporting company ☐
(Do not check if a smaller reporting company)

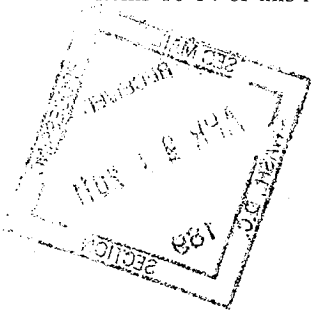
Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act): Yes ☐ No ☑

The aggregate market value of the voting stock held by non-affiliates of the Registrant based upon the last trade price of the common stock reported on the NASDAQ Global Market on June 30, 2010 was approximately $967,573,899, this excludes 17,813,933 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.

The number of shares of common stock outstanding as of February 17, 2011 was 63,033,264.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the Registrant's Definitive Proxy Statement for its 2011 Annual Meeting of Stockholders, which will be filed with the Commission within 120 days of December 31, 2010, are incorporated herein by reference into Part III items 10-14 of this Annual Report on Form 10-K.



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, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. 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.

All references to "the Company," "Onyx," "we," "our," and "us" in this Annual Report on Form 10-K refer collectively to Onyx Pharmaceuticals, Inc. and its wholly-owned subsidiaries.

Item 1. Business

Overview

We are a biopharmaceutical company dedicated to developing innovative therapies that target the molecular mechanisms that cause cancer. Through our internal research programs and in conjunction with our collaborators, we are applying our expertise to develop and commercialize therapies designed to exploit the genetic and molecular differences between cancer cells and normal cells. We are continuing to maximize current commercialization opportunities for Nexavar® (sorafenib) tablets, along with our collaborator, Bayer HealthCare Pharmaceuticals Inc., or Bayer, and we seek to enter the hematologic cancer market through the development of carfilzomib, a selective proteasome inhibitor, for the potential treatment of patients with multiple myeloma and solid tumors. Carfilzomib is a mid-to late-stage compound with the potential for accelerated marketing approval in the United States based on our current clinical trial data and assuming favorable regulatory outcomes. In addition, we continue to expand our development pipeline, with multiple clinical and preclinical stage product candidates.

We were incorporated in California in February 1992 and reincorporated in Delaware in May 1996. Our corporate headquarters are located at 2100 Powell Street, Emeryville, California 94608, and our telephone number is (510) 597-6500.

Our Strategy

We plan to achieve our business strategy of transforming Onyx into a leading biopharmaceutical company in the oncology market by:

- *establishing carfilzomib as a treatment for multiple myeloma*;
- *maximizing current opportunities worldwide for Nexavar* in approved indications;
- *preparing for future commercialization opportunities* of Nexavar and carfilzomib;
- *investing in a broad development program for Nexavar* by pursuing other types of cancer that Nexavar may help in treating, including lung, breast, thyroid, ovarian and colorectal cancers;
- *advancing the development of our pipeline,* including carfilzomib, the ONX 0912, ONX 0914 and ONX 0801 programs, and assessing in-licensing opportunities, such as our option to in-license ONX 0803 and ONX 0805 (both Janus Kinase, or JAK, inhibitors); and
- *continuing to expand our pipeline* by pursuing other investments and opportunities with disciplined financial goals.

Marketed Product — Nexavar

Our first commercially available product, Nexavar, is approved by the United States Food and Drug Administration, or FDA, for the treatment of patients with unresectable liver cancer and advanced kidney cancer. Nexavar is a novel, orally available multiple kinase inhibitor that acts through dual mechanisms of action by inhibiting angiogenesis and the proliferation of cancer cells. 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 called angiogenesis. 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. 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. The RAS signaling pathway plays an integral role in the growth of some tumor types such as colorectal cancer, liver cancer 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

We and Bayer are commercializing Nexavar for the treatment of patients with unresectable liver cancer and advanced kidney cancer. Nexavar has been approved and is marketed for these indications in the United States, European Union and in other territories worldwide. Nexavar was approved for the treatment of patients with advanced kidney cancer by the FDA in December 2005. It was approved by the European Union in July 2006 for the treatment of patients with advanced kidney cancer who have failed prior therapy or are considered unsuitable for other therapies. In the fourth quarter of 2007, Nexavar was approved in the European Union and United States for the treatment of patients with unresectable liver cancer. Nexavar is now approved in more than 90 countries worldwide for the treatment of advanced kidney cancer and unresectable liver cancer. In the United States, we co-promote Nexavar with Bayer. Outside of the United States, Bayer manages all commercialization activities. In 2010, worldwide net sales of Nexavar, as recorded by Bayer, totaled $934.0 million.

Product Candidates in Clinical Trials

The following is a partial listing of the development status of Nexavar, carfilzomib and our other product candidates in clinical trials and the status for select indications.

Product Candidate	Indication	Current Status
Nexavar		
	Liver Cancer	
	• Adjuvant therapy	Phase 3
	• First line, erlotinib +/-	Phase 3
	• Locoregional therapies, e.g. TACE	Phase 2
	Kidney Cancer	
	• Adjuvant therapy	Phase 3
	Non-Small Cell Lung Cancer	
	• Third/fourth line, monotherapy	Phase 3
	Thyroid Cancer	
	• Monotherapy	Phase 3
	Breast Cancer	
	• First/second line, capecitabine +/-	Phase 3
	• First/second line, gemcitabine or capecitabine +/- following treatment with bevacizumab	Phase 2
	• First line, docetaxel and/or letrozole +/-	Phase 2
	Ovarian Cancer	
	• Maintenance therapy	Phase 2
	Colorectal Cancer	
	• First line, combination with mFOLFOX6	Phase 2
Carfilzomib		
	Multiple Myeloma	
	• Monotherapy	Phase 2b
	• Lenalidomide, dexamethasone +/-	Phase 3
	• Comparison to Best Supportive Care (Corticosteroid)	Phase 3
	Solid Tumor	
	• Monotherapy	Phase 2
Cell Cycle Kinase Inhibitor*		Phase 2
ONX 0801		Phase 1
ONX 0912		Phase 1; Phase 1b/2 planned
ONX 0803; ONX 0805****		Phase 2; Phase 1
ONX 0914		Preclinical

* Outlicensed to Pfizer Inc.

** Subject to exercise of our option to in-license.

Nexavar Development Strategy

We and Bayer are executing the Nexavar development strategy with three primary areas of focus. First, we have several ongoing clinical trials that are designed to expand Nexavar's position in the two previously approved indications, unresectable liver cancer and advanced kidney cancer. These include studies in adjuvant therapy (or treatment given in addition to the primary treatment such as surgery) and in combination with other anti-cancer therapies. Secondly, we have ongoing and planned Phase 3 registration studies in cancer types and settings for which we believe Nexavar's unique features and evidence of activity support development.

Finally, we are conducting multiple studies, including large randomized Phase 2 studies, which will serve as screening studies that may provide information for the future design of Phase 3 trials in a variety of cancer types, lines of therapy and in combination with other anti-cancer agents. We believe Nexavar's unique features, including its efficacy, oral availability and tolerability, 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. In addition to conducting company-sponsored clinical trials, we collaborate on clinical trials with government agencies, cooperative groups, and individual investigators. Our goal is to maximize Nexavar's commercial and clinical potential by simultaneously running multiple studies to produce the clinical evidence necessary to determine whether Nexavar can benefit patients with other types of cancers. Additionally, because it is difficult to predict the success of any individual clinical trial, running multiple trials may mitigate the risk of failure of any single clinical trial.

Under our collaboration agreement, we and Bayer are jointly developing Nexavar internationally, with the exception of Japan. In Japan, Bayer funds all product development, and we receive a royalty on sales. The following is a summary of our current key clinical trials with Bayer.

Liver Cancer Program

Phase 3 Trial. In August 2008, we and Bayer initiated an international, randomized, placebo-controlled Phase 3 clinical trial evaluating Nexavar as an adjuvant therapy for patients with liver cancer who have undergone resection or loco-regional treatment with curative intent. This study, known as the Sorafenib as Adjuvant Treatment in the Prevention of Recurrence of Hepatocellular Carcinoma (STORM) trial, completed enrollment in 2010. The primary endpoint of the study is recurrence free survival.

Phase 3 Trial. In May 2009, we and Bayer initiated an international trial examining Nexavar tablets in combination with Tarceva® (erlotinib) tablets as a potential new treatment option for patients with advanced HCC. The randomized, double-blind, placebo-controlled Phase 3 study, known as Sorafenib and Erlotinib, a Randomized Trial Protocol for the Treatment of Patients with HCC (SEARCH), completed enrollment in early 2011. SEARCH will examine whether Nexavar in combination with Tarceva prolongs survival as compared to Nexavar alone. The primary endpoint of the study is overall survival.

Phase 2 Trial. In March 2009, we and Bayer initiated an international, randomized, double-blind, placebo-controlled clinical trial evaluating Nexavar or placebo in combination with transarterial chemoembolization (TACE) performed with drug eluting beads and doxorubicin for patients with intermediate stage HCC. The study, known as the Sorafenib or Placebo in Combination with TACE for Intermediate Hepatocellular Carcinoma (SPACE) trial, completed enrollment in 2010. The primary endpoint of the study is time to progression.

Kidney Cancer Program

Phase 3 Trial. In May 2006, the Eastern Cooperative Oncology Group, or ECOG, initiated an international, randomized, placebo-controlled Phase 3 clinical study, known as the Adjuvant Sorafenib or Sunitinib for Unfavorable Renal Carcinoma (ASSURE) trial, evaluating Nexavar versus sunitinib as an adjuvant therapy for patients with advanced kidney cancer that has been removed by surgery with no evidence of residual disease. The primary endpoint of the study is disease-free survival.

Phase 3 Trial. In June 2007, an international, randomized, double-blind clinical trial comparing Nexavar with placebo in patients with resected primary renal cell carcinoma was initiated. This Phase 3 clinical study is

known as the Sorafenib with Placebo in Patients with Resected Primary Renal Cell Carcinoma at High or Intermediate Risk of Relapse (SORCE). The primary endpoint of the study is disease-free survival.

Non-Small Cell Lung Cancer (NSCLC) Program

Phase 3 Trial. In December 2010, enrollment completed in an international randomized, double-blind placebo-controlled Phase 3 trial to evaluate Nexavar tablets in patients with relapsed or refractory advanced predominantly non-squamous NSCLC who have failed two or three previous treatments. This 3rd/4th line study is known as the Monotherapy Administration of Sorafenib in Patients with NSCLC (MISSION) trial. The primary endpoint of the study is overall survival.

Phase 3 Trial. In June 2009, enrollment completed in a pivotal randomized, double-blind placebo-controlled trial in select locations outside the United States of patients with Stage IIIb-IV NSCLC, who had not received prior systemic anti-cancer treatment. In this trial, known as the NSCLC Research Experience Utilizing Sorafenib (NExUS) trial, patients received gemcitabine and cisplatin in combination with Nexavar or a placebo. The primary endpoint of the study was overall survival. In June 2010, we announced that the study did not meet its primary endpoint.

Phase 3 Trial. In February 2006, we and Bayer initiated a randomized, double-blind, placebo-controlled pivotal clinical trial, called Evaluation of Sorafenib, Carboplatin And Paclitaxel Efficacy (ESCAPE), studying Nexavar administered in combination with the chemotherapeutic agents carboplatin and paclitaxel in patients with NSCLC. This multicenter study compared Nexavar administered in combination with these two agents to treatment with just the two agents alone. In February 2008, this clinical trial was stopped early following a planned interim analysis when an independent DMC concluded that the study would not meet its primary endpoint of improved overall survival.

Thyroid Cancer Program

Phase 3 Trial. In October 2009, we and Bayer began enrolling patients in an international Phase 3 trial to evaluate Nexavar tablets for the treatment of patients with radioactive iodine-refractory, locally advanced or metastatic differentiated thyroid cancer. The trial design called the Study of Sorafenib in Locally Advanced or Metastatic Patients with Radioactive Iodine Refractory Thyroid Cancer (DECISION), is planned to enroll patients with locally advanced or metastatic, radioactive iodine-refractory, differentiated thyroid cancer (papillary, follicular and Hurthle cell) who have received no prior systemic therapy. The primary endpoint of the study is progression-free survival.

Breast Cancer Program

Phase 3 Trial. We and Bayer are actively screening patients for an international Phase 3 trial to evaluate Nexavar tablets in combination with capecitabine for the treatment of patients with locally advanced or metastatic HER2-negative breast cancer who are resistant to or have failed prior taxane and an anthracycline or for whom further anthracycline therapy is not indicated, which is known as the "RESILIENCE" trial. The primary endpoint of the study is progression-free survival.

Phase 2 Trials. In 2007, we and Bayer launched a broad, multinational Phase 2 clinical trial program in advanced breast cancer known as Trials to Investigate the Effects of Sorafenib in Breast Cancer (TIES). The four clinical trials in the TIES program are screening studies intended to provide information that may be used to design a Phase 3 program. The TIES program involves a number of different drug combinations with Nexavar and encompasses various treatment settings.

In September 2009, we presented the results from the first of the collaborative group-sponsored randomized, double-blind, placebo-controlled Phase 2 trials. This first study evaluated Nexavar in combination with the oral chemotherapeutic agent capecitabine. These patients had locally advanced or metastatic HER-2 negative breast cancer and had received no more than one prior chemotherapy in this setting. The trial met its primary endpoint of progression free survival, demonstrating that median progression-free survival was extended in patients treated with Nexavar and capecitabine compared to patients receiving capecitabine and placebo. The

second study evaluated Nexavar in combination with the chemotherapeutic agent paclitaxel. These patients had locally recurrent or metastatic HER-2 negative breast cancer and had not received prior chemotherapy in this setting. While this trial did not meet its primary endpoint of progression free survival, the results demonstrated a positive trend towards improvement of progression-free survival in the Nexavar treatment group with no new toxicities observed and adverse events were clinically manageable. In 2010, the results from the analysis of overall survival from these two trials were presented. A trend toward an improvement in overall survival was observed in the first trial of Nexavar in combination with capecitabine.

The TIES program includes two additional randomized, placebo-controlled Phase 2 trials, and enrollment was completed for both studies in 2010. One of the trials is evaluating Nexavar plus gemcitabine or capecitabine in the first- or second-line setting following progression on bevacizumab, and the second trial is evaluating Nexavar plus docetaxel and/or letrozole in the first-line setting. The primary endpoint of both of these studies is progression-free survival.

Early/Mid Stage Clinical Development

We have additional ongoing and planned studies with Bayer evaluating Nexavar as a single agent and in combination with other anti-cancer agents in tumors such as ovarian, advanced colorectal and other cancers. Based on the results of these ongoing trials, we plan to identify additional potential registration paths for Nexavar.

Carfilzomib

We are developing carfilzomib, a next-generation, selective proteasome inhibitor, as a potential cancer treatment. The proteasome is a protein complex that exists in all cells, whether healthy or cancerous. The proteasome controls the turnover of proteins in cells in a regulated manner, but cancer cells are more susceptible to cell death when the proteasome is inhibited. Carfilzomib is a novel small molecule, belonging to a class known as peptide ketoepoxides, and is designed to inhibit the proteasome and enable sustained suppression of protein degradation in tumor cells. Carfilzomib is currently in multiple clinical trials as summarized below.

Multiple Myeloma Program

We are conducting multiple clinical trials evaluating carfilzomib as a monotherapy in relapsed and/or refractory multiple myeloma patients and in combination with other anti-cancer agents and chemotherapies. Multiple myeloma is the second most common hematologic cancer and results from an abnormality of plasma cells, usually in the bone marrow.

Phase 2b Trial. In December 2010, we presented data results from an ongoing pivotal Phase 2b trial, known as the "003-A1" trial. The primary endpoint of the study was overall response rate. Results demonstrated carfilzomib was well-tolerated in heavily pre-treated relapsed and refractory multiple myeloma patients and could be administered at a full dose over prolonged periods of time, even in a very sick patient population for whom all available treatment options have been exhausted and who have multiple comorbidities. Enrollment consisted of patients who had received prior treatment with bortezomib and either thalidomide or lenalidomide and were unresponsive to their last treatment. The full results of the study will be used to support submission of a New Drug Application (NDA) with the FDA by as early as mid-year 2011. In January 2011, the FDA approved Fast Track review status for the carfilzomib NDA, and in January 2011 we began a rolling submission of the NDA.

Phase 2 Trial. In December 2010, we also presented data from an ongoing study, known as the "004" trial. The primary endpoint is overall response rate and secondary endpoints include time to progression, duration of response, overall survival and safety. Results of 123 evaluable patients demonstrate that single-agent carfilzomib achieves high overall response rates of up to 53% in bortezomib-naïve patients with relapsed myeloma, with minimal neuropathy, even in the setting of high-risk disease. These responses were durable with a median duration of response of greater than 13 months.

Phase 1b/2 Trial. In June 2010, we presented data from a Phase 1b/2 combination study, known as the "006" trial, of carfilzomib with lenalidomide and dexamethasone in patients with relapsed multiple myeloma. The primary endpoint of the study was to evaluate safety and maximum tolerated dose. Results demonstrated the achievement of the safe combination of full dose carfilzomib with full dose lenalidomide and low dose once weekly dexamethasone.

Phase 1/2 Trial. In December 2010, initial results of a Phase 1/2 trial were presented at the American Society of Hematology demonstrating a 100% overall response rate and minimal toxicity. The study, sponsored by University of Michigan Cancer Center, is designed to evaluate the safety and to determine the maximum tolerated dose of carfilzomib plus lenalidomide in combination with dexamethasone in newly diagnosed multiple myeloma patients with no prior treatment.

Phase 3 Trial. In September 2010, we began enrollment in a pivotal Phase 3, international, randomized, open-label trial designed to evaluate the efficacy of carfilzomib in combination with lenalidomide and low dose dexamethasone, versus lenalidomide and low dose dexamethasone alone. The trial, referred to as ASPIRE or the "009" trial, is expected to enroll approximately 700 patients with relapsed multiple myeloma following treatment with one to three prior regimens. The primary endpoint of the study is progression-free survival. The trial is being conducted under a Special Protocol Assessment (SPA) from the FDA. An SPA is an agreement with the FDA on the design and planned analysis for a clinical trial which is intended to form the basis for a marketing application and which may only be changed through a written agreement between the sponsor and the FDA, or if the FDA becomes aware of new public health concerns. We also sought Scientific Advice from the European Medicines Agency (EMA) on the design and planned analysis of the ASPIRE trial. The ASPIRE trial may either serve as the confirmatory trial for full approval, if accelerated approval is granted on the basis of the 003-A1 data, or would allow for initial approval of the NDA if the trial successfully meets the requirements of the SPA.

Phase 3 Trial. In May 2009, we sought Protocol Assistance/Scientific Advice from the EMA on the development of carfilzomib in the European Union. The Committee for Medicinal Products for Human Use of the EMA advised that, in addition to 003-A1, we conduct a controlled study of carfilzomib monotherapy in refractory multiple myeloma patients, using best supportive care as the comparator. In September 2010, we began enrollment in the trial, referred to as FOCUS or the "011" trial, which is designed to evaluate patients with refractory multiple myeloma relapsed after at least three prior regimens who are randomized to receive either carfilzomib or best standard of care. The primary endpoint of the study is progression-free survival. Studies 003-A1 and 011 will be used to support the initial market authorization in the EU for relapsed and refractory multiple myeloma.

ONX 0912

ONX 0912 is an oral proteasome inhibitor in Phase 1 clinical development that is based on similar novel chemistry as carfilzomib. ONX 0912 has demonstrated preclinical anti-tumor activity and a broad therapeutic window in preclinical models. In May 2010, we initiated a Phase 1 study of ONX 0912 in advanced refractory and recurrent solid tumors. This non-randomized, open-label, dose-escalation study will evaluate the safety and tolerability of ONX 0912 and determine its dose limiting toxicity and maximum tolerated dose.

ONX 0801

ONX 0801 is a novel targeted oncology compound in Phase 1 clinical development that is designed to combine two proven approaches to improve outcomes for cancer patients by selectively targeting tumor cells through the alpha-folate receptor, which is overexpressed in a number of tumor types, and inhibiting thymidylate synthase (TS), a key enzyme responsible for cell growth and division. ONX 0801 targets malignant cells that overexpress the alpha-folate receptor, which is located on the cell's surface. ONX 0801 differs from currently marketed TS inhibitors due to its selective tumor cell-specific uptake by the alpha-folate receptor. The alpha-folate receptor is overexpressed in a number of tumor types, including ovarian cancer, lung cancer, breast cancer and colorectal cancer. In September 2009, we initiated a Phase 1 study of ONX 0801 in advanced solid tumors. This open-label, dose-finding study is evaluating the safety and pharmacokinetics of ONX 0801 in patients with advanced solid tumors. We obtained

worldwide product development and commercialization rights to ONX 0801 through a development and license agreement with BTG International Limited, or BTG.

Product Candidate — Earlier Stage Pipeline

ONX 0914

We are developing ONX 0914 to be an inhibitor of the immunoproteasome, with minimal cross-reactivity for the constitutive proteasome. Recent evidence suggests that the immunoproteasome regulates the production of several inflammatory cytokines, including Tumor Necrosis Factor-α(TNF-α), Interleukin-6 (IL-6), IL-17, and IL-23. In preclinical models of rheumatoid arthritis and lupus, ONX 0914 blocked progression of these diseases at well tolerated doses. We are conducting preclinical studies to evaluate the potential clinical applications of ONX 0914 in the treatment of autoimmune disorders, such as rheumatoid arthritis, inflammatory bowel disease and lupus.

Collaboration, Licensing, Option Agreements

Collaboration Agreement with Bayer

Effective February 1994, we executed 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. 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 (IND) application was filed in May 2000. Under our collaboration agreement, we are currently funding 50% of mutually agreed development costs worldwide, excluding Japan. In all foreign countries, except Japan, Bayer first receives a portion of product revenues to repay Bayer for its foreign commercialization infrastructure, after which we receive 50% of net profits on sales of Nexavar. Bayer is funding 100% of development costs in Japan and pays us a single-digit royalty on Nexavar sales in 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% of product development costs, Bayer would retain exclusive, worldwide rights to Nexavar and would pay royalties to us based on net sales.

In March 2006, we and Bayer entered into a co-promotion agreement to co-promote Nexavar in the United States. The co-promotion agreement amends and generally supersedes those provisions of the 1994 collaboration 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 and Bayer share equally in the profits or losses of Nexavar in the United States. If for any reason we do not continue to co-promote in the United States, but continue to co-fund development worldwide (excluding Japan), 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 in the United States.

Our collaboration agreement with Bayer will terminate when patents expire that were issued in connection with product candidates discovered under the agreement, or at the time when neither we nor Bayer are entitled to profit sharing under the agreement, whichever is latest. Our co-promotion agreement with Bayer will terminate upon the earlier of the termination of our collaboration agreement with Bayer or the date products subject to the co-promotion agreement are no longer sold by either party in the United States due to a permanent product withdrawal or recall or a voluntary decision by the parties to abandon the co-promotion of such products in the United States. Either party may also terminate the co-promotion agreement upon failure to cure a material breach of the agreement within a specified cure period.

In addition, our collaboration agreement with Bayer provides that if we are acquired by another entity by reason of merger, consolidation or sale of all or substantially all of our assets, or if a single entity other than Bayer or its affiliate acquires ownership of a majority of the our outstanding voting stock, and Bayer does not consent to the transaction, then for 60 days following the transaction, Bayer may elect to terminate our co-development and co-promotion rights under the collaboration agreement and convert our profit sharing interest under that agreement into

a royalty based on any sales of Nexavar and other collaboration products. The applicable royalty rate would be a function of expected profitability of Nexavar for the remaining patent life of Nexavar. As of December 20, 2010, the fifth anniversary of the initial regulatory approval of Nexavar, in the event of an acquisition transaction, we believe the economic value of a royalty amount should be substantially equivalent to the economic value of the profit share interest for Nexavar during the remaining patent life absent such an acquisition transaction. Bayer has informed us they do not agree with this conclusion. The application of the royalty formula to any transaction that closed prior to the fifth anniversary of the initial regulatory approval of Nexavar would have been different, however, and could have substantially reduced the economic value derived from the sales of Nexavar to us or our successor, compared to the economic value we would have received absent such an acquisition transaction. Also, either party may terminate the agreement upon 30 days' notice within 60 days of specified events relating to insolvency of the other party.

Collaboration Agreement with Pfizer

In May 1995, we entered into a research and development collaboration agreement with Warner-Lambert Company, now a subsidiary of Pfizer Inc., or 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 Pfizer for screening of their compound library. The discovery research term ended in August 2001. Pfizer is responsible for subsequent medicinal chemistry, preclinical and clinical development, regulatory filings, manufacture and sale of any approved collaboration compounds. We are entitled to receive payments upon achievement of certain clinical development milestones and registration of any resulting products and are entitled to receive royalties on worldwide sales. Pfizer identified a small molecule lead compound, PD 0332991, an inhibitor of cyclin-dependent kinase 4/6 (CDK 4/6), and began clinical testing in September 2004. In December 2009, we earned a $1.0 million milestone payment from Pfizer upon initiation of a Phase 2 trial for breast cancer. To date, we have earned $1.5 million in milestone payments relating to this drug candidate, which we refer to as a cell cycle kinase inhibitor.

The May 1995 collaboration agreement with Pfizer will remain in effect until the expiration of all licenses granted pursuant to the agreement. Either party may terminate the agreement for the uncured material breach of the other party. Under this agreement, remaining additional potential milestones payable by Pfizer to Onyx are, in aggregate, up to approximately $15.5 million and royalty payments will be based on a single digit percentage of net sales, if any.

Licensing Agreement with BTG

In November 2008, we licensed a novel targeted oncology compound, ONX 0801, from BTG. Under the terms of the agreement, we obtained a worldwide license for ONX 0801 and its related patents. We also received exclusive worldwide marketing rights and are responsible for all product development and commercialization activities. We paid BTG a $13.0 million upfront payment in 2008 and a $7.0 million milestone payment in 2009. We may be required to make payments of up to an additional $65.0 million upon the attainment of certain global development and regulatory milestones, plus additional milestone payments upon the achievement of certain marketing approvals and commercial milestones. We also are required to pay royalties to BTG on any future product sales.

Our development and license agreement with BTG will expire 10 years after the first commercial sale of the licensed product or until patent coverage expires, whichever is later. We may terminate the agreement at any time without cause by giving BTG prior written notice, and either party may terminate the agreement upon failure to cure a material breach in certain cases. BTG may terminate the agreement by written notice upon the occurrence of certain specified events, including our failure to pay BTG payments due under the agreement after demand for such payments, our challenging the licensed rights under the agreement, our failure to conduct material development activity in relation to a licensed product for a specified period, our decision to cease development of licensed products, or specified events relating to our insolvency. Upon any termination of the agreement, rights to the licensed compounds will revert to BTG. Except in the case of termination for our breach at an early stage of development, we will receive a portion of any compensation received by BTG from the sale of the reverted compounds.

Licensing Agreement with Ono Pharmaceuticals

In September 2010, we entered into an exclusive license agreement with Ono Pharmaceutical Co., Ltd., or Ono, granting Ono the right to develop and commercialize both carfilzomib and ONX 0912 for all oncology indications in Japan. We retain development and commercialization rights for all other countries. We agreed to provide Ono with development and commercial supply of carfilzomib and ONX 0912 on a cost-plus basis. Ono agreed to pay us development and commercial milestone payments based on the achievement of pre-specified criteria. In addition, Ono agreed to share a percentage of costs incurred by us for the global development of carfilzomib and ONX 0912 that support filings for regulatory approval in Japan. The milestone and development support payments could total approximately $283.5 million at current exchange rates. Ono is responsible for all development costs in support of regulatory filings in Japan as well as commercialization costs it incurs. If regulatory approval for carfilzomib and/or ONX 0912 is achieved in Japan, Ono is obligated to pay us double-digit royalties on net sales of the licensed compounds in Japan. The agreement will terminate upon the expiration of the royalty terms specified for each product. In addition, Ono may terminate this agreement for certain scientific or commercial reasons with advance written notice, and either party may terminate this agreement for the other party's uncured material breach or bankruptcy.

*Option Agreement with S*BIO*

In December 2008, we entered into a development collaboration, option and license agreement with S*BIO Pte Ltd, or S*BIO, a Singapore-based company, pursuant to which we acquired options to license rights to each of SB1518 (designated by Onyx as ONX 0803) and SB1578 (designated by Onyx as ONX 0805). Under the terms of the agreement, we were granted options which, if we exercise them, would give us rights to exclusively develop and commercialize ONX 0803 and/or ONX 0805 for all potential indications in the United States, Canada and Europe. Under this agreement, S*BIO will retain responsibility for all development costs prior to the option exercise. After the exercise of our option to license rights to either compound, we are required to assume development costs for the U.S., Canada and Europe subject to S*BIO's option to fund a portion of the development costs in return for enhanced royalties on any future product sales. Upon the exercise of our option of either compound, S*BIO is entitled to receive a one-time option fee, milestone payments upon achievement of certain development and sales levels and royalties on any future product sales. Under the terms of the agreement, in December 2008 we made a $25.0 million payment to S*BIO, including an up-front payment and an equity investment. In May 2010, we expanded our agreement with S*BIO and provided an additional $20.0 million in funding to S*BIO to broaden and accelerate the existing development program for both compounds. S*BIO agreed to utilize the funding to continue to perform the clinical development of ONX 0803 and preclinical through clinical development of ONX 0805.

Our development collaboration, option and license agreement with S*BIO will remain in effect until the expiration of all payment obligations. Because we have not exercised our option in the agreement, we may terminate the agreement at any time without cause by giving S*BIO prior written notice. In addition, either party may terminate the agreement for the uncured material breach of the other party.

ONX 0803 and ONX 0805

ONX 0803 is an orally available, potent and selective inhibitor of JAK that has been designed to suppress over-activity of mutant JAK. S*BIO is conducting trials for ONX 0803 in multiple Phase 1 studies. In February 2010, S*BIO initiated two Phase 2 trials using ONX 0803 in myelofibrosis. ONX 0805 is a JAK inhibitor and is in preclinical development. Under normal circumstances, activation of JAK stimulates blood cell production. Genetic mutations in the JAK enzyme result in up-regulated activity and are implicated in myeloproliferative diseases, conditions characterized by an overproduction of blood cells in the bone marrow. The conditions where JAK mutations are most common include polycythemia vera, essential thrombocytopenia and primary myelofibrosis. The JAK signaling pathway has been shown to play a critical role in the proliferation of certain types of cancer cells and in the anti-inflammatory pathway, suggesting JAK inhibitors may also be able to play a role in the treatment of solid tumors and other diseases such as rheumatoid arthritis.

Acquisition Agreement and Plan of Merger

In November 2009, we acquired Proteolix, Inc., or Proteolix, under the terms of an Agreement and Plan of Merger, or the Merger Agreement, with Proteolix, Shareholder Representative Services LLC (SRS) and Profiterole Acquisition Corp., which was entered into in October 2009. The acquisition provided us with an opportunity to expand into the hematological malignancies market and expand our mid-to-late stage development portfolio.

Under the original Merger Agreement, the aggregate cash consideration paid to former Proteolix stockholders at closing was $276.0 million and an additional $40.0 million earn-out payment was made in April 2010, 180 days after completion of enrollment in an ongoing pivotal Phase 2b clinical study involving relapsed and refractory multiple myeloma patients, known as the "003-A1" trial. We may be required to pay up to an additional $535.0 million in earn-out payments payable in up to four installments upon the achievement of certain regulatory approvals for carfilzomib in the U.S. and Europe within pre-specified timeframes. In January 2011, we entered into Amendment No. 1 to the Merger Agreement, or the Amendment, with SRS. Under the original Merger Agreement, the first of these additional earn-out payments would be in the amount of $170.0 million if achieved by the date originally contemplated, and would be triggered by accelerated marketing approval for carfilzomib in the United States for relapsed/refractory multiple myeloma. This obligation is unchanged in the Amendment. The Amendment modifies this payment if the milestone is not achieved by the date originally contemplated on a sliding scale basis, as follows:

- if accelerated marketing approval in the United States for relapsed/refractory multiple myeloma is achieved after the date originally contemplated, but within six months of the original date, subject to extension under certain circumstances, then the amount payable will be reduced to $130.0 million; and
- if accelerated marketing approval in the United States for relapsed/refractory multiple myeloma is achieved more than six months after the date originally contemplated, but within 12 months of the original date, subject to extension under certain circumstances, then the amount payable will be reduced to $80.0 million.

The remaining earn-out payments will continue to become payable in up to three additional installments as follows:

- $65.0 million would be triggered by marketing approval in the European Union for relapsed/refractory multiple myeloma.
- $150.0 million would be triggered by marketing approval in the United States for relapsed multiple myeloma.
- $150.0 million would be triggered by marketing approval for relapsed multiple myeloma in the European Union.

Under certain circumstances, including if we fail to satisfy regulatory approval-related diligence obligations under the Merger Agreement, we may be required to make one or more earnout payments even if the associated regulatory approvals are not received. Subject to the terms and conditions set forth in the Merger Agreement, Onyx may, in its sole discretion, make any of the remaining earnout payments that become payable to former holders of Proteolix preferred stock in the form of cash, shares of Onyx common stock or a combination thereof.

In accordance with the Merger Agreement, 10% of each of the total cash payments to date, or $31.6 million, was placed in an escrow account to secure the indemnification rights of Onyx and other indemnitees with respect to certain matters and was to be held until December 31, 2010. However, in December 2010, we filed a claim notice in good faith describing circumstances that we believed entitled us to indemnification, compensation and/or reimbursement under the Merger Agreement. This escrow amount was paid to the former Proteolix stockholders in February 2011 after the settlement of the claim through the Amendment of the original Merger Agreement in January 2011.

Research and Development

A significant portion of our operating expenses relates to the development of Nexavar. We and Bayer share development expenses for Nexavar, except in Japan where Bayer is responsible for development costs of Nexavar. Starting in 2010, a percentage of our costs for the global development of carfilzomib and ONX 0912 will be reimbursed by Ono. In 2010, our development staff was primarily focused on the clinical development of Nexavar,

carfilzomib, ONX 0801, and ONX 0912. We expect to continue to make significant product development investments in 2011. Those investments will be primarily for the clinical development of Nexavar and carfilzomib, as well as for the development of our early stage product candidates. In addition, if we exercise our option for either ONX 0803 or ONX 0805, we are required to assume development costs for the U.S., Canada and Europe subject to S*BIO's option to fund a portion of the development costs in return for enhanced royalties on any future product sales.

For the years ended December 31, 2010, 2009 and 2008, our research and development costs were $185.7 million, $128.5 million and $123.7 million, respectively, and are included in the research and development expense line item in our Consolidated Statements of Operations for the years ended December 31, 2010, 2009 and 2008.

Marketing and Sales

Under our agreements with Bayer, we have co-promotion rights for Nexavar in the United States, where we and Bayer each have complementary sales, marketing and medical affairs capabilities with particular expertise in commercializing oncology products. We and Bayer each provide one-half of the field-based sales and medical affairs staffing in the United States. Individuals hired into this organization have significant experience relevant to the field of pharmaceuticals in general and to the specialty of oncology in particular. In addition, we and Bayer have added sales and medical staff that has experience in the specialty of hepatology, as it applies to the detection and treatment of liver cancer. We and Bayer have also established comprehensive patient support services to maximize patient access to Nexavar. This includes Resources for Expert Assistance and Care Hotline, or REACH, 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 contracts with multiple specialty pharmacies that ship Nexavar directly to patients. NexConnect, another support program also established by Onyx and Bayer, provides patient education materials on Nexavar to help patients take an active role in their treatment. Under the collaboration agreement, outside the United States, Bayer is responsible for all commercial activities relating to Nexavar. Future commercialization of carfilzomib and/or any of our other product candidates, if any receive marketing approval, would require us to make significant investments to build on our current marketing and sales capabilities.

Manufacturing

Under our collaboration agreement with Bayer, Bayer has the responsibility to manufacture and supply Nexavar for commercial requirements and to support 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.

Under our license agreement with BTG, we are responsible for manufacturing ONX 0801. If we exercise our options under our agreement with S*BIO, S*BIO is responsible for supplying clinical and commercial quantities of drug product. If S*BIO fails to supply us, or if other specified events occur, we will have co-exclusive manufacturing rights (with S*BIO) to make and have made ONX 0803 and ONX 0805 for use and sale in the United States, Canada and Europe.

We currently manufacture carfilzomib, ONX 0801, ONX 0912 and ONX 0914 through agreements with third-party contract manufacturers. At this time, we plan to continue with the use of third-party manufacturers on a commercial scale. In the future, we could consider developing in-house manufacturing capabilities.

International Operations

Our product development pipeline expansion has led us to begin building our presence internationally, with particular focus on Europe. In 2010, we established Zug, Switzerland as our European headquarters. International expansion will assist in carrying out various functions relating to product sales, interfacing with regulatory agencies, research and development and management of our clinical and future commercial product supply chain.

Intellectual Property

Patents and other intellectual property rights are crucial to our success. It is our policy to protect our intellectual property rights through available means, including filing patent and prosecuting applications in the United States and other countries. We also develop and protect confidential information and know-how, for example, we include restrictions regarding use and disclosure of our proprietary information in our contracts with third parties. We regularly enter into agreements with our employees, consultants, clinical investigators and scientific advisors to protect our confidential information and know-how. 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. It is also our policy to operate without infringing on, or misappropriating, the proprietary rights of others.

Intellectual Property Related to Nexavar

Patents and patent applications covering Nexavar are owned by Bayer. Those Nexavar patents that arose out of our collaboration agreement with Bayer are licensed to us, including two United States patents covering Nexavar. Both patents will expire January 12, 2020. These two patents are listed in the FDA's Approved Drug Products with Therapeutic Equivalence Evaluations (Orange Book).

Bayer also has patents in several European countries covering Nexavar, which will expire in 2020. Bayer has other patents and patent applications pending worldwide that cover Nexavar alone or in combination with other drugs for treating cancer. Certain of these patents may be subject to possible patent-term extension, the entitlement to and the term of which cannot presently be calculated. In 2009, we became aware that a third-party had filed an opposition proceeding with the Chinese patent office to invalidate the patent that covers Nexavar. Unlike other countries, China has a heightened requirement for patentability, and specifically requires a detailed description of medical uses of a claimed drug, such as Nexavar. Bayer also has a patent in India the covers Nexavar. Cipla Limited, an Indian generic drug manufacturer, applied to the Drug Controller General of India (DCGI) for market approval for Nexavar, which Bayer sought to block based on its patent. Bayer sued the DCGI and Cipla Limited in the Delhi High Court requesting an injunction to bar the DCGI from granting Cipla Limited market authorization. The Court ruled against Bayer, stating that in India, unlike the U.S., there is no link between regulatory approval of a drug and its patent status. Bayer appealed with the ruling to the Indian Supreme Court, which has rejected the appeal. Bayer has also filed a patent infringement suit against Cipla that is currently pending before the Delhi High Court. If Nexavar patents are invalidated, nullified, or otherwise held unenforceable in these other proceedings, we and Bayer could face increased competition, including by generic companies, prior to the normal expiration date of the Nexavar patents. Although Bayer intends to defend the patent and we believe that the Nexavar patents are valid, we cannot predict the final outcomes of these proceedings.

In addition to and separate from patent protection, Nexavar enjoys marketing exclusivity under the Orphan Drug Act of 1983, as amended, which was enacted to provide incentives to pharmaceutical companies who create treatments for rare diseases. It does so by granting seven years of exclusivity after approval of a drug in the rare disease, or "orphan" indication. During the seven year period, the FDA may not grant marketing authorization (*e.g.*, to a generic manufacturer) for the same drug for the orphan indication, but FDA may grant marketing authorization for the same drug in a common disease or other non-protected rare disease. Nexavar has orphan drug exclusivity until December 20, 2012 in advanced kidney cancer and until November 16, 2014 in unresectable liver cancer.

The Hatch Waxman Act authorizes the FDA to approve Abbreviated New Drug Applications (ANDAs) for generic versions of innovative pharmaceuticals that were previously approved via a NDA. In an ANDA, the generic manufacturer is not required to prove safety and efficacy, but must demonstrate "bioequivalence" between its generic version and the NDA-approved drug. An ANDA filer may allege that one or more of the patents covering the approved, innovative pharmaceutical and listed with the FDA (the "Orange Book patents") are invalid, unenforceable and/or not infringed in order to obtain FDA approval to market a generic version of the approved drug. This patent challenge is commonly known as a Paragraph IV certification. The owner of the Orange Book patents may then file a lawsuit against the ANDA filer to enforce its patents. If the lawsuit is filed in a timely fashion, the FDA is prohibited from approving the ANDA for thirty months after the patent owner's receipt of notice of the Paragraph IV certification if the certification is after the five year NCE. If the certification and patent infringement lawsuit is filed before the end of the five year NCE, then the FDA is prohibited from approving the ANDA until

seven and one half years after the NDA approval unless prior to that date the Orange Book patents are found to be invalid, unenforceable and/or not infringed. This period can also be shortened or extended by a trial court judge hearing the patent challenge if a party to the litigation fails to cooperate reasonably in expediting the action. The period may also be shortened if the court enters final judgment that the patents are not infringed, invalid, or unenforceable. The first filer of a Paragraph IV certification may be entitled to a 180-day period of market exclusivity over all other generic manufacturers, which may encourage generic manufacturers to file ANDAs. In recent years, generic manufacturers have used Paragraph IV certifications extensively to challenge patents on a wide array of innovative pharmaceuticals, and we expect this trend to continue. In addition, generic companies have shown an increasing willingness to launch "at risk," *i.e.*, after receiving ANDA approval but before final resolution of their patent challenge. Outside the United States, the legal doctrines and processes by which pharmaceutical patents can be challenged vary widely.

As of December 20, 2009, generic manufacturers were permitted to submit ANDAs seeking FDA authorization to manufacture and market generic versions of Nexavar that contained Paragraph IV certifications as to one or more of the Orange Book-listed Nexavar patents. Thus far, we are not aware of any ANDA filing for sorafenib. It is possible, however, that one or more such ANDAs for Nexavar may have been submitted; however, Bayer and we may not learn about the ANDAs and any challenge to the Nexavar patents until receipt of a notice letter from a generic manufacturer that such an application has been filed. Upon notification of an ANDA filing for Nexavar, Bayer (as the owner of the Nexavar patents) may file a patent infringement lawsuit against each ANDA filer. If there are multiple ANDA filers, Bayer may be required to file multiple patent infringement lawsuits in multiple jurisdictions. Under our collaboration agreement with Bayer, we are responsible for sharing the costs incurred for such ANDA lawsuits. If one or more ANDAs are filed, we may need to spend significant resources to enforce and defend the Nexavar patents. Upon each timely filed ANDA lawsuit, the FDA will impose a stay on the approval of the corresponding ANDA, pending resolution of the lawsuit or the expiration of the stay period. If Bayer fails to timely file a lawsuit against an ANDA filer, that ANDA filer may not be subject to an FDA stay, and upon approval of the ANDA, the ANDA filer may elect to launch a generic version of Nexavar at the risk of a lawsuit and injunction. If Bayer timely commences lawsuits against ANDA filers for patent infringement, as we expect Bayer to do, the FDA cannot approve the ANDAs until seven and one-half years have elapsed from the date of Nexavar's initial approval (*i.e.*, until June 20, 2013). This period of protection, referred to as the statutory litigation stay period, may end early however, in the event of an adverse court action, such as if Bayer were to lose a patent infringement case against an ANDA filer before the statutory litigation stay period expires (*i.e.*, if the court finds both patents invalid, unenforceable or not infringed) or if Bayer fails to reasonably cooperate in expediting the litigation. On the other hand, if Bayer were to prevail in an infringement action against an ANDA filer, the ANDA with respect to such generic company cannot be approved until expiration of the patents held to be infringed.

Issued patents may be challenged by third parties, including competitors and generic companies, through litigation, nullity proceedings and the like. Patents covering Nexavar may be challenged and possibly invalidated in one or more countries, which could expose us and Bayer to generic competition prior to the normal expiration date of the Nexavar patents. In light of the increasingly aggressive challenges by generic companies to innovator intellectual property, we and Bayer are continually assessing and seeking to strengthen our patent estate for Nexavar around the world.

Intellectual Property Related to Carfilzomib and Other Proteolix Assets

We own a patent portfolio covering carfilzomib, including 4 United States patents and 3 United States patent applications, which will begin to expire in 2025 without patent term extension, together with their foreign counterparts. We also own a patent portfolio covering ONX 0912 and ONX 0914, including 2 United States patents and 7 United States patent applications, which will begin to expire in 2027, without patent term extension together with their foreign counterparts. In addition, carfilzomib was granted orphan drug designation by the FDA for the treatment of multiple myeloma in 2008. Orphan drug designation is granted to assist and encourage companies to develop safe and effective therapies for the treatment of rare diseases and disorders. Under the designation, the sponsor may be eligible for grant funding towards clinical trial costs, tax advantages, FDA user-fee benefits, and seven years of market exclusivity in the United States following drug approval by the FDA.

Intellectual Property Related to ONX 0801, 0803 and 0805

In the United States and Europe, ONX 0801 is covered by an issued patent. The United States patent expires in 2023, and the European patent expires in 2022. Both may be entitled to term extensions. There are patent applications pending in the United States and European Union that cover ONX 0803 and ONX 0805 and, if granted, will expire in 2026. Both may be entitled to term extensions.

Other Intellectual Property

In addition to the patents and patent applications discussed above, as of December 31, 2010, we owned or had licensed rights to 71 United States patents and 31 United States patent applications and, generally, the 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 Pfizer or Bayer, or aspects of our discontinued therapeutic virus program.

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, both large pharmaceutical companies and biotechnology companies, are actively seeking to develop oncology products, including those that have disease targets similar to those we are pursuing. Some of these competitive product candidates are in clinical trials and others are approved. Many of these companies with competitive products and/or product candidates have greater capital resources than we do, which provide them with potentially greater flexibility in the development and marketing of their products. Most pharmaceutical companies devote significant operating resources to the research and development of new oncology drugs or additional indications for oncology drugs that are already marketed. We expect these trends to continue.

Nexavar for unresectable liver cancer. Currently, there are no other systemic therapies approved for unresectable liver cancer. However, there are several other therapies in development, including Bristol-Myers Squibb's brivanib and regorafenib, referred to by us as fluoro-sorafenib, which is the subject of litigation between ourselves and Bayer. Other trials in HCC include a Phase 2 trial of bevacizumab plus erlotinib, a Phase 3 trial of ABT 869 versus Nexavar and a Phase 2 trial of TKI 1258 versus Nexavar. Other drugs being studied in HCC include ramucirumab and everolimus. In addition, there are many existing approaches used in the treatment of unresectable liver cancer including alcohol injection, radiofrequency ablation, chemoembolization, cryoablation and radiation therapy.

Nexavar for advanced kidney cancer. Currently, five novel agents besides Nexavar have been approved for the treatment of advanced kidney cancer — Sutent, Torisel, Avastin, Afinitor and Votrient. Pfizer, Inc. announced that its drug axitinib achieved its primary endpoint of improved progression free survival versus Nexavar in patients with renal cell carcinoma. In addition, we anticipate that AVEO Pharmaceuticals, Inc. will announce the results of its randomized Phase 3 trial of AV- 951. Additional agents being studied versus Nexavar include Novartis's Dovitinib/ TKI 1258.

Carfilzomib. Currently, there are three commonly-used agents approved in the U.S. for the treatment of patients with multiple myeloma — Velcade and two immunomodulatory drugs (IMiDs), Revlimid and Thalomid, that could be used in combination with or instead of carfilzomib if it is approved for marketing. In addition, other potentially-competitive therapies are in clinical development for multiple myeloma. Vorinistat, being developed by Merck & Co., and panobinostat, being developed by Novartis AG, are being studied in combination with bortezomib for relapsed myeloma. Pomalidomide, being developed by Celgene Corporation, is in an ongoing randomized Phase 2 trial that could be used for U.S. approval in the relapsed and refractory patient population. We anticipate our first marketing application will be in patients who have relapsed and refractory multiple myeloma and who have already received and progressed on or after bortezomib and at least one of the IMiDs.

Government Regulation

Regulation by government authorities in the United States, individual states and other countries is a significant factor in the development, manufacturing and marketing of any products that we currently market or may develop.

Pharmaceutical companies must comply with comprehensive regulation by the FDA, the Centers for Medicare and Medicaid Services and other regulatory agencies in the United States and comparable authorities in other countries.

FDA Regulation

We must obtain regulatory approvals by FDA and foreign government agencies prior to clinical testing and commercialization of any product and for post-approval clinical studies for additional indications in approved drugs. This is also true internationally. We anticipate that any product candidate will be subject to rigorous preclinical and clinical testing and pre-market approval procedures by the FDA and similar health authorities in foreign countries. Various federal statutes and regulations also govern or influence the preclinical and clinical testing, record-keeping, approval, labeling, manufacture, quality, shipping, distribution, storage, marketing and promotion, export and reimbursement 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 in the desired indication for use;
- the submission of an NDA to the FDA, together with payment of a substantial user fee; and
- FDA approval of the NDA, including inspection and approval of the product manufacturing facility and select sites at which human clinical trials were conducted.

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. The results of 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. 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 investigators seek to evaluate the effects of various dosages and to establish an optimal dosage level and schedule. 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. Investigators also gather additional safety data. Phase 3 clinical trials consist of expanded, large-scale, multi-center 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. Phase 3 trials are designed to more rigorously test the efficacy of a product candidate and are normally randomized and double-blinded. Phase 3 trials are typically monitored by an independent DMC which periodically reviews data as a trial progresses. A DMC may recommend that a trial be stopped before completion for a number of reasons including safety concerns, patient benefit or futility.

Data obtained from this development program are submitted as an NDA to the FDA and possibly to corresponding agencies in other countries for review, and requires agency approval prior to marketing in the relevant country. Extensive regulations define the form, content and methods of gathering, compiling and analyzing the product candidate's safety and efficacy data.

The process of obtaining regulatory approval can be costly, time consuming and subject to unanticipated delays. Regulatory agencies may refuse to approve an application if they believe that applicable regulatory criteria are not satisfied and may also require additional testing for safety and efficacy and/or post-marketing surveillance or other ongoing requirements for post-marketing studies. In some instances, regulatory approval may be granted with the condition that confirmatory Phase 4 clinical trials are carried out, and if these trials do not confirm the results of previous studies, regulatory approval for marketing may be withdrawn. Moreover, each regulatory approval of a product is limited to specific indications. 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, may include Risk Evaluation and Mitigation Strategies and, if overly restrictive, may limit a sponsor's ability to successfully market the product. Regulatory agencies routinely revise or issue new regulations, which can affect and delay regulatory approval of product candidates.

In addition to the FDA's internal review, the FDA may request the Oncology Drugs Advisory Committee, or ODAC, to review and evaluate data concerning the safety and effectiveness of marketed and investigational human drug products for use in the treatment of cancer. The ODAC subsequently makes non-binding recommendations to the FDA about the advisability of approving new medications to treat cancer. The ODAC consists of a core of 13 voting members from among authorities knowledgeable in the fields of general oncology, pediatric oncology, hematologic oncology, immunologic oncology, biostatistics and other related professions.

For Nexavar, we rely on Bayer to manage communications with regulatory agencies, including filing new drug applications, submitting promotional materials and generally directing the regulatory processes. We also rely on Bayer to complete the necessary government reporting obligations such as price calculation reporting and clinical study disclosures to federal and state regulatory agencies. If we have disagreements as to ownership of clinical trial results or regulatory approvals, and the FDA refuses to recognize Onyx as holding, or having access to, the regulatory approvals necessary to commercialize Nexavar, we may experience delays in or be precluded from marketing or further developing Nexavar.

For carfilzomib, we are responsible for managing communications with regulatory agencies, including filing investigational new drug applications, filing new drug applications, submission of promotional materials and generally directing the regulatory processes in all territories except Japan. In Japan, Ono will be responsible for managing communications with regulatory agencies, including filing new drug applications, submitting promotional materials and generally directing the regulatory processes. We have limited experience directing such activities and may not be successful with our planned development strategies, on the planned timelines, or at all. Even if carfilzomib or any other product candidate is designated for "fast track" or "priority review" status or if we seek approval under accelerated approval (Subpart H) regulations, such designation or approval pathway does not necessarily mean a faster development process or regulatory review process or necessarily confer any advantage with respect to approval compared to conventional FDA procedures. Accelerated development and approval procedures will only be available if the indications for which we are developing products remain unmet medical needs and if our clinical trial results support use of surrogate endpoints, respectively. Even if these accelerated development or approval mechanisms are available to us, depending on the results of clinical trials, we may elect to follow the more traditional approval processes for strategic and marketing reasons, since drugs approved under accelerated approval procedures are more likely to be subjected to post-approval requirements for clinical studies to provide confirmatory evidence that the drugs are safe and effective. If we fail to conduct any such required post-approval studies or if the studies fail to verify that any of our product candidates are safe and effective, our FDA approval could be revoked. It can be difficult, time-consuming and expensive to enroll patients in such clinical trials because physicians and patients are less likely to participate in a clinical trial to receive a drug that is already commercially available. Drugs approved under accelerated approval procedures also require regulatory pre-approval of promotional materials which may delay or otherwise hinder commercialization efforts.

Some of our product candidates may be based on new technologies, which may affect our ability or the time we require to obtain necessary regulatory approvals. The regulatory requirements governing these types of products may be more rigorous than for conventional products. As a result, we may experience a longer development or regulatory process in connection with any products (e.g. carfilzomib) that we develop based on these new technologies or new therapeutic approaches.

Pharmaceutical manufacturing processes must conform to current good manufacturing practices, or cGMPs. Manufacturers, including a drug sponsor's third party contract manufacturers, must expend time, money and effort in the areas of production, quality control and quality assurance, including compliance with stringent record-keeping requirements. Manufacturing establishments are subject to periodic inspections by the FDA or other health authorities, in order to assess, among other things, compliance with cGMP. Before approval of the initiation of commercial manufacturing processes, the FDA will usually perform a preapproval inspection of the facility to determine its compliance with cGMP and other rules and regulations. In addition, foreign manufacturing establishments must also comply with cGMPs in order to supply products for use in the United States, and are subject to periodic inspection by the FDA or by regulatory authorities in certain countries under reciprocal agreements with the FDA. Manufacturing processes and facilities for pharmaceutical products are highly regulated. Regulatory authorities may choose not to certify or may impose restrictions, or even shut down existing manufacturing facilities which they determine are non-compliant.

We also must comply with clinical trial and post-approval safety and adverse event reporting requirements. Adverse events related to our products must be reported to the FDA in accordance with regulatory timelines based on their severity and expectedness. Failure to make timely safety reports and to establish and maintain related records could result in withdrawal of marketing authorization.

Violations of regulatory requirements, at any stage, including after approval, may result in various adverse consequences, including the delay by a regulatory agency in approving or refusal to approve a product, withdrawal or recall of an approved product from the market, other voluntary agency-initiated action that could delay further development or marketing, as well as the imposition of criminal penalties against the manufacturer and NDA holder.

Other Regulations

Pharmaceutical companies, including Onyx, 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 Statute 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. Some of the state prohibitions apply to referral of patients for healthcare services reimbursed by any source, not only the Medicare and Medicaid programs.

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 — so-called "off-label use." The FDA does not ordinarily 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 diseases other than advanced kidney cancer and unresectable liver cancer, and neither we nor Bayer may market Nexavar for any unapproved use. 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. The United States False Claims Act prohibits, among other things, anyone from knowingly and willfully presenting, or causing to be presented for payment to third party payers (including Medicare and Medicaid) claims for reimbursed drugs or services that are false or fraudulent, claims for items or services not provided as claimed or claims for medically unnecessary items or services. Violations of fraud and abuse laws may be punishable by criminal and/or civil sanctions, including imprisonment, fines and civil monetary penalties, as well as possible exclusion from federal health care programs (including Medicare and Medicaid). In addition, under this and other applicable laws, such as the Food, Drug and Cosmetic Act, there is an ability for private individuals to bring similar actions. Further, there are an increasing number of state laws that require manufacturers to make reports to states on pricing and marketing information. Many of these laws contain ambiguities as to what is required to comply with the law.

Increased industry trends in U.S. regulatory scrutiny of promotional activity by the FDA, Department of Justice, Office of Inspector General and Offices of State Attorney Generals resulting from healthcare fraud and abuse,

including, but not limited to, violations of the Food, Drug and Cosmetic Act, False Claims Act and Federal Anti-kickback Statute, have led to significant penalties for those pharmaceutical companies alleged of non-compliance. If we or Bayer fail to comply with applicable regulatory requirements, including strict regulation of marketing and sales activities, we could be subject to penalties, including fines, suspensions of regulatory approval, product recall, seizure of products and criminal prosecution.

We have adopted the voluntary Code on Interactions with Healthcare Professionals, or PhRMA Code, promulgated by the Pharmaceutical Research and Manufacturers of America, including its 2009 revisions. The PhRMA Code addresses interactions with respect to marketed products and related pre- and post-launch activities and reinforces the intention that interactions with healthcare professionals are professional exchanges designed to benefit patients and to enhance the practice of medicine.

We are subject to various laws and regulations regarding laboratory practices and the experimental use of animals in connection with our research. In each of these areas, as above, the FDA and other regulatory authorities have broad regulatory and enforcement powers, including the ability to suspend or delay issuance of approvals, seize or recall products, withdraw approvals, enjoin violations and institute criminal prosecution, any one or more of which could have a material adverse effect upon our business, financial condition and results of operations.

We must comply with regulations under the Occupational Safety and Health Act, the Environmental Protection Act, the Toxic Substances Control Act and other federal, state and local regulations. We are subject to federal, state and local laws and regulations governing the use, generation, manufacture, storage, air emission, effluent discharge, handling and disposal of certain hazardous or potentially hazardous materials. We may be required to incur significant costs to comply with environmental and health and safety regulations in the future. Our research and development involves the controlled use of hazardous materials, including, but not limited to, certain hazardous chemicals and radioactive materials.

Our activities are also potentially subject to federal and state consumer protection and unfair competition laws. We are also subject to the U.S. Foreign Corrupt Practices Act, or the FCPA, which prohibits companies and individuals from engaging in specified activities to obtain or retain business or to influence a person working in an official capacity. Under the FCPA, it is illegal to pay, offer to pay, or authorize the payment of anything of value to any foreign government official, governmental staff members, political party or political candidate in an attempt to obtain or retain business or to otherwise influence a person working in an official capacity. In addition, federal and state laws protect the confidentiality of certain health information, in particular, individually identifiable information, and restrict the use and disclosure of that information. At the federal level, the Department of Health and Human Services promulgated health information privacy and security rules under the Health Insurance Portability and Accountability Act of 1996. In addition, many state laws apply to the use and disclosure of health information.

Employees

We believe our success is dependent on our ability to attract and retain qualified employees. As of December 31, 2010, we had 299 full-time employees, of whom 52 hold Ph.D., M.D. or Pharm.D. degrees. Of our employees, 116 are in research and development, 105 are in operations, sales and marketing and 78 are in finance, administration and corporate development. No employee is represented by a labor union and we believe our employee relations to be good.

Available Information

Our website is located at *http://www.onyx-pharm.com*. However, information found on our website is not incorporated by reference into this Annual Report on Form 10-K. 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 Conduct

In 2003, we adopted a code of conduct that applies to our principal officers, directors and employees. We have posted the text of our code of conduct on our website at *http://www.onyx-pharm.com* in connection with "Investors" materials under "Corporate Governance." However, information found on our website is not incorporated by reference into this report. In addition, we intend to promptly disclose (1) the nature of any amendment to our code of conduct 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 conduct 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.

Nexavar® is our only approved product and we may never obtain regulatory approval for carfilzomib or any other future product candidate. If Nexavar fails and we are unable to develop, obtain approval for and commercialize alternative product candidates our business would fail.

Nexavar is the only approved product that generated commercial revenues for the year ended December 31, 2010 and which we rely on to fund our operations. Unless we can successfully commercialize one of our other product candidates, we will continue to rely on Nexavar to generate substantially all of our revenues and fund our operations. All of our other product candidates are still development stage and we may never obtain approval of or earn revenues from any of our product candidates.

Carfilzomib is in mid-to-late stage clinical development and our other product candidates are in early clinical stage. Successful development and commercialization of these compounds and our other product candidates is highly uncertain and depends on a number of factors, many of which are beyond our control. The NDA for accelerated approval of carfilzomib may take longer to file than we expect or may not be filed at all. We have limited experience managing filing and managing regulatory filings and we may not succeed in obtaining accelerated approval, or full approval of carfilzomib on anticipated timelines or at all.

Our stock price is volatile, our operating results are unpredictable, we have a history of losses and we may be unable to sustain profitability.

Our stock price is volatile and is likely to continue to be volatile. A variety of factors may have a significant effect on our stock price, including:

- fluctuations in our results of operations;
- results from or speculation about clinical trials or the regulatory status of Nexavar, carfilzomib or other product candidates;
- decisions by regulatory agencies, or changes in regulatory requirements;
- announcements by us regarding, or speculation about, our business development activities;
- ability to accrue patients into clinical trials or submit regulatory filings;
- developments in our relationship with Bayer;
- changes in healthcare reimbursement policies or other government regulations;
- changes in generally accepted accounting principles and changes in tax laws;
- announcements by us or our competitors of innovations or new products;

- sales by us of our common stock or debt securities; and
- foreign currency fluctuations, which would affect our share of collaboration profits or losses.

In the past, following our or Bayer's announcements regarding lower than anticipated Nexavar sales, and disappointing clinical trials in melanoma and NSCLC, our stock price has declined in some cases significantly.

Our operating results and Nexavar sales will likely fluctuate from quarter to quarter and from year to year, and are difficult to predict. Our operating expenses are highly dependent on expenses incurred by Bayer and in certain regions are independent of Nexavar sales. We have to date incurred losses principally from costs incurred in our research and development programs, from our general and administrative costs and the development of our commercialization infrastructure. We might incur operating losses in the future as we expand our development and commercial activities for Nexavar and our product candidates. We expect to incur significant operating expenses associated with the development activities of carfilzomib and additional products.

As a result of the acquisition of Proteolix, we may be required to pay up to an additional $535.0 million in four earn-out payments upon the receipt of certain regulatory approvals and the satisfaction of other milestones. We recorded a liability for this contingent consideration for the four earn-out payments with a fair value of $253.5 million at December 31, 2010 based upon a discounted cash flow model that uses significant estimates and assumptions. Any changes to these estimates and assumptions could significantly impact the fair values recorded for this liability resulting in significant charges to our Consolidated Statements of Operations. Moreover, we may, at our discretion, make any of the remaining earn-out payments in the form of cash, shares of Onyx common stock or a combination thereof. If we elect to issue shares of our common stock in lieu of making an earn-out payment in cash, this would have a dilutive effect on our common stock and could cause the trading price of our common stock to decline.

It is, therefore, difficult for us to accurately forecast profits or losses. It is possible that in some quarters our operating results could disappoint securities analysts or investors. Many factors, including, but not limited to disappointing operating results and/or the other factors outlined above, could cause the trading price of our common stock to decline, perhaps substantially.

Our clinical trials for Nexavar or carfilzomib could take longer to complete than we project or may not be completed at all, and we may never obtain regulatory approval for carfilzomib or any other product candidate.

The timing of initiation and completion of clinical trials may be subject to significant delays resulting from various causes, including actions by Bayer for Nexavar clinical trials, 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 for clinical and commercial purposes. We may face difficulties developing relationships with carfilzomib development partners, including clinical research organizations, contract manufacturing organizations, key opinion leaders and clinical investigators. We may not complete clinical trials involving Nexavar, carfilzomib or any of our other product candidates as projected or at all.

We may not have the necessary capabilities to successfully manage the execution and completion of clinical trials in a way that leads to approval of Nexavar, carfilzomib or other product candidates for their target indications. In addition, we rely on Bayer, academic institutions, cooperative oncology organizations and clinical research organizations to conduct, supervise or monitor the majority of clinical trials involving Nexavar and carfilzomib. We have less control over the timing and other aspects of these clinical trials than if we conducted them entirely on our own. The timing of review by regulatory authorities is uncertain. We may not obtain priority review from the FDA for our application for accelerated approval of carfilzomib, and we may not receive accelerated approval or any approval for carfilzomib.

Development and commercialization of compounds that appear promising in research or development, including Phase 2 clinical trials, may be delayed or fail to reach later stages of development or the market for a variety of reasons including:

- nonclinical tests may show the product to be toxic or lack efficacy in animal models;
- clinical trial results may show the product to be less effective than desired or to have harmful or problematic side effects;

- regulatory approvals may not be received, or may be delayed due to factors such as slow enrollment in clinical studies, extended length of time to achieve study endpoints, additional time requirements for data analysis or preparation of an IND, discussions with regulatory authorities, requests from regulatory authorities for additional preclinical or clinical data, analyses or changes to study design, including possible changes in acceptable trial endpoints, or unexpected safety, efficacy or manufacturing or quality issues;
- difficulties formulating the product, scaling the manufacturing process or in validating or getting approval for manufacturing;
- manufacturing costs, pricing or reimbursement issues, or other factors may make the product uneconomical;
- proprietary or contractual rights of others and their competing products and technologies may prevent our product from being developed or commercialized or may increase the cost of doing so; and
- contractual rights of our collaborators or others may prevent our product from being developed or commercialized or may increase the cost of doing so.

Failure to successfully commercialize carfilzomib or to complete additional development of Nexavar for these or any other reasons would significantly harm our business and could cause the trading price of our common stock to decline significantly.

If Nexavar is not broadly adopted for the treatment of unresectable liver cancer, our business would be harmed. If our ongoing and planned clinical trials fail to demonstrate that Nexavar is safe and effective for additional indications or we are unable to obtain necessary approvals for other uses, we will be unable to expand the commercial market for Nexavar and our business may fail.

The rate of adoption of Nexavar for unresectable liver cancer and the ultimate market size will be dependent on several factors including educating treating physicians on the appropriate use of Nexavar and the management of patients who are receiving Nexavar. This may be difficult as liver cancer patients typically have underlying liver disease and other comorbidities and can be treated by a variety of medical specialists. In addition, screening, diagnostic and treatment practices can vary significantly by region. Further, liver cancer is common in many regions in the developing world where the healthcare systems are limited and reimbursement for Nexavar is limited or unavailable, which will likely limit or slow adoption. If we are unable to change the treatment paradigms for this disease, we may be unable to successfully achieve the market potential of Nexavar in this indication, which could harm our business.

Outside the United States and European Union, some regulatory authorities have not completed their review of our submissions for the use of Nexavar for unresectable liver cancer. These submissions may not result in marketing approval by these authorities in this indication. In addition, certain countries require pricing to be established before reimbursement for this indication may be obtained and in some Asian Pacific countries in particular these approvals require prolonged negotiations with the governments. In addition, we may not receive or maintain pricing approvals at favorable levels or at all, which could harm our ability to broadly market Nexavar.

Nexavar has not been approved in any indications other than unresectable liver cancer and advanced kidney cancer. We and Bayer are currently conducting a number of clinical trials of Nexavar; however, our clinical trials may fail to demonstrate that Nexavar is safe and effective in other indications, and Nexavar may not gain additional regulatory approval, which would limit the potential market for the product causing our business to fail.

Success in one or even several cancer types does not indicate that Nexavar would be approved or have successful clinical trials in other cancer types. Bayer and Onyx have conducted Phase 3 trials in melanoma and non-small cell lung cancer, or NSCLC,that were not successful. In addition, in the NSCLC Phase 3 trial, higher mortality was observed in the subset of patients with squamous cell carcinoma of the lung treated with Nexavar and carboplatin and paclitaxel than in the subset of patients treated with carboplatin and paclitaxel alone. Based on this observation, further enrollment of squamous cell carcinoma of the lung was suspended from other NSCLC trials sponsored by us. Other cancer types with a histology similar to squamous cell carcinoma of the lung may yield a similar adverse treatment outcome. If so, patients having this histology may be excluded from ongoing and future clinical trials, which could potentially delay clinical trial enrollment and would reduce the number of patients that could potentially receive Nexavar. Regulatory requirements change over time, including acceptable clinical endpoints.

We may be unable to satisfy new requirements or expectations of regulatory authorities and hence, Nexavar may never be approved in additional indications.

We face intense competition and many of our competitors have substantially greater experience and resources than we have.

We are engaged in a rapidly changing and highly competitive field. We are seeking to develop and market oncology products that face significant competition from other products and therapies that currently exist or are being developed.

Nexavar faces significant competition. There are many existing approaches used in the treatment of unresectable liver cancer including alcohol injection, radiofrequency ablation, chemoembolization, cryoablation and radiation therapy. Several other therapies are in development, including Bristol-Myers Squibb's brivanib, a Vascular Endothelial Growth Factor Receptor 2 (VEGFR 2) inhibitor and regorafenib, to which we refer as fluoro-sorafenib, a multiple kinase inhibitor, and which is the subject of litigation between us and Bayer. If Nexavar is unable to compete or be combined successfully with existing approaches or if new therapies are developed for unresectable liver cancer, our business would be harmed.

There are several competing therapies approved for the treatment of advanced kidney cancer, including Sutent, a multiple kinase inhibitor marketed in the United States, the European Union and other countries by Pfizer; Torisel, an mTOR inhibitor marketed in the United States, the European Union and other countries by Wyeth; Avastin, an angiogenesis inhibitor approved for the treatment of advanced kidney cancer in the United States and the European Union and marketed by Genentech, a member of the Roche Group; Afinitor, an mTOR inhibitor marketed in the United States and the European Union by Novartis; and GlaxoSmithKline's Votrient, a multiple kinase inhibitor recently approved by the FDA. Nexavar's U.S. market share in advanced kidney cancer has declined following the introduction of these products into the market. Bayer is conducting clinical trials of fluoro-sorafenib in kidney cancer. We expect competition to increase as additional products are approved to treat advanced kidney cancer. The successful introduction of other new therapies, including generic versions of competing therapies, to treat advanced kidney cancer could significantly reduce the potential market for Nexavar in this indication.

Beyond unresectable liver cancer and advanced kidney cancer, 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 Bayer, Pfizer, Roche, Wyeth, Novartis International AG, Amgen, AstraZeneca PLC, Astellas Pharma Inc., GlaxoSmithKline, Eli Lilly and several others. A number of companies have agents such as small molecules or antibodies targeting VEGF, VEGF receptors, Epidermal Growth Factor, or EGF, EGF receptors, and other enzymes. In addition, many other pharmaceutical companies are developing novel cancer therapies that, if successful, would also provide competition for Nexavar.

A demonstrated survival benefit is often an important element in determining standard of care in oncology. We did not demonstrate a statistically significant overall survival benefit for patients treated with Nexavar in our Phase 3 kidney cancer trial, which we believe was due in part to the crossover of patients from placebo to Nexavar during the conduct of our pivotal clinical trial. Competitors with statistically significant overall survival data could be preferred in the marketplace. The FDA approval of Nexavar permits Nexavar to be marketed as an initial, or first-line, therapy and subsequent lines of therapy for the treatment of advanced kidney cancer, but approvals in some other regions do not. For example, the European Union approval indicates Nexavar only for advanced kidney cancer patients that have failed prior cytokine therapy or whose physicians deem alternate therapies inappropriate. We may be unable to compete effectively against competitive products with broader or different marketing authorizations in one or more countries.

Nexavar may face challenges and competition from generic products. Generic manufacturers may file ANDAs in the U.S. seeking FDA authorization to manufacture and market generic versions of Nexavar, together with Paragraph IV certifications that challenge the scope, validity or enforceability of the Nexavar patents. If Bayer or we fail to timely file a lawsuit against any ANDA filer, that ANDA filer may not be subject to an FDA stay, and upon approval of the ANDA, the ANDA filer may elect to launch a generic version of Nexavar, thereby harming our business. Even if a lawsuit is timely filed, Bayer and we may be unable to successfully enforce and defend the Nexavar patents and we may face generic competition prior to expiration of the Nexavar patents in 2020.

Similarly, outside the United States, generic companies or other competitors may challenge the scope, validity or enforceability of the Nexavar patents, requiring Bayer and us to engage in complex, lengthy and costly litigation or other proceedings. Generic companies may develop, seek approval for, and launch generic versions of Nexavar. For example, a generic version of Nexavar has been launched in Peru and Cipla recently received approval to launch its version of sorafenib in India at a price that is significantly less than that charged for Nexavar in India. Bayer has ongoing litigations with Cipla, including a patent infringement case in India, and has requested the court to issue an injunction against Cipla. Bayer may be unsuccessful in defending or enforcing the Nexavar patents in one or more countries and could face generic competition prior to expiration of the Nexavar patents, which would harm our business.

We have not developed or marketed products for any hematological cancer, including multiple myeloma, and may be at a disadvantage to our competitors. Carfilzomib, if approved for multiple myeloma, would compete directly with products marketed by Millennium Pharmaceuticals, Inc., a wholly owned subsidiary of Takeda Pharmaceutical Company Limited, Celgene Corporation and potentially against agents currently in development for treatment of this disease by Merck & Co. Inc., Bristol-Myers Squibb, Keryx Biopharmaceuticals, Inc., Nereus Pharmaceuticals Cephalon, Inc., and other companies.

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:

- discovering and patenting products;
- undertaking preclinical testing and human clinical trials;
- obtaining FDA and other regulatory approvals;
- manufacturing products; and
- marketing and obtaining reimbursement for products.

Accordingly, our competitors may be more successful than we in any or all of these areas. 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.

We are dependent upon our collaborative relationship with Bayer to further develop, manufacture and commercialize Nexavar. Bayer's interest in other anti-cancer drugs, including fluoro-sorafenib, may reduce its incentive to develop and commercialize Nexavar.

Our success for developing, manufacturing and commercializing Nexavar depends in large part upon our relationship with Bayer. If we are unable to maintain our collaborative relationship with Bayer, we may be unable to continue development, manufacturing and marketing activities at our own expense. If we were able to do so on our own, this would significantly increase our capital and infrastructure requirements, would necessarily impose delays on development programs, may limit the indications we are able to pursue and could prevent us from effectively developing and commercializing Nexavar. Disputes with Bayer may delay or prevent us from further developing, manufacturing or commercializing or increasing the sales of Nexavar, and could lead to additional litigation or arbitration against Bayer, which could be time consuming and expensive.

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

- the outcome of our pending lawsuit against Bayer and the development and commercialization by Bayer of fluoro-sorafenib;
- decisions by Bayer regarding the amount and timing of resource expenditures for the development and commercialization of Nexavar;
- possible disagreements as to development plans, clinical trials, regulatory marketing or sales;

- our inability to co-promote Nexavar in any country outside the United States, which makes us solely dependent on Bayer to promote Nexavar in foreign countries;
- Bayer's right to terminate the collaboration agreement on limited notice in certain circumstances involving our insolvency or material breach of the agreement;
- loss of significant rights if we fail to meet our obligations under the collaboration agreement;
- adverse regulatory or legal action against Bayer resulting from failure to meet healthcare industry compliance requirements in the promotion and sale of Nexavar, including federal and state reporting requirements;
- changes in key management personnel at Bayer, including Bayer's representatives on the collaboration's executive team; and
- disagreements with Bayer regarding interpretation or enforcement of the collaboration agreement.

We have limited ability to direct Bayer in its promotion of Nexavar and we may be unable to obtain any remedy against Bayer. Bayer may not have sufficient expertise to promote or obtain reimbursement for oncology products in foreign countries and may fail to devote appropriate resources to this task. In addition, 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 potential regulatory approvals. 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.

Bayer's development of other products, including fluoro-sorafenib, may affect Bayer's incentives to develop and commercialize Nexavar that are different from our own. Our litigation against Bayer regarding fluoro-sorafenib, may be time consuming and expensive, and may be a distraction to our management. If it is ultimately determined that Onyx has no rights to fluoro-sorafenib and if Bayer obtains approval for this product, it would likely compete with and cannibalize sales of Nexavar, thereby harming our business. Bayer has disclosed a clinical development plan for fluoro-sorafenib that includes tumor types for which Nexavar has been approved (renal cell carcinoma and hepatocellular carcinoma), as well as tumor types for which Nexavar is in development (colorectal cancer and NSCLC). In June 2010, we filed an amended complaint in our pending litigation against Bayer to include an allegation that Bayer has prejudiced the value of Nexavar by reason of its interest in other drugs, including fluoro-sorafenib; Bayer may continue to prejudice the value of Nexavar.

Under the terms of the collaboration agreement, 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. Further, if we or Bayer cease funding development of Nexavar under the collaboration agreement, then that party will be entitled to receive a royalty, 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, further development of Nexavar could be delayed and we may be unable to fund the development costs on our own and may be unable to find a new collaborator.

In addition, Bayer has the right, which it is not currently exercising, to nominate a member 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 not be able to effectively control the election of all members of the board of directors and determine all corporate actions.

Moreover, we are highly dependent on Bayer for timely and accurate information regarding any revenues realized from sales of Nexavar and the costs incurred in developing and selling it, in order to accurately report our results of operations. If we do not receive timely and accurate information or incorrectly estimate activity levels associated with the co-promotion and development of Nexavar at a given point in time, we could be required to record adjustments 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 collaboration agreement with Bayer will terminate when patents expire that were issued in connection with product candidates discovered under that agreement, or at the time when neither we nor Bayer are entitled to profit sharing under that agreement, whichever is later. The worldwide patents and patent applications covering Nexavar are owned by Bayer and certain Nexavar patents are licensed to us through our collaboration agreement. We have no control over the filing, strategy, or prosecution of the Nexavar patent applications nor of enforcement or defense of the Nexavar patents outside the United States.

Our operating results could be adversely affected by product sales occurring outside the United States and fluctuations in the value of the United States dollar against foreign currencies or unintended consequences from our currency contracts.

A majority of Nexavar sales are generated outside of the United States, and a significant percentage of Nexavar commercial and development expenses are incurred outside of the United States. Under our collaboration agreement, when these sales and expenses are translated into U.S. dollars by Bayer in determining amounts payable to us or payable by us, we are exposed to fluctuations in foreign currency exchange rates. In July 2010 we began entering into transactions to manage our exposure to fluctuations in foreign currency exchange rates. Such transactions may expose us to the risk of financial loss in certain circumstances, including instances in which there is a change in the expected differential between the underlying exchange rate in the contracts and actual exchange rate.

The primary foreign currencies in which we have exchange rate fluctuation exposure are the Euro and the Japanese Yen. As we expand our business geographically, we could be exposed to exchange rate fluctuation in other currencies. Exchange rates between these currencies and the U.S. dollar have fluctuated significantly in recent years and may do so in the future. Hedging foreign currencies can be difficult, especially if the currency is not freely traded. We cannot predict the impact of future exchange rate fluctuations on our operating results.

We may be unsuccessful in launching, maintaining adequate supply or obtaining reimbursement for carfilzomib, if it receives regulatory approval.

In order to commercialize carfilzomib, if approved, we must ensure an adequate supply chain, including validation of commercial manufacturing processes, build capabilities for managed care and reimbursement by private and public insurers, and expand our U.S. sales force and must develop and maintain an international sales, marketing and distribution infrastructure. We have limited experience building and maintaining a commercialization infrastructure in the U.S., no experience in building such an infrastructure internationally, and no experience in building or maintaining a supply chain or managed care and reimbursement infrastructure, which is difficult and time consuming, and requires substantial financial and other resources. Factors that may hinder our efforts to expand our U.S. presences and develop an international sales, marketing, supply chain, managed care and distribution infrastructure include:

- inability to recruit, retain and effectively manage adequate numbers of effective sales and marketing, supply chain and managed care personnel;
- inability to establish or maintain relationships with pharmaceutical manufacturers, suppliers, wholesalers, insurers and distributors;
- delay in launch due to the need to validate manufacturing processes;
- inability to sufficiently manufacture adequate quantities of our products;
- the inability of sales personnel to obtain access to or convince adequate numbers of physicians to prescribe our products;
- the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and
- unforeseen delays, costs and expenses associated with creating international capabilities, including an international sales and marketing organization and international supply chain and reimbursement capabilities.

If serious adverse side effects are associated with Nexavar or carfilzomib, our business could be harmed.

The FDA-approved package insert for Nexavar includes several warnings relating to observed adverse reactions. With continued commercial use of Nexavar and additional clinical trials of Nexavar, we and Bayer have updated and expect to continue to update adverse reactions listed in the package insert to reflect current information. If additional adverse reactions 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. In addition, if patients receiving Nexavar were to suffer harm as a result of their use of Nexavar, these patients or their representatives may bring claims against us. These claims, or the mere threat of these claims, could have a material adverse effect on our business and results of operations. We plan to seek regulatory approval of carfilzomib, and we expect that its package insert will include information related to safety and adverse events.

If previously unforeseen and unacceptable side effects are observed in Nexavar or carfilzomib, we may be unable to proceed with further clinical trials, to seek regulatory approval in one or more indications, or to realize full commercial benefits of our products. In our clinical trials, we may treat patients with Nexavar or carfilzomib as a single agent or in combination with other therapies. During the course of treatment, these patients may die or suffer adverse medical effects for reasons unrelated to our products, including adverse effects related to the products that are administered in combination with our products. These adverse effects may impact the interpretation of clinical trial results, which could lead to adverse conclusions regarding the toxicity or efficacy of Nexavar or carfilzomib.

We are dependent on Bayer and third parties to manufacture and distribute our products, and do not have the manufacturing expertise or capabilities to manufacture or distribute any current or future products.

Under our collaboration agreement with Bayer, Bayer has the manufacturing responsibility to supply Nexavar for clinical trials and for commercialization. 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. In addition, we have manufacturing responsibility for carfilzomib and ONX 0912, which we currently manufacture through third-party contract manufacturers, and have not yet established back-up manufacturers for these compounds.

We lack the resources, experience and capabilities to manufacture Nexavar, carfilzomib or any other product candidate on our own and would require substantial funds and time to establish these capabilities. Consequently, we are, and expect to remain, dependent on third parties for manufacturing. These parties may encounter difficulties and delays in production scale-up, production yields, control and quality assurance, validation, regulatory status or shortage of qualified personnel. They may not perform as agreed or may not continue to manufacture our products for the time required to test or market our products. They may fail to deliver the required quantities of our products or product candidates on a timely basis and at commercially reasonable prices. For example, we utilize a sole manufacturer for carfilzomib, and if this manufacturer became unable to deliver our required quantities of carfilzomib on a timely basis, or ceased production, we would experience delays in the clinical trial schedule of our drugs and drug candidates, the regulatory approval process, ability to timely ship product, and may be required to find an alternative manufacturer. In addition, marketed drugs and their contract manufacturing organizations are subject to continual review, including review and approval of their manufacturing facilities and the manufacturing processes, which can result in delays in the regulatory approval process. For example, in October 2010, we announced a delay in our planned NDA filing for accelerated approval of carfilzomib from 2010 to no earlier than the middle of 2011. The delay was based on pre-NDA discussions with the Chemistry, Manufacturing and Controls, or CMC, reviewing division of the FDA regarding CMC information to support the commercial manufacturing of carfilzomib.

In addition, discovery of previously unknown problems with a medicine may result in restrictions on its permissible uses, or on the manufacturer, including withdrawal of the medicine from the market. The FDA and similar foreign regulatory authorities may also implement additional new standards, or change their interpretation and enforcement of existing standards and requirements for the manufacture, packaging or testing of products at any time. Manufacturing processes and facilities for pharmaceutical products are highly regulated. Regulatory authorities may chose not to certify or may impose restrictions, or even shut down existing manufacturing facilities which they

determine are non-compliant. If we or our third party manufacturers are unable to comply, we may be unable to obtain regulatory approval, or if we fail to maintain regulatory approval, this will impair our ability to meet the market demand for our approved drugs, delay ongoing clinical trials of our product candidates or delay our drug 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. In addition, we could be subject to regulatory or civil actions or penalties that could significantly and adversely affect our business.

Our success also 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 accurate or timely information regarding their inventories, the number of patients who are using Nexavar or complaints about Nexavar;
- reduce their efforts or discontinue to sell or support or otherwise not effectively 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/or
- cease operations.

We are subject to extensive government regulation, which can be costly, time consuming and subject us to unanticipated delays. We may incur significant liability if it is determined that we are in violation of federal and state regulations related to the promotion of drugs in the United States or elsewhere.

If we have disagreements with Bayer regarding ownership of clinical trial results or regulatory approvals for Nexavar, and the FDA refuses to recognize Onyx as holding, or having access to, the regulatory approvals necessary to commercialize Nexavar, we may experience delays in or be precluded from marketing Nexavar.

For carfilzomib, we are responsible for managing communications with regulatory agencies, including filing investigational new drug applications, filing new drug applications, submission of promotional materials and generally directing the regulatory processes. We have limited experience directing such activities and may not be successful with our planned development strategies, on the planned timelines, or at all. Even if carfilzomib or any other product candidate is designated for "fast track" or "priority review" status or if we seek approval under accelerated approval (Subpart H) regulations, such designation or approval pathway does not necessarily mean a faster development process or regulatory review process or necessarily confer any advantage with respect to approval compared to conventional FDA procedures. If we fail to conduct any required post-approval studies or if the studies fail to verify that any of our product candidates are safe and effective, our FDA approval could be revoked.

If we or Bayer 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.

To date, the FDA has approved Nexavar only for the treatment of advanced kidney cancer and unresectable liver cancer. Physicians are not prohibited from prescribing Nexavar for the treatment of diseases other than advanced kidney cancer or unresectable liver cancer, however, we and Bayer are prohibited from promoting Nexavar for any non-approved indication, often called "off label" promotion. The FDA and other regulatory agencies actively enforce regulations prohibiting off label promotion and the promotion of products for which marketing authorization has not been obtained. A company that is found to have improperly promoted an off label use 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 medical and scientific communication concerning their products. We engage in the support of medical education activities and engage investigators and

potential investigators interested in 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.

The market may not accept our products and we may be subject to pharmaceutical pricing and third-party reimbursement pressures.

Nexavar, carfilzomib or our product candidates that may be approved may not gain market acceptance among physicians, patients, healthcare payers and/or the medical community or the market may not be as large as forecasted. A significant factor that affects market acceptance of our products 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 payers, such as government and private health insurers and managed care organizations. Third-party payers are increasingly challenging the pricing of medical products and services, especially in global markets, and their reimbursement practices may affect the price levels for Nexavar, if approved, carfilzomib or any other future product. Governments outside of the US may increase their use of risk-sharing programs, which will only pay for a drug after it demonstrates efficacy in a given patient. In addition, governments may increasingly rely on Heath Technology Assessments to determine payment policy for cancer drugs. Health Technology Assessments are used by governments to assess if health services are safe and cost-effective. In addition, the market for our products may be limited by third-party payers who establish lists of approved products and do not provide reimbursement for products not listed. If our products are not on the approved lists in one or more countries, our sales may suffer. Non-government organizations can influence the use of our products and reimbursement decisions for our products in the United States and elsewhere. For example, the National Comprehensive Cancer Network, or NCCN, a not-for-profit alliance of cancer centers, has issued guidelines for the use of Nexavar in the treatment of advanced kidney cancer and unresectable liver cancer. These guidelines may affect treating physicians' use of Nexavar.

Nexavar's success in Europe and other regions, particularly in Asia Pacific, will also depend largely on obtaining and maintaining government reimbursement. For example, in Europe and in many other international markets, most patients will not use prescription drugs that are not reimbursed by their governments. Negotiating prices with governmental authorities can delay commercialization by twelve months or more. Even if reimbursement is available, reimbursement policies may adversely affect sales and profitability of Nexavar. In addition, in Europe and 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. In the Asia-Pacific region, excluding Japan, China leads in Nexavar sales, however, reimbursement typically requires multiple steps. Also, in December 2009, health authorities in China published a new National Reimbursement Drug List, or NRDL, which lists medicines that are expected to be sold at government-controlled prices. There were no targeted oncology drugs, including Nexavar, on the NRDL, however, we believe that the Ministry of Human Resource and Social Security, the group responsible for developing the NDRL, plans to establish a mechanism and framework for reimbursement of high-value innovative products, such as targeted oncology drugs. Reimbursement policies are subject to change due to economic, political or competitive factors. 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 and commercialization of our products, including the following:

- rate of adoption by healthcare practitioners;
- treatment guidelines issued by government and non-government agencies;
- types of cancer for which the product is approved;
- rate of a product's acceptance by the target patient population;
- timing of market entry relative to competitive products;
- availability of alternative therapies;

- price of our product relative to alternative therapies, including generic versions of our products, or generic versions of innovative products that compete with our products;
- patients' reliance on patient assistance programs, under which we provide free drug;
- 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, carfilzomib or any of our future products 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 realize the potential financial or strategic benefits of our acquisition of Proteolix, or any future business acquisitions or strategic investments, which could hurt our ability to grow our business, develop new products or sell our products.

In 2009 we acquired Proteolix, and in the future we may enter into other acquisitions of, or investments in, businesses, in order to complement or expand our current business or enter into a new product area. Achieving the anticipated benefits of the Proteolix acquisition, or any future acquisition, depends upon the successful integration of the acquired business' operations and personnel in a timely and efficient manner. The difficulties of integration include, among others:

- consolidating research and development operations;
- retaining key employees;
- consolidating corporate and administrative infrastructures, including integrating and managing information technology and other support systems and processes;
- preserving relationships with third parties, such as regulatory agencies, clinical investigators, key opinion leaders, clinical research organizations, contract manufacturing organizations, licensors and suppliers;
- appropriately identifying and managing the liabilities of the combined company;
- utilizing potential tax assets of the acquired business; and
- managing risks associated with acquired facilities, including environmental risks and compliance with laws regulating laboratories.

We cannot assure stockholders that we will receive any benefits of the Proteolix acquisition or any other merger or acquisition, or that any of the difficulties described above will not adversely affect us. In addition, integration efforts, such as those for Proteolix, place a significant burden on our management and internal resources, which could result in delays in clinical trial and product development programs and otherwise harm our business, financial condition and operating results.

Negotiations associated with an acquisition or strategic investment could divert management's attention and other company resources. Any of the following risks associated with future acquisitions or investments could impair our ability to grow our business, develop new products, or sell Nexavar or carfilzomib, and ultimately could have a negative impact on our growth or our financial results:

- difficulty in operating in a new or multiple new locations;
- difficulty in realizing the potential financial or strategic benefits of the transaction;
- difficulty in maintaining uniform standards, controls, procedures and policies;
- disruption of or delays in ongoing research, clinical trials and development efforts;
- diversion of capital and other resources;
- assumption of liabilities and unanticipated expenses resulting from litigation arising from potential or actual business acquisitions or investments; and

- difficulties in entering into new markets in which we have limited or no experience and where competitors in such markets have stronger positions.

In addition, the consideration for any future acquisition could be paid in cash, shares of our common stock, the issuance of convertible debt securities or a combination of cash, convertible debt and common stock. If we make an investment in cash or use cash to pay for all or a portion of an acquisition, our cash and investment balances would be reduced which could negatively impact our liquidity, the growth of our business or our ability to develop new products. However, if we pay the consideration with shares of common stock, or convertible debentures, the holdings of our existing stockholders would be diluted. The significant decline in the trading price of our common stock would make the dilution to our stockholders more extreme and could negatively impact our ability to pay the consideration with shares of common stock or convertible debentures. We cannot forecast the number, timing or size of future strategic investments or acquisitions, or the effect that any such investments or acquisitions might have on our operations or financial results.

If we lose our key employees or are unable to attract or retain qualified personnel, our business could suffer. Our planned move of our headquarters may cause additional disruption and turnover of employees.

The loss of the services of key employees may have an adverse impact on our business unless or until we hire a suitably qualified replacement. 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 order to succeed in our research and development efforts, we will need to continue to hire individuals with the appropriate scientific skills.

In 2011, we plan to move our corporate headquarters from Emeryville, California to South San Francisco, California. As a result, we expect to incur additional expenses, including exit costs, and may encounter disruption of operations related to the move, all of which could have an adverse effect on our financial condition and results of operations. In addition, relocation of our corporate headquarters may make it more difficult to retain certain of our employees, and any resulting need to recruit and train new employees could be disruptive to our business.

Provisions in our collaboration agreement with Bayer may impact certain change in control transactions.

Our collaboration agreement with Bayer provides that if we are acquired by another entity by reason of merger, consolidation or sale of all or substantially all of our assets, or if a single entity other than Bayer or its affiliate acquires ownership of a majority of the Company's outstanding voting stock, and Bayer does not consent to the transaction, then for 60 days following the transaction, Bayer may elect to terminate our 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 happens, we, or our successor, would receive a royalty based on any sales of Nexavar and other collaboration products, rather than a share of any profits. Under the royalty formula, an acquisition transaction that occurred prior to the fifth anniversary of the initial regulatory approval of Nexavar, or December 20, 2010, could have substantially reduced the economic value derived from the sales of Nexavar to us or our successor as compared to the economic value of the profit share interest we would have received absent such an acquisition. However, for an acquisition transaction that closes after December 20, 2010, we believe the economic value of the royalty amount, which would depend in part on the expected profitability of Nexavar for the remaining patent life of Nexavar, could be substantially equivalent to the economic value of the profit share interest for Nexavar during the remaining patent life absent such an acquisition transaction. Bayer has notified us that they disagree with this conclusion.

The potential for disagreements and disputes with Bayer regarding interpretation and implementation of these provisions could have the effect of delaying or preventing a change in control, or a sale of all or substantially all of our assets, or could reduce the number of companies interested in acquiring us. However, we believe that a reorganization transaction in which the persons who held majority ownership of Onyx prior to the transaction continue to hold majority ownership of Onyx, directly or through a parent company, after the transaction would be outside the scope of the foregoing provision of the collaboration agreement. Moreover, we believe that a merger

transaction in which Onyx was the surviving entity would also be outside the scope of the foregoing provision of the collaboration agreement.

Healthcare policy changes, including recently enacted legislation, may have a material adverse effect on us.

Healthcare costs have risen significantly over the past decade. On March 23, 2010, the President signed one of the most significant health care reform measures in decades. The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act (collectively, the Healthcare Reform Act), substantially changes the way health care is financed by both governmental and private insurers, and significantly impacts the pharmaceutical industry. The Healthcare Reform Act contains a number of provisions, including those governing enrollment in federal healthcare programs, the increased use of comparative effectiveness research on healthcare products, reimbursement and fraud and abuse changes, which will impact existing government healthcare programs and will result in the development of new programs. A significant portion of the U.S. Nexavar revenue recorded by Bayer is derived from U.S. government healthcare programs, including Medicare. An expansion in the government's role in the U.S. healthcare industry may lower reimbursements for pharmaceutical products and adversely affect our business and results of operations. Furthermore, beginning in 2011, the Healthcare Reform Act will impose a non-deductible excise tax on pharmaceutical manufacturers or importers who sell "branded prescription drugs," which includes innovator drugs and biologics (excluding orphan drugs or generics) to U.S. government programs.

In addition to this recently enacted legislation, there are expected to be other proposals by legislators at both the federal and state levels, regulators and third-party payors to keep healthcare costs down while expanding individual healthcare benefits. Certain of these anticipated changes could impose limitations on the prices we or our collaborators will be able to charge for our products or the amounts of reimbursement available for these products from governmental agencies or third-party payors or may increase the tax requirements for pharmaceutical companies such as ours. While it is too early to predict what affect the recently enacted Health Reform Act or any future legislation or regulation will have on us, such laws could have a material adverse effect on our business, financial position and results of operations.

We may need additional funds, our future access to capital is uncertain, and unstable market and economic conditions may have serious adverse consequences on our business.

We may need additional funds to conduct the costly and time-consuming activities related to the development and commercialization of Nexavar and carfilzomib, including manufacturing, clinical trials and regulatory approval. Also, we may need funds to develop our early stage product candidates, to acquire rights to additional product candidates, or acquire new or complementary businesses. Our future capital requirements will depend upon a number of factors, including:

- revenue from our product sales;
- global product development and commercialization activities;
- the cost involved in enforcing patents against third parties and defending claims by third parties;
- the costs associated with acquisitions or licenses of additional products;
- the cost of acquiring new or complementary businesses;
- competing technological and market developments; and
- future fee and milestone payments to BTG, S*BIO and former stockholders of Proteolix.

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 on terms that are unfavorable to us.

We believe that our existing capital resources and interest thereon will be sufficient to fund our current development plans beyond 2011. However, if we change our development plans, acquire rights to or license additional products, or seek to acquire new or complementary businesses, we may need additional funds sooner than we expect. In

addition, we anticipate that our expenses related to carfilzomib and our share of expenses under our collaboration with Bayer will increase over the next several years. While these costs are unknown at the current time, we may need to raise additional capital and may be unable to do so.

Our general business may be adversely affected by the recent economic downturn and volatile business environment and continued unpredictable and unstable market conditions. If the current equity and credit markets do not sustain improvement or begin to deteriorate again, it may make any necessary future debt or equity financing more difficult, more costly and more dilutive, and may result in adverse changes to product reimbursement and pricing and sales levels, which would harm our operating results. Failure to secure any necessary financing in a timely manner and on favorable terms could have a material adverse effect on our growth strategy, financial performance and stock price and could require us to delay or abandon clinical development plans or plans to acquire additional technology. There is also a possibility that our stock price may decline, due in part to the volatility of the stock market and the general economic downturn, such that we would lose our status as a Well-Known Seasoned Issuer, which allows us to more rapidly and more cost-effectively raise funds in the public markets.

Additionally, other challenges resulting from the current economic environment include fluctuations in foreign currency exchange rates, global pricing pressures, increases in national unemployment impacting patients' ability to access drugs, increases in uninsured or underinsured patients affecting their ability to afford pharmaceutical products and increased U.S. free goods to patients. There is a risk that one or more of our current service providers, manufacturers and other partners may not survive these difficult economic times, which would directly affect our ability to attain our operating goals on schedule and on budget. Further dislocations in the credit market may adversely impact the value and/or liquidity of marketable securities owned by us.

We incurred significant indebtedness through the sale of our 4.0% convertible senior notes due 2016, and we may incur additional indebtedness in the future. The indebtedness created by the sale of the notes and any future indebtedness we incur exposes us to risks that could adversely affect our business, financial condition and results of operations.

We incurred $230.0 million of senior indebtedness in August 2009 when we sold $230.0 million aggregate principal amount of 4.0% convertible senior notes due 2016, or the 2016 Notes. We may also incur additional long-term indebtedness or obtain additional working capital lines of credit to meet future financing needs. Our indebtedness could have significant negative consequences for our business, results of operations and financial condition, including:

- increasing our vulnerability to adverse economic and industry conditions;
- limiting our ability to obtain additional financing;
- requiring the dedication of a substantial portion of our cash flow from operations to service our indebtedness, thereby reducing the amount of our cash flow available for other purposes;
- limiting our flexibility in planning for, or reacting to, changes in our business; and
- placing us at a possible competitive disadvantage with less leveraged competitors and competitors that may have better access to capital resources.

We cannot assure stockholders that we will continue to maintain sufficient cash reserves or that our business will continue to generate cash flow from operations at levels sufficient to permit us to pay principal, premium, if any, and interest on our indebtedness, or that our cash needs will not increase. If we are unable to generate sufficient cash flow or otherwise obtain funds necessary to make required payments, or if we fail to comply with the various requirements of the 2016 Notes, or any indebtedness which we may incur in the future, we would be in default, which would permit the holders of the 2016 Notes and such other indebtedness to accelerate the maturity of the notes and such other indebtedness and could cause defaults under the 2016 Notes and such other indebtedness. Any default under the notes or any indebtedness which we may incur in the future could have a material adverse effect on our business, results of operations and financial condition.

In the event the conditional conversion features of the 2016 Notes are triggered, holders of the 2016 Notes will be entitled to convert the 2016 Notes at any time during specified periods at their option. If one or more holders elect to

convert their 2016 Notes, unless we elect to satisfy our conversion obligation by delivering solely shares of our common stock, we would be required to make cash payments to satisfy all or a portion of our conversion obligation based on the applicable conversion rate, which could adversely affect our liquidity. In addition, even if holders do not elect to convert their 2016 Notes, we could be required under applicable accounting rules to reclassify all or a portion of the outstanding principal of the 2016 Notes as a current rather than long-term liability, which could result in a material reduction of our net working capital.

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

The sale of Nexavar and the use of it and other products and product candidates in clinical trials expose us to product liability claims. In the United States, FDA approval of a drug may not offer protection from liability claims under state law (i.e., federal preemption defense), the tort duties for which may vary state to state. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of Nexavar and/or future products.

We may not be able to maintain insurance product liability 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. Whether or not we are insured, a product liability claim or product recall may result in significant losses. Regardless of merit or eventual outcome, product liability claims may result in:

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

We or Bayer may not be able to protect or enforce our or their intellectual property and we may not be able to operate our business without infringing 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, effectively maintained as trade secrets, or otherwise protected as confidential information or know-how. 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, particularly generic drug manufacturers.

Patents and patent applications covering Nexavar are owned by Bayer. Those Nexavar patents that arose out of our collaboration agreement with Bayer are licensed to us, including two United States patents covering Nexavar and pharmaceutical compositions of Nexavar. Both patents will expire January 12, 2020. These two patents are listed in the FDA's Approved Drug Product List (Orange Book). Based on publicly available information, Bayer also has patents in several European countries covering Nexavar, which will expire in 2020. Bayer has other patents and patent applications pending worldwide that cover Nexavar alone or in combination with other drugs for treating cancer. Certain of these patents may be subject to possible patent-term extension, the entitlement to and the term of which cannot presently be calculated, in part because Bayer does not share with us information related to its Nexavar patent portfolio. We cannot be certain that these issued patents and future patents if they issue will provide adequate protection for Nexavar or will not be challenged by third parties in connection with the filing of an ANDA, or otherwise. Similarly, we cannot be certain that the patents and patent applications acquired in the Proteolix acquisition, or licensed to us by any licensor, will provide adequate protection for carfilzomib or any other product, or will not be challenged by third parties in connection with the filing of an ANDA, or otherwise. The patents related

to carfilzomib and 0912 will begin to expire in 2025 and 2027, respectively. Third parties may claim to have rights in the assets that we acquired with Proteolix, including carfilzomib, or to have intellectual property rights that will be infringed by our commercialization of the assets that we acquired with Proteolix. If third parties were to succeed in such claims, our business and company would be harmed.

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. Third party patents may cover the materials, methods of treatment or dosage related to our product, or compounds to be used in combination with our products; those third parties may make allegations of infringement. We cannot provide assurances that our products or activities, or those of our licensors or licensees, will not infringe patents or other intellectual property owned by third parties. Competitors may have independently developed technologies similar or complementary to ours, including compounds to be used in combination with our products. We may need to license the right to use third-party patents and intellectual property to develop and market our product candidates. We may be unable to 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 in the United States Patent and Trademark Office. These activities are uncertain, making any outcome difficult to predict and costly and may be a substantial distraction for our management team.

Bayer may have rights to publish data and information in which we have rights. In addition, we sometimes engage individuals, entities or consultants, including clinical investigators, to conduct research that may be relevant to our business. The ability of these third parties to publish or otherwise publicly disclose information generated during the course of their research is subject to certain contractual limitations; however, these contracts may be breached and we may not have adequate remedies for any such breach. If we do not apply for patent protection prior to publication or if we cannot otherwise maintain the confidentiality of our confidential information, then our ability to receive patent protection or protect our proprietary information will be harmed.

Limited foreign intellectual property protection and compulsory licensing could limit our revenue opportunities.

The laws of some foreign countries do not protect intellectual property rights to the same extent as the laws of the United States. The requirements for patentability may differ in certain countries, particularly developing countries. In 2009, we became aware that a third-party had filed an opposition proceeding with the Chinese patent office to invalidate the patent that covers Nexavar. Unlike other countries, China has a heightened requirement for patentability, and specifically requires a detailed description of medical uses of a claimed drug, such as Nexavar. Bayer also has a patent in India the covers Nexavar. Cipla Limited, an Indian generic drug manufacturer, applied to the Drug Controller General of India (DCGI) for market approval for Nexavar, which Bayer sought to block based on its patent. Bayer sued the DCGI and Cipla Limited in the Delhi High Court requesting an injunction to bar the DCGI from granting Cipla Limited market authorization. The Court ruled against Bayer, stating that in India, unlike the U.S., there is no link between regulatory approval of a drug and its patent status. Bayer appealed, which it recently lost. Consequently, Bayer has appealed to the Indian Supreme Court, and has filed a patent infringement suit against Cipla that is currently pending before the Delhi high court. Some companies have encountered significant problems in protecting and defending such rights in foreign jurisdictions. Many countries, including certain countries in Europe and developing countries, have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In those countries, Bayer, the owner of the Nexavar patent estate, may have limited remedies if the Nexavar patents are infringed or if Bayer is compelled to grant a license of

Nexavar to a third party, which could materially diminish the value of those patents that cover Nexavar. If compulsory licenses were extended to include Nexavar, this could limit our potential revenue opportunities. Moreover, the legal systems of certain countries, particularly certain developing countries, do not favor aggressive enforcement of patent and other intellectual property protection, which may make it difficult to stop infringement. Many countries limit the enforceability of patents against government agencies or government contractors. These factors could also negatively affect our revenue opportunities in those countries.

If we use hazardous or potentially hazardous materials in a manner that causes injury or violates applicable law, we may be liable for damages.

Our research and development activities involve the controlled use of hazardous or potentially hazardous materials, including chemical, biological and radioactive materials. In addition, our operations produce hazardous waste products. Federal, state and local laws and regulations govern the use, manufacture, storage, handling and disposal of hazardous materials. We may incur significant additional costs to comply with these and other applicable laws in the future. Also, even if we are in compliance with applicable laws, we cannot completely eliminate the risk of contamination or injury resulting from hazardous materials and we may incur liability as a result of any such contamination or injury. In the event of an accident, we could be held liable for damages or penalized with fines, and the liability could exceed our resources. We do not have any insurance for liabilities arising from hazardous materials. Compliance with applicable environmental laws and regulations is expensive, and current or future environmental regulations may impair our research, development and manufacturing efforts, which could harm our business.

A portion of our investment portfolio is invested in auction rate securities, and if auctions continue to fail for amounts we have invested, our investment will not be liquid. If the issuer of an auction rate security that we hold is unable to successfully close future auctions and their credit rating deteriorates, we may be required to adjust the carrying value of our investment through an impairment charge to earnings.

A portion of our investment portfolio is invested in auction rate securities. The underlying assets of these securities are student loans substantially backed by the federal government. Due to adverse developments in the credit markets, beginning in February 2008, these securities have experienced failures in the auction process. When an auction fails for amounts we have invested, the security becomes illiquid. In the event of an auction failure, we are not able to access these funds until a future auction on these securities is successful. We have reclassified these securities from current to non-current marketable securities, and if the issuer is unable to successfully close future auctions and their credit rating deteriorates, we may be required to adjust the carrying value of the marketable securities through an impairment charge to earnings.

Existing stockholders have significant influence over us.

Our executive officers, directors and 5% stockholders own, in the aggregate, approximately 21% 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.

Provisions in the indenture for the 2016 Notes may deter or prevent a business combination.

If a fundamental change occurs prior to the maturity date of the 2016 Notes, holders of the notes will have the right, at their option, to require us to repurchase all or a portion of their notes. In addition, if a fundamental change occurs prior to the maturity date of 2016 Notes, we will in some cases be required to increase the conversion rate for a holder that elects to convert its notes in connection with such fundamental change. In addition, the indenture for the notes prohibits us from engaging in certain mergers or acquisitions unless, among other things, the surviving entity assumes our obligations under the 2016 Notes. These and other provisions could prevent or deter a third party from acquiring us even where the acquisition could be beneficial to our stockholders.

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 a Delaware corporation from engaging in a merger or sale of more than 10% of its assets with any stockholder, including all affiliates and associates of the stockholder, who owns 15% or more of the corporation's outstanding voting stock, for three years following the date that the stockholder acquired 15% or more of the corporation's stock unless:

- the board of directors approved the transaction where the stockholder acquired 15% or more of the corporation's stock;
- after the transaction in which the stockholder acquired 15% or more of the corporation's stock, the stockholder owned at least 85% 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 10% 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. The change in control severance agreements may have the effect of preventing a change in control.

Item 1B. Unresolved Staff Comments

None.

Item 2. Properties

Our corporate headquarters, including our principal offices, are currently located in Emeryville, California. We began occupying these premises in December 2004 and lease a total 60,000 square feet of office space, which will expire in 2013. We also acquired a lease for 67,000 square feet of office and laboratory space in South San Francisco, California, which has a remaining period of four years with the option to extend the lease for two additional one-year terms. In addition, we leased 9,000 square feet of space in Richmond, California that was subleased through the expiration of that lease in September 2010.

In 2011, we plan to move our corporate headquarters from Emeryville, California to South San Francisco, California. In July 2010, we entered into arrangements to lease and sublease a total of approximately 126,493 square

feet located at 249 East Grand Avenue, South San Francisco, California. The lease and the sublease expire in 2021 and 2015, respectively. Upon expiration of the sublease, the lease will be automatically expanded to include the premises subject to the sublease. The lease includes two successive five-year options to extend the term of the lease. The lease also includes a one-time option exercisable until 2014 to lease additional premises that will be constructed after the exercise of the option. If the option is exercised, the term of the lease will be automatically extended by ten years. Please refer to Note 12, "Facility Leases," of the accompanying Consolidated Financial Statements for further information regarding our lease obligations.

We believe that our current facilities are sufficient to meet our present requirements. We anticipate that additional space will be available, when needed, on commercially reasonable terms.

Item 3. Legal Proceedings

In May 2009, we filed a complaint against Bayer Corporation and Bayer A.G. in the United States District Court for the Northern District of California under the caption *Onyx Pharmaceuticals, Inc. v. Bayer Corporation and Bayer AG*, Case No. CV09-2145 MHP (N.D. Cal.). In the complaint, we have asserted our rights under the Collaboration Agreement to fluoro-sorafenib, an anti-cancer compound that Bayer is developing and to which Bayer refers as regorafenib, its International Nonproprietary Name. Fluoro-sorafenib has the same chemical structure as sorafenib (Nexavar), except that a single fluorine atom has been substituted for a hydrogen atom. Bayer is currently conducting trials of fluoro-sorafenib in mixed solid tumors, gastrointestinal stromal tumors (GIST), kidney, colorectal and liver cancer and non-squamous non-small cell lung cancer (NSCLC) and has initiated Phase 3 clinical trials in metastatic colorectal carcinoma and GIST. In the lawsuit, we allege that fluoro-sorafenib was discovered during joint research between us and Bayer and we are seeking monetary damages and a court ruling that we have certain rights to fluoro-sorafenib under the collaboration agreement. Bayer has asserted that we have no such rights. In June 2010, we filed an amended complaint to include an allegation that Bayer has prejudiced the value of Nexavar by reason of its interest in other drugs, including fluoro-sorafenib. The litigation is currently in the discovery phase, with trial scheduled to begin in June 2011.

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

No matters were submitted to a vote of our stockholders during the quarter ended December 31, 2010.

PART II.

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

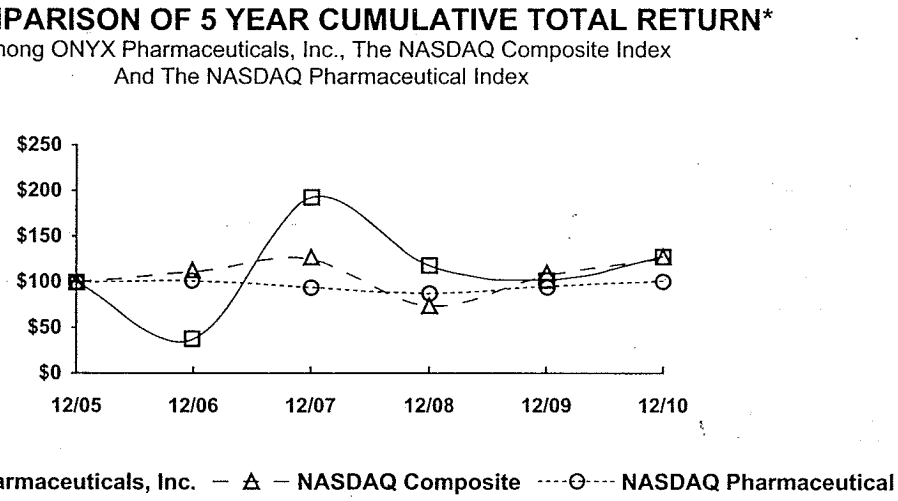
Our common stock is traded on the NASDAQ Global Market (NASDAQ) under the symbol "ONXX." We commenced trading on NASDAQ on May 9, 1996. The following table presents the high and low closing sales prices per share of our common stock reported on NASDAQ.

	Common Stock			
	2010		2009	
	High	Low	High	Low
First Quarter	$32.46	$27.76	$36.50	$26.27
Second Quarter	31.18	21.59	28.77	22.17
Third Quarter	28.11	19.90	36.55	27.23
Fourth Quarter	37.10	25.53	30.04	25.13

On February 17, 2011, the last reported sales price of our common stock on NASDAQ was $37.64 per share.

Stock Performance Graph

The following 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.



* $100 invested on 12/31/05 in stock or index, including reinvestment of dividends.
Fiscal year ending December 31.

Holders

There were approximately 151 holders of record of our common stock as of February 17, 2011.

Dividends

We have not paid cash dividends on our common stock and do not plan to pay any cash dividends in the foreseeable future.

Recent Sales of Unregistered Securities

None.

Issuer Purchases of Equity Securities

None.

Item 6. Selected Financial Data

This section presents our selected historical financial data. You should carefully read the consolidated 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, 2010, 2009 and 2008 and the Balance Sheet data as of December 31, 2010 and 2009 has been derived from our audited consolidated financial statements included elsewhere in this report. The Statement of Operations data for the years ended December 31, 2007 and 2006 and the Balance Sheet data as of December 31, 2008, 2007 and 2006 has been derived from our audited consolidated financial statements that are not included in this report. Historical results are not necessarily indicative of future results.

	Year Ended December 31,				
	2010	2009	2008	2007	2006
	(In thousands, except per share data)				
Statement of Operations Data:					
Revenue from collaboration agreement	$ 265,350	$ 250,390	$ 194,343	$ 90,429	$ 29,274
License revenue	59,165	-	-	-	250
Contract revenue from collaboration	-	1,000	-	-	-
Total operating expenses(1)	(392,837)	(231,166)	(204,743)	(143,852)	(134,188)
Income (loss) from operations	(68,322)	20,224	(10,400)	(53,423)	(104,664)
Investment income, net	2,829	4,028	12,695	19,256	11,983
Interest expense	(19,400)	(6,858)	-	-	-
Other expense	(773)	-	-	-	-
Provision (benefit) for income taxes	(819)	1,233	347	-	-
Net income (loss)	$ (84,847)	$ 16,161	$ 1,948	$ (34,167)	$ (92,681)
Basic net income (loss) per share	$ (1.35)	$ 0.27	$ 0.03	$ (0.67)	$ (2.20)
Diluted net income (loss) per share	$ (1.35)	$ 0.27	$ 0.03	$ (0.67)	$ (2.20)
Shares used in computing basic net income (loss) per share	62,618	59,215	55,915	51,177	42,170
Shares used in computing diluted net income (loss) per share	62,618	59,507	56,765	51,177	42,170

	December 31,				
	2010	2009	2008	2007	2006
			(In thousands)		
Balance Sheet Data:					
Cash, cash equivalents, and current and non-current marketable securities	$ 577,868	$ 587,282	$ 458,046	$ 469,650	$ 271,403
Goodwill(2)	193,675	193,675	-	-	-
Intangible assets — in-process research and development(2)	438,800	438,800	-	-	-
Total assets	1,352,635	1,324,680	509,767	484,083	286,246
Working capital	572,324	530,945	428,755	469,215	256,699
Advance from collaboration partner, non-current	-	-	-	39,234	40,000
Liability for contingent consideration, current and non-current(2)	253,458	200,528	-	-	-
Convertible senior notes due 2016(3)	152,701	143,669	-	-	-
Accumulated deficit	(539,396)	(454,549)	(470,710)	(472,658)	(438,491)
Total stockholders' equity	697,574	750,556	475,200	432,237	222,780

(1) Total operating expenses in 2010 includes a $92.9 million expense associated with the change in the fair value of the non-current contingent consideration liability related to the acquisition of Proteolix in November 2009.

(2) In November 2009, we completed our acquisition of Proteolix for an aggregate purchase price with a fair value of $475.0 million. As a result of the acquisition, we acquired $438.8 million of in-process research and development and $193.7 million of goodwill, and we recorded $157.1 million of deferred tax liabilities primarily related to the difference between the book basis and tax basis of the intangible assets related to the IPR&D projects. We also recorded a liability for contingent consideration for amounts payable to former Proteolix stockholders upon the achievement of specified regulatory approvals within pre-specified timeframes for carfilzomib.

(3) In August 2009, we issued, through an underwritten public offering, $230.0 million aggregate principal amount of 4.0% convertible senior notes due 2016.

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 Annual Report on Form 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. Through our internal research programs and in conjunction with our collaborators, we are applying our expertise to develop and commercialize therapies designed to exploit the genetic and molecular differences between cancer cells and normal cells. We are continuing to maximize current commercialization opportunities for Nexavar® (sorafenib) tablets, along with our collaborator, Bayer HealthCare Pharmaceuticals Inc., or Bayer, and we seek to enter the hematologic cancer market through the development of carfilzomib, a selective

proteasome inhibitor, for the potential treatment of patients with multiple myeloma and solid tumors. Carfilzomib is a mid-to late-stage compound with the potential for accelerated marketing approval in the United States based on our current clinical trial data and assuming favorable regulatory outcomes. In addition, we continue to expand our development pipeline, with multiple clinical and preclinical stage product candidates.

Our first commercially available product, Nexavar® (sorafenib) tablets, being developed with our collaborator Bayer is approved by the United States Food and Drug Administration, or FDA, for the treatment of patients with unresectable liver cancer and advanced kidney cancer. Nexavar is a novel, orally available multiple kinase inhibitor and is one of a new class of anti-cancer treatments that target both cancer cell proliferation and tumor growth through the inhibition of key signaling pathways. In December 2005, Nexavar became the first newly approved drug for patients with advanced kidney cancer in over a decade. In November 2007, Nexavar was approved as the first and is currently the only systemic therapy for the treatment of patients with unresectable liver cancer. Nexavar is now approved in more than 90 countries worldwide for the treatment of advanced kidney cancer and unresectable liver cancer. In 2010, worldwide net sales of Nexavar as recorded by Bayer were $934.0 million. We and Bayer are also conducting clinical trials of Nexavar in several important cancer types in addition to advanced kidney cancer and unresectable liver cancer, including lung, thyroid, breast, ovarian and colon cancers.

In collaboration with Bayer, we initially focused on demonstrating Nexavar's ability to benefit patients suffering from a cancer for which there were no or few established therapies. With the approval of Nexavar for the treatment of advanced kidney cancer and unresectable liver cancer, the two companies have established the Nexavar brand and created a global commercial oncology presence. In order to benefit as many patients as possible, we and Bayer are investigating the administration of Nexavar with previously approved and investigational anti-cancer therapies in more common cancers, with the objective of enhancing the anti-tumor activity of existing therapies through combination with Nexavar.

We and Bayer are developing and marketing Nexavar under our collaboration and co-promotion agreements. We fund 50% of the development costs for Nexavar worldwide, excluding Japan. With Bayer, we co-promote Nexavar in the United States and share equally in any profits or losses. Outside of the United States, excluding Japan, Bayer has exclusive marketing rights and we share profits equally. In Japan, Bayer funds all product development, and we will receive a royalty on any sales. Our collaboration agreement with Bayer will terminate when patents expire that were issued in connection with product candidates discovered under the agreement, or at the time when neither we nor Bayer are entitled to profit sharing under the agreement, whichever is latest. Our co-promotion agreement with Bayer will terminate upon the earlier of the termination of our collaboration agreement with Bayer or the date products subject to the co-promotion agreement are no longer sold by either party in the United States. Either party may also terminate the co-promotion agreement upon failure to cure a material breach of the agreement within a specified cure period.

Our collaboration agreement with Bayer provides that if we are acquired by another entity by reason of merger, consolidation or sale of all or substantially all of our assets, or if a single entity other than Bayer or its affiliate acquires ownership of a majority of the our outstanding voting stock, and Bayer does not consent to the transaction, then for 60 days following the transaction, Bayer may elect to terminate our co-development and co-promotion rights under the collaboration agreement and convert our profit sharing interest under that agreement into a royalty based on any sales of Nexavar and other collaboration products. The applicable royalty rate would be a function of expected profitability of Nexavar for the remaining patent life of Nexavar. As of December 20, 2010, the fifth anniversary of the initial regulatory approval of Nexavar, in the event of an acquisition transaction, we believe the economic value of a royalty amount should be substantially equivalent to the economic value of the profit share interest for Nexavar during the remaining patent life absent such an acquisition transaction. Bayer has informed us they do not agree with this conclusion. The application of the royalty formula to any transaction that closed prior to the fifth anniversary of the initial regulatory approval of Nexavar would have been different, however, and could have substantially reduced the economic value derived from the sales of Nexavar to us or our successor, compared to the economic value we would have received absent such an acquisition transaction. Also, either party may terminate the agreement upon 30 days' notice within 60 days of specified events relating to insolvency of the other party.

In November 2009, we made a significant move towards achieving our goal of becoming a multi-product portfolio company by acquiring Proteolix, Inc., or Proteolix, a privately-held biopharmaceutical company located in South

San Francisco, California. Proteolix focused primarily on the discovery and development of novel therapies that target the proteasome for the treatment of hematological malignancies, solid tumors and autoimmune disorders. This acquisition, which included carfilzomib, has provided us with an opportunity to expand into the hematological malignancies market. The aggregate cash consideration paid to former Proteolix stockholders at closing was $276.0 million with another $40.0 million paid in April 2010 upon the achievement of a pre-specified milestone. In addition, we may be required to pay up to an additional $535.0 million in earn-out payments upon the receipt of certain regulatory approvals and the satisfaction of other milestones.

We have also expanded our development pipeline through the acquisition of rights to development-stage novel anti-cancer agents. In November 2008, we entered into an agreement to license worldwide development and commercialization rights to ONX 0801, previously known as BGC 945, from BTG International Limited, or BTG, a London-based specialty pharmaceuticals company. ONX 0801 is in preclinical development and is believed to work by combining two established approaches to improve outcomes for cancer patients, selectively targeting tumor cells through the alpha-folate receptor, which is overexpressed in a number of tumor types, and inhibiting thymidylate synthase, a key enzyme responsible for cell growth and division. In September 2009, we initiated Phase 1 studies of ONX 0801 in advanced solid tumors, triggering a $7.0 million milestone payment to BTG. In December 2008, we acquired options to license SB1518 (designated by Onyx as ONX 0803) and SB1578 (designated by Onyx as ONX 0805), which are both Janus Kinase, or JAK, inhibitors, from S*BIO Pte Ltd, or S*BIO, a Singapore-based company. The activation of JAK stimulates blood cell production and the JAK pathway is known to play a critical role in the proliferation of certain types of cancer cells and in the anti-inflammatory pathway. ONX 0803 is in multiple Phase 1 studies and ONX 0805 is in preclinical development. We have not yet exercised our options to license rights to ONX 0803 and ONX 0805.

In December 2009, our collaborator, Warner-Lambert Company, now a subsidiary of Pfizer Inc., initiated a Phase 2 clinical trial administering PD 0332991, a small molecule cell cycle inhibitor resulting from our collaboration that targets a cyclin-dependent kinase 4/6, or CDK 4/6. In accordance with our collaboration agreement, we received a $1.0 million milestone payment from Pfizer in 2009.

Our product development pipeline expansion has led us to begin building our presence internationally, with particular focus on Europe. In 2010, we established Zug, Switzerland as our European headquarters. International expansion will assist in carrying out various functions relating to product sales, interfacing with regulatory agencies, research and development and management of our clinical and future commercial product supply chain.

For the year ended December 31, 2010, we reported a net loss of $84.8 million, which is principally attributed to a $92.9 million expense associated with the change in the fair value of the non-current contingent consideration liability for amounts payable to former Proteolix stockholders upon the achievement of specified regulatory approvals within pre-specified timeframes for carfilzomib. With the exception of the years ended December 31, 2009 and 2008, we have incurred annual net losses since our inception. Our ability to achieve sustainable profitability is uncertain and is dependent on a number 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, investments in sales and marketing efforts to support the sales of Nexavar, Bayer and our investments in the research and development of Nexavar, fluctuations in foreign exchange rates, revenues, including milestone payments from development and commercialization partnerships, expenses associated with the change in the fair value of the non-current contingent consideration liability, and expenditures we may incur to acquire or develop and commercialize carfilzomib and other additional products. Our operating results will likely fluctuate from quarter to quarter and from year to year, and are difficult to predict. Since inception, we have relied on public and private financings, combined with milestone payments from our collaborators, to fund our operations and may continue to do so in future periods. As of December 31, 2010, our accumulated deficit was approximately $539.4 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 in approved indications, 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.

2010 Business Highlights

In 2010, we continued to execute on our value building strategy by increasing worldwide sales of Nexavar, producing cash flow for expansion and strengthening our pipeline.

Nexavar margins remained stable year over year, and sales of Nexavar as recorded by Bayer in countries around the world increased from $843.5 million in 2009 to $934.0 million in 2010 despite pricing pressures in European countries and the strengthening of the U.S. Dollar against the Euro.

In September 2010, we entered into an exclusive license agreement with Ono Pharmaceutical Co., Ltd., or Ono. The agreement grants Ono the right to develop and commercialize both carfilzomib and ONX 0912 for all oncology indications in Japan. We retain development and commercialization rights for all other countries. If regulatory approval for carfilzomib and/or ONX 0912 is achieved in Japan, Ono is obligated to pay us double-digit royalties on net sales of the licensed compounds in Japan.

Significant highlights of our product candidates included:

- In December 2010, we presented complete data results from an ongoing pivotal Phase 2b trial, known as the "003-A1" trial, for carfilzomib in multiple myeloma patients. Results demonstrated carfilzomib was well-tolerated in heavily pre-treated relapsed and refractory multiple myeloma patients and could be administered at a full dose over prolonged periods of time, even in a very sick patient population for whom all available treatment options have been exhausted and who have multiple comorbidities.
- We began enrollment in two Phase 3 trials to evaluate the efficacy of carfilzomib in multiple myeloma patients. One trial, referred to as the ASPIRE trial, will evaluate carfilzomib in combination with lenalidomide and low dose dexamethasone, versus lenalidomide and low dose dexamethasone alone. The other trial, referred to as the FOCUS trial, was initiated after seeking Protocol Assistance/Scientific Advice from the Committee for Medicinal Products for Human Use of the European Medical Agency on the development of cafilzomib in the European Union. The FOCUS trial will evaluate carfilzomib monotherapy in refractory multiple myeloma patients in Europe using best supportive care as the comparator.
- We completed enrollment in two trials to evaluate the efficacy of Nexavar in hepatocellular carcinoma (HCC), or liver cancer, patients. One trial, referred to as the SPACE trial, is Phase 2 trial which will evaluate Nexavar or placebo in combination with transarterial chemoembolization (TACE) performed with drug eluting beads and doxorubicin for patients with intermediate stage HCC. The other trial, referred to as the STORM trial, is a Phase 3 clinical trial which will evaluate the efficacy of Nexavar as an adjuvant therapy for patients with liver cancer who have undergone resection or loco-regional treatment with curative intent. In early 2011, we also completed enrollment in another Phase 3 trial, referred to as the SEARCH trial, which will examine Nexavar tablets in combination with Tarceva® (erlotinib) tablets as a potential new treatment option for patients with advanced HCC.
- We also completed enrollment in a Phase 3 trial, referred to as the MISSION trial, which will evaluate the efficacy of Nexavar tablets in patients with relapsed or refractory advanced predominantly non-squamous NSCLC who have failed two or three previous treatments.

In July 2010, we entered into arrangements to lease and sublease additional premises in South San Francisco, California, which will consolidate our facilities and serve as our new company headquarters in 2011.

2010 Financial Highlights

Our operating results for the year included revenue from the Nexavar collaboration agreement of $265.4 million, an increase of $15.0 million, or 6%, from $250.4 million in 2009. The increase in revenue from the Nexavar collaboration agreement was driven primarily by an increase in Nexavar net sales. Our operating results for the year also included $59.2 million in license revenue from our license agreement with Ono.

Total operating expenses for the year were $392.8 million, an increase of $161.7 million, or 70%, from $231.2 million in 2009. The increase in operating expenses was primarily driven by an expense associated with

the increase in the fair value of the non-current contingent consideration liability of $92.9 million for estimated amounts payable to former Proteolix stockholders upon the achievement of specified regulatory approvals within pre-specified timeframes for carfilzomib and a full year of research and development expenses to further develop carfilzomib.

Cash, cash equivalents and current and non-current marketable securities at December 31, 2010 were $577.9 million, a decrease of $9.4 million, or 2%, from $587.3 million at December 31, 2009. Cash, cash equivalents and current and non-current marketable securities remained relatively consistent despite increases in expenses incurred for our continued expansion and the development of carfilzomib.

2011 Outlook

Our initiatives for fiscal year 2011 are intended to promote the development of carfilzomib, the growth of Nexavar and the growth of our development pipeline. These initiatives include continuing momentum in the clinical program for carfilzomib and continuing to invest in the development of carfilzomib, for which we expect to submit an NDA with the FDA as early as mid-year 2011. We also expect data from the Phase 3 FOCUS trial for patients with refractory multiple myeloma in the first half of 2012, which will be used to support initial market authorization in the European Union.

We expect to continue to support clinical activities for the development of Nexavar in liver cancer, breast cancer, colorectal cancer, lung cancer and thyroid cancer. In 2011, we expect data from several clinical trials, including the Phase 2 SPACE trial for patients with intermediate stage HCC, the Phase 2 TIES trial for patients with HER-2 negative breast cancer, and the Phase 3 MISSION trial for patients with non-small cell lung cancer. We also expect to complete enrollment in a Phase 3 trial, referred to as the DECISION trial, which will evaluate the efficacy of Nexavar in the treatment of patients with radioactive iodine-refractory, locally advanced or metastatic differentiated thyroid cancer. In addition, South Korea will begin reimbursements for Nexavar in liver cancer in 2011.

We expect to continue to invest in the development of our earlier-stage product candidates, including ONX 0912 and ONX 0914. In 2011, we expect to also evaluate our options to license rights to exclusively develop and commercialize ONX 0803 and ONX 0805 for all potential indications in the United States, Canada and Europe under our development collaboration, option and license agreement with S*BIO.

We are mindful that conditions in our current macroeconomic environment could affect our ability to achieve our goals, including healthcare policy changes in the United States and continued government pricing pressures internationally. We will continue to monitor these factors and will adjust our business processes to mitigate these risks to our business.

The successes we experienced in 2010 have helped us execute our strategy and as we continue to grow our business and achieve greater operational leverage, we remain focused on profitable revenue growth and prudent expense management that we believe will enable execution of our operating objectives for 2011.

Critical Accounting Policies, Estimates and Judgments

The accompanying discussion and analysis of our financial condition and results of operations are based upon our Consolidated Financial Statements, which have been prepared in accordance with accounting principles generally accepted in the United States. The preparation of these Consolidated Financial Statements requires us to make significant estimates, assumptions and judgments that affect the amounts of assets, liabilities, revenues and expenses and related disclosures. 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 2010 include assumptions used in the determination of the fair value of marketable securities, revenue from collaboration agreement, multiple element arrangements, the effect of business combinations, fair value measurement of tangible and intangible assets and liabilities, goodwill and other intangible assets, fair value of convertible senior notes, research and development expenses, stock-based compensation and the provision for income taxes. Actual results may differ materially from these estimates.

We believe the following critical accounting policies reflect the more significant judgments and estimates used in the preparation of our Consolidated Financial Statements.

Marketable Securities: Marketable securities consist primarily of corporate debt securities, corporate commercial paper, debt securities of United States government agencies, auction rate notes and money market funds and are classified as available-for-sale securities. Concentration of risk is limited by diversifying investments among a variety of industries and issuers. 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). For securities with unobservable quoted market prices, such as the AAA rated auction rate securities collateralized by student loans that are included in our investment portfolio, the fair value is determined using a discounted cash flow analysis. The discounted cash flow model used to value these securities is based on a specific term and liquidity assumptions. An increase or decrease in either of these assumptions could result in a $1.2 million decrease or increase in value. Unrealized losses are charged against "investment income" when a decline in fair value is determined to be other-than-temporary. We review several factors to determine whether a loss is other-than-temporary. These factors include but are not limited to: (i) the extent to which the fair value is less than cost and the cause for the fair value decline, (ii) the financial condition and near-term prospects of the issuer, (iii) the length of time a security is in an unrealized loss position and (iv) our ability to hold the security for a period of time sufficient to allow for any anticipated recovery in fair value. We do not intend to sell our marketable securities and it is not more likely than not that we will be required to sell our marketable securities prior to the recovery of their amortized cost bases. Available-for-sale securities with remaining maturities of greater than one year are classified as long-term. 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. The cost of securities sold or the amount reclassified out of accumulated other comprehensive income into earnings is based on the specific identification method. Realized gains and losses and declines in value judged to be other than temporary are included in the statements of operations. Interest and dividends on securities classified as available-for-sale are included in investment income.

Revenue from Collaboration Agreement: In accordance with Accounting Standards Codification (ASC) Subtopic 808-10, *Collaborative Arrangements,* we record our share of the pre-tax commercial profit generated from the collaboration with Bayer, reimbursement of our shared marketing costs related to Nexavar and royalty revenue in one line item, "Revenue from collaboration agreement." Our portion of shared collaboration research and development expenses is not included in the line item "Revenue from collaboration agreement," but is reflected under operating expenses. According to the terms of the collaboration agreement, the companies share all research and development, marketing and non-U.S. sales expenses. We and Bayer each bear our own U.S. sales force and medical science liaison expenses. These costs related to our U.S. sales force and medical science liaisons are recorded in selling, general and administrative expenses. Bayer recognizes all revenue under the Nexavar collaboration and incurs the majority of expenses relating to the development and marketing of Nexavar. We are highly dependent on Bayer for timely and accurate information regarding any revenues realized from sales of Nexavar and the costs incurred in developing and selling it, in order to accurately report our results of operations. For the periods covered in the financial statements presented, there have been no significant or material changes to prior period estimates of revenues and expenses. However, if we do not receive timely and accurate information or incorrectly estimate activity levels associated with the collaboration of Nexavar at a given point in time, we could be required to record adjustments in future periods and may be required to restate our results for prior periods.

Multiple Element Arrangements: Beginning in 2010, we account for multiple element arrangements, such as license and development agreements in which a customer may purchase several deliverables, in accordance with Accounting Standard Update (ASU) No. 2009-13, *Multiple Deliverable Revenue Arrangements*, For these multiple element arrangements, we allocate revenue to each non-contingent element based upon the relative selling price of each element. When applying the relative selling price method, we determine the selling price for each deliverable using vendor-specific objective evidence (VSOE) of selling price, if it exists, or third-party evidence (TPE) of selling price, if it exists. If neither VSOE nor TPE of selling price exist for a deliverable, we use best estimated selling price (BESP) for that deliverable. Revenue allocated to each element is then recognized based on when the basic four revenue recognition criteria are met for each element.

Determining whether and when some of these criteria have been satisfied often involves assumptions and judgments that can have a significant impact on the timing and amount of revenue we report. Changes in assumptions or

judgments or changes to the elements in an arrangement could cause a material increase or decrease in the amount of revenue that we report in a particular period.

Business Combinations: We accounted for the acquisition of Proteolix in 2009 in accordance with ASC Topic 805, *Business Combinations*. ASC Topic 805 establishes principles and requirements for recognizing and measuring the total consideration transferred to and the assets acquired and liabilities assumed in the acquired target in a business combination. The consideration paid to acquire Proteolix is required to be measured at fair value and included cash consideration and contingent consideration, which are earn-out payments that will be paid upon the receipt of certain regulatory approvals and the satisfaction of other milestones. After the total consideration transferred was calculated by determining the fair value of the contingent consideration plus the cash consideration, we assigned the purchase price of Proteolix to the fair value assets acquired and liabilities assumed. This resulted in recognition of intangible assets related to in-process research and development (IPR&D) projects and goodwill. The determination and allocation of the consideration transferred requires management to make significant estimates and assumptions, especially at the acquisition date with respect to the fair value of the contingent consideration and intangible assets acquired. We believe the fair values assigned to our liability for contingent consideration and acquired intangible assets are based on reasonable estimates and assumptions given the available facts and circumstances as of the acquisition dates. Discounted cash flow models are used in valuing these assets and liabilities, and these models require the use of significant estimates and assumptions including but not limited to:

- estimated cash flows projected from the success of unapproved product candidates;
- the probability of technical and regulatory success for unapproved product candidates considering their stages of development;
- the time and resources needed to complete the development and approval of product candidates;
- the life of the potential commercialized products and associated risks, including the inherent difficulties and uncertainties in developing a product candidate such as obtaining FDA and other regulatory approvals; and
- risk associated with uncertainty, achievement and payment of the milestone events.

In determining the probability of technical and regulatory success, we utilized data regarding similar milestone events from several sources, including industry studies. We based the time needed to complete the development and approval of product candidates on the current stages of development of the product candidates, resources needed to complete the development and approval of product candidates and the inherent difficulties and uncertainties in developing a product candidate, such as obtaining FDA and other regulatory approvals. Inputs related to the time needed to complete the development and approval of product candidates is highly judgmental as they are not readily determinable because the drug development process can be unpredictable. We established a discount rate based on future cash flows that would be required by a market participant for similar instruments, based on the estimated cost of capital and the inherent risk premium associated with repayment. That discount rate, representative of the rate of return required by a market participant, has been determined by us to be 9%, and has been applied to the contingent payment amounts to determine their present values.

Changes to any of these estimates and assumptions could significantly impact the fair values recorded for these assets and liabilities resulting in significant charges to our Consolidated Statement of Operations. In addition, unanticipated events and circumstances may occur which may affect the accuracy or validity of such assumptions, estimates or actual results.

Goodwill and Other Intangible Assets: We account for goodwill and other intangible assets in accordance with ASC Topic 805, and ASC Topic 350, *Intangibles — Goodwill and Other.* ASC Topic 805 requires that the purchase method of accounting be used for all business combinations and specifies the criteria that must be met in order for intangible assets acquired in a business combination to be recognized and reported apart from goodwill. Our intangible assets and goodwill are determined to have indefinite lives and, therefore, are not amortized. Instead they are tested for impairment at least annually or whenever events or circumstances occur that indicate impairment might have occurred in accordance with ASC Topic 350. Judgment regarding the existence of impairment indicators will be based on historical and projected future operating results, changes in the manner of our use of the acquired

assets or our overall business strategy, and market and economic trends. In the future, events could cause us to conclude that impairment indicators exist and that certain other intangibles with determinable lives and other long-lived assets are impaired resulting in an adverse impact on our financial position and results of operations.

Convertible Senior Notes: In August 2009, we issued, through an underwritten public offering, $230.0 million aggregate principal amount of 4.0% convertible senior notes due 2016, or the 2016 Notes. The 2016 Notes are accounted for in accordance with ASC Subtopic 470-20, *Debt with Conversion and Other Options*. Under ASC Subtopic 470-20 issuers of certain convertible debt instruments that have a net settlement feature and may be settled in cash upon conversion, including partial cash settlement, are required to separately account for the liability (debt) and equity (conversion option) components of the instrument. The carrying amount of the liability component of the 2016 Notes, as of the issuance date, was computed by estimating the fair value of a similar liability issued at a 12.5% effective interest rate, which was determined by considering the rate of return investors would require in our capital structure as well as taking into consideration effective interest rates derived by comparable companies. The amount of the equity component was calculated by deducting the fair value of the liability component from the principal amount of the 2016 Notes and results in a corresponding increase to debt discount. Subsequently, the debt discount is amortized as interest expense through the maturity date of the 2016 Notes.

Stock-Based Compensation: We account for stock-based compensation of stock options granted to employees and directors and of employee stock purchase plan shares by estimating the fair value of stock-based awards using the Black-Scholes option-pricing model and amortizing the fair value of the stock-based awards granted over the applicable vesting period. The Black-Scholes option pricing model includes assumptions regarding dividend yields, expected volatility, expected option term and risk-free interest rates. We estimate expected volatility based upon a combination of historical and implied stock prices. The risk-free interest rate is based on the U.S. treasury yield curve in effect at the time of grant. The expected option term calculation incorporates historical employee exercise behavior and post-vesting employee termination rates. We account for stock-based compensation of restricted stock award grants by amortizing the fair value of the restricted stock awards grants, which is the grant date market price, over the applicable vesting period.

Net income (loss) for the years ended December 31, 2010 and 2009 includes employee stock-based compensation expense of $22.1 million, or $0.35 per diluted share, and $21.1 million, or $0.35 per diluted share, respectively. The net loss for the year ended December 31, 2008 includes employee stock-based compensation expense of $18.8 million, or $0.33 per diluted share. As of December 31, 2010, the total unrecorded stock-based compensation expense for unvested stock options, net of expected forfeitures, was $37.5 million, which is expected to be amortized over a weighted-average period of 2.7 years. As of December 31, 2010, the total unrecorded stock-based compensation expense for unvested restricted stock awards, net of expected forfeitures, was $6.8 million, which is expected to be amortized over a weighted-average period of 1.6 years.

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. The option arrangements are subject to periodic remeasurement over their vesting terms. We recorded compensation expense related to option grants to non-employees of $0.7 million, $1.5 million and $1.7 million for the years ended December 31, 2010, 2009 and 2008, respectively.

The assumptions used in computing the fair value of stock-based awards reflect our best estimates, but involve uncertainties relating to market and other conditions, many of which are outside of our control. In addition, 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. As a result, if other assumptions or estimates had been used, the stock-based compensation expense that was recorded for the years ended December 31, 2010, 2009 and 2008 could have been materially different. Furthermore, if different assumptions are used in future periods, stock-based compensation expense could be materially impacted in the future.

Research and Development Expense: Research and development costs are charged to expense when incurred. The major components of research and development costs include clinical manufacturing costs, preclinical study expenses, 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. Preclinical

study expenses include, but are not limited to, costs incurred for the laboratory evaluation of a product candidate's chemistry and its biological activities and costs incurred to assess the potential safety and efficacy of a product candidate and its formulations. Clinical trial expenses include, but are not limited to, investigator fees, site costs, comparator drug costs and clinical research organization costs. 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. 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, cooperative groups and clinical research organizations. 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 incorrectly estimate activity levels associated with various studies at a given point in time, we could be required to record adjustments to research and development expenses in future periods.

In instances where we enter into agreements with third parties for clinical trials and other consulting activities, up-front payment amounts are capitalized and expensed as services are performed or as the underlying goods are delivered. If we do not expect the services to be rendered or goods to be delivered, any remaining capitalized amounts for non-refundable up-front payments are charged to expense immediately. 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.

Non-refundable option payments, including those made under our agreement with S*BIO, that do not have any future alternative use are recorded as research and development expense. Not all research and development costs are incurred by us. A significant portion of our total research and development expenses, approximately 49% in 2010, 63% in 2009 and 55% in 2008, relates to our cost sharing arrangement with Bayer and represents our share of the research and development costs incurred by Bayer. As a result of the cost sharing arrangement between us and Bayer, there was a net reimbursable amount of $78.8 million, $63.7 million and $50.7 million to Bayer for the years ended December 31, 2010, 2009 and 2008, respectively. Such amounts were recorded based on invoices and estimates we receive from Bayer. When such invoices have not been received, we must estimate the amounts owed to Bayer based on discussions with Bayer. For the periods covered in the financial statements presented, there have been no significant or material differences between actual amounts and estimates. However, if we underestimate or overestimate the amounts owed to Bayer, we may need to adjust these amounts in a future period, which could have an effect on earnings in the period of adjustment.

Income Taxes: We use the asset and liability method to account for income taxes in accordance with ASC 740-10, Income Taxes. Under this method, deferred tax assets and liabilities are determined based on differences between the financial reporting and tax bases of assets and liabilities. At each balance sheet date, we evaluate the available evidence about future taxable income and other possible sources of realization of deferred tax assets, and record a valuation allowance that reduces the deferred tax assets to an amount that represents our best estimate of the amount of such deferred tax assets that more likely than not will be realized. Deferred tax assets and liabilities are measured using the enacted tax rates and laws that will be in effect when the differences are expected to reverse. The effect on deferred tax assets and liabilities of a change in tax rates is recognized in income in the period that includes the enactment date.

Realization of deferred tax assets is dependent upon future earnings, if any, the timing and the amount of which are uncertain. Accordingly, we continue to maintain a full valuation allowance against most of our net operating loss carryforwards and other deferred tax assets. On a quarterly basis, we reassess our valuation allowance for deferred income taxes. We will consider reducing the valuation allowance when it becomes more likely than not the benefit of those assets will be realized.

As part of our accounting for the acquisition of Proteolix in 2009, we recorded goodwill and intangible assets. Amortization expenses associated with acquired intangible assets are generally not tax deductible; therefore,

deferred taxes have been recorded for future non- deductible amortization expenses related to intangible assets as a part of the business combination. In the event of an impairment charge associated with goodwill, such charges are generally not tax deductible and would increase the effective tax rate in the quarter any impairment is recorded.

ASC 740 also clarifies the accounting for uncertainty in tax positions recognized in the financial statements. We adopted this guidance on uncertain tax positions on January 1, 2007. Under this guidance, we may recognize the tax benefit from an uncertain tax position only if it is more likely than not that the tax position will be sustained on examination by the taxing authorities based on technical merits of the position. The tax benefits recognized in the financial statements from such a position would be measured based on the largest benefit that has a greater than 50% likelihood of being realized upon ultimate settlement. We are in the process of completing an analysis of our tax credit carryforwards. Any uncertain tax positions identified in the course of this analysis will not impact our consolidated financial statements due to the full valuation allowance.

We are subject to taxation in the U.S. and various state and foreign jurisdictions. Our calculation of our tax liabilities involves uncertainties in the application of complex tax laws and regulations in various taxing jurisdictions that is subject to legal and factual interpretation, judgment and uncertainty. Tax laws and regulations themselves are subject to change as a result of changes in fiscal policy, changes in legislation, the evolution of regulations and court rulings. Therefore, the actual liability for U.S. taxes, or the various state and foreign jurisdictions, may be materially different from our estimates. If, based on new facts that arise within a period, we ultimately determine that the payment of these liabilities will be unnecessary, the liability will be reversed and we will recognize a tax benefit during the period in which it is determined the liability no longer applies. Conversely, we record additional tax charges in a period in which it is determined that a recorded tax liability is less than the ultimate assessment is expected to be. Interest and penalties are included in tax expense.

Results of Operations

Years Ended December 31, 2010, 2009 and 2008

Revenue. Nexavar is our only marketed product. In accordance with our collaboration agreement with Bayer, Bayer recognizes all revenue from the sale of Nexavar. As such, for the years ended December 31, 2010, 2009 and 2008, we reported no product revenue related to Nexavar. Nexavar net sales as recorded by Bayer were $934.0 million, $843.5 million and $677.8 million for the years ended December 31, 2010, 2009 and 2008, respectively, primarily from sales in the United States, the European Union, Asia-Pacific and other territories worldwide and includes the impact in the U.S. of the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act.

Contract Revenue from Collaborations. Contract revenue from collaborations was zero in 2010, $1.0 million in 2009 and zero in 2008. Contract revenue from collaborations in 2009 relates to a milestone fee earned when Pfizer initiated Phase 2 clinical testing to advance a lead candidate from our previous cell cycle kinase discovery collaboration.

Revenue from Collaboration Agreement. Nexavar is currently approved in more than 90 countries worldwide for the treatment of unresectable liver cancer and advanced kidney cancer. We co-promote Nexavar in the United States with Bayer under collaboration and co-promotion agreements. Under the terms of the co-promotion agreement and consistent with the collaboration agreement, we and Bayer 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 outside of Japan and our continued co-promotion of Nexavar in the United States. Outside of the United States, excluding Japan, Bayer incurs all of the sales and marketing expenditures, and we reimburse Bayer for half of those expenditures. In addition, for sales generated outside of the United States, excluding Japan, we reimburse Bayer a fixed percentage of sales for their marketing infrastructure. Research and development expenditures on a worldwide basis, excluding 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 receive a royalty on net sales of Nexavar.

In the United Sates, Bayer provides all product distribution and all marketing support services for Nexavar, including managed care, customer service, order entry and billing. We compensate Bayer for distribution expenses based on a fixed percentage of gross sales of Nexavar in the United States. We reimburse Bayer 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 and is reimbursed at an agreed transfer price per unit for the cost of goods sold in the United States.

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. We and Bayer each bear our own sales force and medical science liaison expenses. These expenses are not included in the calculation of the profits or losses of the collaboration.

Revenue from collaboration agreement consists of our share of the pre-tax commercial profit generated from our collaboration with Bayer, reimbursement of our shared marketing costs related to Nexavar and royalty revenue. Under the collaboration, Bayer recognizes all sales of Nexavar worldwide. We record revenue from collaboration agreement on a quarterly basis. Revenue from collaboration agreement 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 and allocable overhead costs. Reimbursement by Bayer of our shared marketing costs related to Nexavar and royalty revenue are also included in the "Revenue from collaboration agreement" line item.

Our portion of shared collaboration research and development expenses is not included in the "Revenue from collaboration agreement" line item, but is reflected under operating expenses. According to the terms of the collaboration agreement, the companies share all research and development, marketing and non-U.S. sales expenses. U.S. 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 used to derive the revenue from collaboration agreement 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 periods covered in the financial statements presented, there have been no significant or material changes to prior period estimates of revenues and expenses. However, if we do not receive timely and accurate information or incorrectly estimate activity levels associated with the collaboration of Nexavar at a given point in time, we could be required to record adjustments in future periods and may be required to restate our results for prior periods. Revenue from collaboration agreement increases with increased Nexavar net revenue, or decreases with decreased Nexavar net revenue, over and above the associated cost of goods sold, distribution, selling and general administrative expenses. Increases to the associated costs of goods sold, distribution, selling and general and administrative expenses will decrease revenue from collaboration agreement and decreases to these costs will increase revenue from collaboration agreement. Additionally, prolonged or profound economic downturn may result in adverse changes to product reimbursement and pricing and sales levels, which would harm our operating results. We expect Nexavar sales and 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, particularly from certain Asia-Pacific countries.

Revenue from collaboration agreement was $265.4 million, $250.4 million and $194.3 million and for the years ended December 31, 2010, 2009 and 2008, respectively. The increase in revenue from collaboration agreement is primarily a result of increased net product revenue on sales of Nexavar as recorded by Bayer of $934.0 million for the year ended December 31, 2010 as compared to $843.5 million for the year ended December 31, 2009 and $677.8 million for the year ended December 31, 2008. The increase in net product revenue was adversely impacted by pricing pressures in Europe and strengthening of the U.S. Dollar against the Euro and was partially offset by increased costs to sell, distribute and market in countries around the world, including certain Asia-Pacific countries

in advance of anticipated government reimbursement. Revenue from collaboration agreement is calculated as follows:

	Year Ended December 31,		
	2010	2009	2008
	(In thousands)		
Nexavar product revenue, net (as recorded by Bayer)	$934,038	$843,470	$677,806
Nexavar revenue subject to profit sharing (as recorded by Bayer)	$794,977	$753,340	$637,459
Combined cost of goods sold, distribution, selling, general and administrative expenses	329,989	312,205	298,792
Combined collaboration commercial profit	$464,988	$441,135	$338,667
Onyx's share of collaboration commercial profit	$232,494	$220,567	$169,334
Reimbursement of Onyx's shared marketing expenses	23,122	23,514	22,185
Royalty revenue	9,734	6,309	2,824
Revenue from collaboration agreement	$265,350	$250,390	$194,343

License Revenue. License revenue, as compared to prior years, was as follows:

	For the Year Ending December 31,			Change 2010 vs 2009		Change 2009 vs 2008	
	2010	2009	2008	$	%	$	%
	(In thousands, except percentages)						
License revenue	$59,165	$-	$-	$59,165	-	$-	-

In September 2010, we entered into an exclusive license agreement with Ono granting Ono the right to develop and commercialize both carfilzomib and ONX 0912 for all oncology indications in Japan. We retain development and commercialization rights for all other countries of the world.

In accordance with ASU 2009-13, we identified the license as one of the non-contingent deliverables under this agreement with stand-alone value. Because VSOE or TPE of selling price for this element was unavailable, we utilized BESP to apply the relative selling price method to allocate revenue to this element. The objective of BESP is to determine the price at which we would transact a sale if the product were sold on a stand-alone basis. Therefore, BESP for the license is based on discounted future projected cash flows relating to the licensed territory. Revenue allocated to the license of $59.2 million was recognized in September 2010 when all related knowledge and data had been transferred.

Research and Development Expenses. Research and development expenses, as compared to prior years, were as follows:

	For the Year Ending December 31,			Change 2010 vs 2009		Change 2009 vs 2008	
	2010	2009	2008	$	%	$	%
	(In thousands, except percentages)						
Research and development	$185,740	$128,506	$123,749	$57,234	45%	$4,757	4%

The 2010 increase in research and development expenses compared to 2009 is primarily due to increases to further develop carfilzomib, which was acquired in November 2009. Research and development expenses in 2010 also included $5.8 million in expenses related to the amortization of the $20.0 million payment made to S*BIO in May 2010 for the expansion and acceleration of the development collaboration program for ONX 0803 and ONX 0805. The increase in research and development expenses was partially offset by an $8.5 million reimbursement received from Ono and by lower expenses for the ONX 0801 program compared to 2009, when a milestone payment of $7.0 million was made to BTG International Limited. Under the terms of the license agreement with Ono, a percentage of the global development costs we incur for the development of carfilzomib and ONX 0912 is reimbursed by Ono. Refer to Note 3 in the Consolidated Financial Statements for further information. Research and development expenses also included stock-based compensation of $4.3 million in 2010 compared to $3.6 million in

2009. We expect that Bayer and we will continue to invest in the development of Nexavar by conducting clinical trials to test Nexavar's efficacy in more prevalent tumor types in future periods. Additionally, we expect our research and development activities to include developing carfilzomib and our other product candidates.

The 2009 increase in research and development expenses compared to 2008 is primarily due to planned increases in the development program for Nexavar across additional tumor types, such as thyroid, colorectal and adjuvant liver cancer, as well as increased costs to further develop ONX 0801, including a milestone payment of $7.0 million to BTG, partially offset by decreased spending for lung cancer trials. Research and development expenses also included stock-based compensation of $3.6 million in 2009 compared to $2.7 million in 2008.

A significant portion of our total research and development expenses, approximately 49% in 2010, 63% in 2009 and 55% in 2008, relates to our cost sharing arrangement with Bayer and represents our share of the research and development costs incurred by Bayer. As a result of the cost sharing arrangement between us and Bayer, there was a net reimbursable amount of $78.8 million, $63.7 million and $50.7 million to Bayer for the years ended December 31, 2010, 2009 and 2008, respectively. Such amounts were recorded based on invoices and estimates we receive from Bayer. When such invoices have not been received, we must estimate the amounts owed to Bayer based on discussions with Bayer. If we underestimate or overestimate the amounts owed to Bayer, we may need to adjust these amounts in a future period, which could have an effect on earnings in the period of adjustment.

The major components of research and development costs include clinical manufacturing costs, clinical trial expenses, non-refundable upfront payments, 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.

Products/ Product Candidates	Description	Collaborator	Phase of Development — Estimated Completion	Research and Development Expenses For the Year Ended December 31, 2010	2009	2008
					(In millions)	
Nexavar (sorafenib) Tablets(1)	Small molecule inhibitor of tumor cell proliferation and angiogenesis, targeting RAF, VEGFR-2, PDGFR-ß, KIT, FLT-3 and RET.	Bayer	Phase 1 — 2004 Phase 2 — Unknown Phase 3 — Unknown	$103.0(2)	$101.4(2)	$89.8(2)
Carfilzomib	Proteasome inhibitor	Ono	Phase 2 — Unknown Phase 3 — Unknown	65.4	8.5(3)	-
ONX 0801	Compound targeting apha-folate receptor and inhibiting thymidylate synthase	BTG	Phase 1 — Unknown Phase 2 — Planned	5.2	16.7(4)	13.1(4)
ONX 0912	Oral proteasome inhibitor	Ono	Phase 1 — Unknown Phase 1b & Phase 2 — Planned	3.3	-	-
ONX 0914	Immunoproteasome inhibitor	-	Preclinical	1.4	0.1(3)	-
ONX 0803, ONX 0805	Janus Kinase Inhibitors	S*BIO	Phase 1& Phase 2 — Unknown	6.8(6)	0.7	20.8(5)
Other	-	-	-	0.6	1.1	-
			Total research and development expenses	$ 185.7	$ 128.5	$ 123.7

(1) Aggregate research and development costs to date through December 31, 2010 incurred by us since fiscal year 2000 for the Nexavar project is $596.5 million.

(2) Costs reflected include our share of product development costs incurred by Bayer for Nexavar.

(3) Costs reflected are from the date of acquisition, November 16, 2009, through December 31, 2009.

(4) Costs include a $13.0 million upfront payment in fiscal year 2008 and $7.0 million milestone payment in fiscal year 2009 made to BTG under our development and license agreement.

(5) Costs include the nonrefundable upfront payment of $25.0 million made to S*BIO under our development collaboration, option and license agreement.

(6) Costs include $5.8 million in expenses related to the amortization of the $20.0 million payment made to S*BIO in May 2010 for the expansion and acceleration of the development collaboration program for ONX 0803 and ONX 0805. The $20.0 million payment was initially capitalized as prepaid research and development expense and is being amortized as research and development expense each period based on the actual expenses incurred by S*BIO for the development of ONX 0803 and ONX 0805.

Selling, General and Administrative Expenses. Selling, general and administrative expenses, as compared to prior years were as follows:

	For the Year Ending December 31,			Change 2010 vs 2009		Change 2009 vs 2008	
	2010	2009	2008	$	%	$	%
			(In thousands, except percentages)				
Selling, general and administrative	$114,167	$101,132	$80,994	$13,035	13%	$20,138	25%

The 2010 increase in selling, general and administrative expenses compared to 2009 is primarily due to planned increases in spending as a result of the acquisition of Proteolix, an increase in external commercial expenses and an

increase in employee-related costs. Selling, general and administrative expenses also included stock-based compensation of $17.9 million in 2010 compared to $17.5 million in 2009.

The 2009 increase in selling, general and administrative expenses compared to 2008 is primarily due to increased headcount and increased employee-related expenses to support Nexavar's commercial growth, as well as increased headcount and legal and employee-related expenses to support our growth. Selling, general and administrative expenses also included stock-based compensation of $17.5 million in 2009 compared to $17.8 million in 2008.

Selling, general and administrative expenses consist primarily of salaries, employee benefits, consulting, advertising and promotion expenses, legal costs, other third party costs, corporate functional expenses and allocations for overhead and occupancy costs. We expect our selling, general and administrative expenses to increase due to increases in marketing expenses related to Nexavar and increases in personnel due to preparations for the potential launch of carfilzomib.

Contingent Consideration Expense. Contingent consideration expense, as compared to prior years, was as follows:

	For the Year Ending December 31,			Change 2010 vs 2009		Change 2009 vs 2008	
	2010	2009	2008	$	%	$	%
	(In thousands, except percentages)						
Contingent consideration	$92,930	$1,528	$-	$91,402	5982%	$1,528	—

As a result of the acquisition of Proteolix in November 2009 under the terms of an Agreement and Plan of Merger, or the Merger Agreement, which was entered into in October 2009, we made a payment of $40.0 million in April 2010 and may be required to pay up to an additional $535.0 million payable in up to four earn-out payments upon the achievement of certain regulatory approvals for carfilzomib in the U.S. and Europe within pre-specified timeframes. In January 2011, we entered into Amendment No. 1 to the Merger Agreement, or the Amendment. Under the original Merger Agreement, the first of these additional earn-out payments would be in the amount of $170.0 million if achieved by the date originally contemplated, and would be triggered by accelerated marketing approval for carfilzomib in the United States for relapsed/refractory multiple myeloma. This obligation is unchanged in the Amendment. The Amendment modifies this payment if the milestone is not achieved by the date originally contemplated on a sliding scale basis, as follows:

- if accelerated marketing approval in the United States for relapsed/refractory multiple myeloma is achieved after the date originally contemplated, but within six months of the original date, subject to extension under certain circumstances, then the amount payable will be reduced to $130.0 million; and
- if accelerated marketing approval in the United States for relapsed/refractory multiple myeloma is achieved more than six months after the date originally contemplated, but within 12 months of the original date, subject to extension under certain circumstances, then the amount payable will be reduced to $80.0 million.

The remaining earnout payments will continue to become payable in up to three additional installments as follows:

- $65.0 million would be triggered by marketing approval in the European Union for relapsed/refractory multiple myeloma;
- $150.0 million would be triggered by marketing approval in the United States for relapsed multiple myeloma; and
- $150.0 million would be triggered by marketing approval for relapsed multiple myeloma in the European Union.

We recorded a non-current liability for the contingent consideration related to the four remaining earn-out payments with a fair value of $253.5 million at December 31, 2010 based upon a discounted cash flow model that uses significant estimates and assumptions, including the probability of technical and regulatory success (PTRS) of the product candidate, carfilzomib. Contingent consideration expense is due to the change in the fair value of the recognized amount of the non-current liability for contingent consideration. For the year ended December 31, 2010, the increase in the fair value of the non-current liability primarily resulted from a $74.6 million increase due to a change in the PTRS in the second quarter of 2010, partially offset by a benefit recorded as a result of the

Amendment. In June 2010, positive data was presented for the 006 carfilzomib trial, a Phase 1b multicenter dose escalation study of carfilzomib plus lenalidomide and low-dose dexamethasone in relapsed and refractory multiple myeloma patients. In July 2010, positive data was also presented for the 003-A1 carfilzomib trial, an open label, single-arm Phase 2b study of single-agent carfilzomib in relapsed and refractory multiple myeloma patients. The data from the 006 and 003-A1 trials positively impacted the PTRS. The remaining increase in the fair value of the non-current liability for contingent consideration resulted from an $18.4 million increase due to the passage of time. Any further changes to these estimates and assumptions could significantly impact the fair values recorded for this liability resulting in significant charges to our Consolidated Statements of Operations.

Investment Income, net. Investment income consists of interest income and realized gains or losses from the sale of marketable equity investments. We had investment income of $2.8 million for the year ended December 31, 2010, a decrease of $1.2 million, or 30%, from $4.0 million in the same period in 2009. These decreases were primarily due to lower effective interest rates in the market as well as a change in the asset allocation of our investment portfolio. Excluding restricted cash of $31.9 million attributable primarily to the escrow account for the acquisition of Proteolix, which was paid to former Proteolix stockholders in February 2011, our average cash balances in 2010 decreased by $9.4 million from 2009, primarily as a result of a $40.0 million payment to former Proteolix shareholders in April 2010 for the achievement of a development milestone, a $20.0 million payment to S*BIO in May 2010 for the expansion and acceleration of the development collaboration program for ONX 0803 and ONX 0805 and a $9.3 million interest payment on our 2016 Notes, which were partially offset by $59.2 million in license revenue received from Ono.

We had investment income of $4.0 million for the year ended December 31, 2009, a decrease of $8.7 million, or 69%, from $12.7 million in the same period in 2008. These decreases were primarily due to lower effective interest rates in the market as well as a change in the asset allocation of our investment portfolio. Excluding restricted cash of $27.6 million attributable to the escrow account for the acquisition of Proteolix, our average cash balances in 2009 increased by $129.2 million from 2008, primarily as a result of net proceeds raised by our 2016 Notes and equity financings in August 2009 secondary offering from which we received $356.7 million, net of underwriting discounts and commissions, and cash from operations of $35.1 million partially offset by total cash consideration of $276.0 million paid to former Proteolix stockholders as a result of our recent acquisition of Proteolix.

Interest Expense. Interest expense of $19.4 million in 2010 primarily relates to the 2016 Notes issued in August 2009, and includes non-cash imputed interest expense of $9.0 million as a result of the application of ASC Subtopic 470-20.

Other Expense. Other expense of $0.8 million in 2010 primarily relates to net losses on certain foreign currency option contracts that were entered into in July 2010 and October 2010. These foreign currency option contracts are measured at fair value. Any changes to the fair value of foreign currency option contracts that are not designated as hedging instruments flow through earnings and are recorded in the line item "Other expense" in the Consolidated Statements of Operations.

Income Taxes. For the years ended December 31, 2010, 2009 and 2008, we recorded a benefit for income taxes of $0.8 million and a provision for income taxes of $1.2 million and $0.3 million, respectively, related to continuing operations. In 2010, our benefit for income taxes primarily related to our election to carryback net operating losses under the Worker, Homeownership and Business Association Act of 2009. The election enabled the Company to eliminate all federal Alternative Minimum Taxes (AMT) previously recorded in 2009. In 2009 and 2008, our tax expense was related primarily to federal alternative minimum tax and state income taxes.

As of December 31, 2010, our net operating loss carryforwards for federal and state income tax purposes were approximately $271.2 million and $434.6 million. These net operating losses can be utilized to reduce future taxable income, if any. Approximately $28.8 million of the federal and $27.1 million of the state valuation allowance for the deferred tax assets relate to net operating loss carryforwards representing the stock option deduction arising from activity under our stock option plan, the benefit of which will increase additional paid in capital when realized. The federal net operating loss carryforwards expire beginning in 2025 through 2029, and the state net operating loss carryforwards expire beginning in 2014 through 2031 and may be subject to certain limitations. We also had research tax credit and orphan drug credit carryforwards of approximately $68.8 million

for federal income tax purposes that expire beginning in 2011 through 2030 and $12.1 million for California income tax purposes that do not expire.

Utilization of the net operating loss and tax credit carryforwards may be subject to substantial annual limitations due to ownership change limitations provided by the Internal Revenue Code of 1986, as amended, and similar state provisions. As a result of these provisions, utilization of our net operating losses would be limited in the event of any future significant ownership changes. These annual limitations may result in the expiration of net operating losses and tax credit carryforwards before utilization. Please refer to Note 17 of the accompanying consolidated financial statements for further information regarding income taxes.

Acquired In-Process Research and Development

Intangible assets for in-process research and development, or IPR&D, consist of product candidates resulting from our acquisition of Proteolix, including carfilzomib, ONX 0912 and ONX 0914. We determined that the combined estimated fair values of carfilzomib, ONX 0912 and ONX 0914 was $438.8 million as of November 16, 2009, or the Acquisition Date. We used an income approach, which is a measurement of the present value of the net economic benefit or cost expected to be derived from an asset or liability, to measure the fair value of carfilzomib and a cost approach to measure the fair values of ONX 0912 and ONX 0914. Under the income approach, an intangible asset's fair value is equal to the present value of the incremental after-tax cash flows (excess earnings) attributable solely to the intangible asset over its remaining useful life. Under the cost approach, an intangible asset's fair value is equal to the costs incurred to-date to develop the asset to its current stage.

To calculate fair value of carfilzomib under the income approach, we used probability-weighted cash flows discounted at a rate considered appropriate given the inherent risks associated with this type of asset. We estimated the fair value of this asset using a present value discount rate based on the estimated weighted-average cost of capital for companies with profiles substantially similar to that of Proteolix. This is comparable to the estimated internal rate of return for Proteolix's operations and represents the rate that market participants would use to value this asset. Cash flows were generally assumed to extend either through or beyond the patent life of the asset, depending on the circumstances particular to the asset. In addition, we compensated for the phase of development for this program by probability-adjusting our estimation of the expected future cash flows. We believe that the level and timing of cash flows appropriately reflect market participant assumptions. The projected cash flows from this project were based on key assumptions such as estimates of revenues and operating profits related to the project considering its stage of development; the time and resources needed to complete the development and approval of the related product candidate; the life of the potential commercialized product and associated risks, including the inherent difficulties and uncertainties in developing a drug compound such as obtaining marketing approval from the FDA and other regulatory agencies; and risks related to the viability of and potential alternative treatments in any future target markets. The resultant probability-weighted cash flows were then discounted using a rate we believe is appropriate and representative of a market participant assumption.

For the other two intangible assets acquired, ONX 0912 and 0914, we used the costs incurred to-date by Proteolix to develop these assets to their current stage as their fair value as result of the lack of financial projections for these assets in their current development stages.

These IPR&D programs represent Proteolix's incomplete research and development projects which had not yet reached technological feasibility at acquisition. A summary of these programs and estimated fair values at the Acquisition Date is as follows:

Product Candidates	Description	Estimated Acquisition Date Fair Value (In thousands)
Carfilzomib	First in a new class of selective and irreversible proteasome inhibitors associated with prolonged target suppression, improved antitumor activity and low neurotoxicity for treatment against multiple myeloma and solid tumors.	$435,000
ONX 0912	Oral proteasome inhibitor for treatment against hematologic and solid tumors.	3,500
ONX 0914	Immunoproteasome inhibitor for treatment against rheumatoid arthritis andinflammatory bowel disease.	300
		$438,800

Liquidity and Capital Resources

With the exception of the profitability we achieved for the years ended December 31, 2009 and 2008, we have incurred significant annual net losses since our inception and have relied primarily on public and private financing, combined with milestone payments we received from our collaborators, to fund our operations.

At December 31, 2010, we had cash, cash equivalents and current and non-current marketable securities of $577.9 million, excluding $31.9 million of restricted cash, compared to $587.3 million at December 31, 2009. The decrease of $9.4 million was primarily attributable to a $40.0 million payment to former Proteolix shareholders in April 2010 for the achievement of a development milestone, a $20.0 million payment to S*BIO in May 2010 for the expansion and acceleration of the development collaboration program for ONX 0803 and ONX 0805 and a $9.3 million interest payment on our 2016 Notes, which were partially offset by $59.2 million in license revenue received from Ono.

At December 31, 2009, we had cash, cash equivalents and current and non-current marketable securities of $587.3 million, excluding $27.6 million of restricted cash, compared to $458.0 million at December 31, 2008. The increase of $129.3 million was primarily attributable to $356.7 million in net proceeds raised by our 2016 Notes and equity financings in August 2009 and cash from operations of $35.1 million, partially offset by our cash payment, net of cash acquired, of $252.5 million to former Proteolix stockholders in conjunction with our acquisition of Proteolix in November 2009 and a $7.0 milestone payment to BTG.

In 2010, our cash provided by operations was $28.4 million, compared to cash provided by operations of $35.1 million in 2009 and cash used in operations of $8.4 million in 2008. In 2010, the cash provided by operations primarily related to license revenue received from Ono of $59.2 million. In 2009, the cash provided by operations primarily related to net income earned for the year. Expenditures for capital equipment amounted to approximately $7.0 million in 2010, $1.3 million in 2009, and $1.6 million in 2008. Capital expenditures in 2010 were primarily for construction of facilities in South San Francisco, California that we leased and subleased beginning in July 2010 and for equipment to accommodate our employee growth. Please refer to Note 12, "Facility Leases," of the accompanying consolidated financial statements for further information. Capital expenditures in 2009 and 2008 were primarily for equipment to accommodate our employee growth.

At December 31, 2010, our investment portfolio includes $32.7 million of AAA rated securities with an auction reset feature ("auction rate securities") that are collateralized by student loans. In January 2011, $2.7 million in securities were redeemed at par and, accordingly, we classified these securities as current marketable securities in the accompanying Consolidated Balance Sheet at December 31, 2010. The remaining balance of $29.9 million of par value auction rate securities is currently outstanding in our investment portfolio. Since February 2008, these types of securities have experienced failures in the auction process. However, a limited number of these securities have been redeemed at par by the issuing agencies. As a result of the auction failures, interest rates on these

securities reset at penalty rates linked to LIBOR or Treasury bill rates. The penalty rates are generally higher than interest rates set at auction. Based on the overall failure rate of these auctions, the frequency of the failures, the underlying maturities of the securities, a portion of which are greater than 30 years, and our belief that the market for these student loan collateralized instruments may take in excess of twelve months to fully recover, we have classified the auction rate securities with a par value of $29.9 million as non-current marketable securities on the accompanying Consolidated Balance Sheet. We have determined the fair value to be $28.6 million for these securities, based on a discounted cash flow model, and have reduced the carrying value of these marketable securities by $1.4 million through accumulated other comprehensive income (loss) instead of earnings because we have deemed the impairment of these securities to be temporary. Further adverse developments in the credit market could result in an impairment charge through earnings in the future. The discounted cash flow model used to value these securities is based on a specific term and liquidity assumptions. An increase in either of these assumptions could result in a $1.2 million decrease in value. Alternatively, a decrease in either of the assumptions could result in a $1.2 million increase in value.

Currently, we believe these investments are not other-than-temporarily impaired as all of them are substantially backed by the federal government, but it is not clear in what period of time they will be settled. We do not intend to sell the securities and we believe it is not more likely than not that we will be required to sell the securities prior to the recovery of their amortized cost bases. We believe that, even after reclassifying these securities to non-current assets and the possible requirement to hold all such securities for an indefinite period of time, our remaining cash and cash and current marketable securities will be sufficient to meet our anticipated cash needs beyond 2011.

We anticipate our operating costs to increase in 2011 as we continue to incur expenses towards the development of carfilzomib, ONX 0912 and ONX 0914. In addition, the terms of the agreement and plan of merger for Proteolix provide that we may be required to pay up to an additional $535.0 million in earn-out payments upon the receipt of certain regulatory approvals and the satisfaction of other milestones.

In July 2010, we entered into arrangements to lease and sublease a total of approximately 126,493 square feet located at 249 East Grand Avenue, South San Francisco, California and anticipate that we will incur cash outlays associated with the lease and sublease of these premises. The total monthly base rent in the first year for both the lease and sublease was approximately $294,000 beginning in September 2010. The total obligations under both of these operating leases will be approximately $45.9 million.

We believe that our existing capital resources and interest thereon will be sufficient to fund our current and planned operations beyond 2011. However, if we change our development plans, including acquiring or developing additional product candidates or complementary businesses, we may need additional funds sooner than we expect. We anticipate that we will incur cash outlays to conduct and support additional clinical trials both currently underway and planned for the development of carfilzomib and our other development candidates. We also expect to incur cash outlays as we prepare for a potential commercial launch of carfilzomib, should it receive marketing approval. If we exercise one or both of our options, ONX 0803 and ONX 0805, we will be required to pay significant license fees and will incur development expenses. Further, we may be obligated to make up to an additional $535.0 million of contingent earn-out payments upon the achievement of regulatory approvals for carfilzomib in the U.S. and Europe, payable in either cash or common stock, at our discretion. The terms of the development and license agreement dated November 6, 2008 with BTG provide that we may be required to make payments to BTG of up to $65.0 million upon the attainment of certain global development and regulatory milestones, plus additional milestone payments upon the achievement of certain marketing approvals and commercial milestones.

While most of our anticipated development costs are unknown at the current time, we may need to raise additional capital to continue the funding of our product development programs and our development plans in future periods beyond 2011. 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:

Contractual Obligations	Payments Due by Period				
	Total	Less than 1 Year	1-3 Years	3-5 Years	After 5 Years
			(In thousands)		
Convertible senior notes due 2016	$285,200	$ 9,200	$18,400	$18,400	$239,200
Operating leases, net of sublease income	61,494	7,345	15,608	10,036	28,505
Liability for contingent consideration	535,000	(1)	(1)	(1)	(1)
Milestone payments — BTG	65,000	(2)	(2)	(2)	(2)
Milestone payments — S*BIO	(3)	(3)	(3)	(3)	(3)
	$946,694	$16,545	$34,008	$28,436	$267,705

(1) The terms of the Agreement and Plan of Merger dated October 12, 2009 and Amendment No. 1 to the Agreement and Plan of Merger dated January 27, 2011 for the acquisition of Proteolix provide that we may be required to pay up to an additional $535.0 million in earn-out payments upon the receipt of certain regulatory approvals and the satisfaction of other milestones. This amount is not included in the above table as the timing and payment amounts are unknown. See Note 5 "Acquisition of Proteolix" of the accompanying consolidated financial statements for further information regarding the amounts payable to former stockholders of Proteolix.

(2) The terms of the development and license agreement dated November 6, 2008 with BTG provide that we may be required to make payments to BTG of up to $65.0 million upon the attainment of certain global development and regulatory milestones, plus additional milestone payments upon the achievement of certain marketing approvals and commercial milestones. We are also required to pay royalties to BTG on any future product sales.

(3) Under the terms of the agreement dated December 24, 2008 with S*BIO, we were granted options which, if we exercise them, would give us rights to exclusively develop and commercialize ONX 0803 and/or ONX 0805 for all potential indications in the United States, Canada and Europe. Under this agreement, S*BIO will retain responsibility for all development costs prior to the option exercise. After the exercise of our option to license rights to either compound, we are required to assume development costs for the U.S., Canada and Europe subject to S*BIO's option to fund a portion of the development costs in return for enhanced royalties on any future product sales. Upon the exercise of our option of either compound, S*BIO we are required to pay a one-time option fee, milestone payments upon achievement of certain development and sales levels and royalties on any future product sales.

Our corporate headquarters, including our principal offices, are located in Emeryville, California. We began occupying these premises in December 2004 and lease a total 60,000 square feet of office space, which expire in 2013. We also acquired a lease for 67,000 square feet of office and laboratory space in South San Francisco, California, which has a remaining period of four years with the option to extend the lease for two additional one-year terms. In addition, we leased 9,000 square feet of space in Richmond, California that was subleased through the expiration of that lease in September 2010. In July 2010, we entered into arrangements to lease and sublease a total of approximately 126,493 square feet located in South San Francisco, California. The lease and the sublease expire in 2021 and 2015, respectively. Upon expiration of the sublease, the lease will be automatically expanded to include the premises subject to the sublease. The lease includes two successive five-year options to extend the term of the lease. The lease also includes a one-time option exercisable until 2014 to lease additional premises that will be constructed after the exercise of the option. If the option is exercised, the term of the lease will be automatically extended by ten years. Please refer to Note 12 in the accompanying Consolidated Financial Statements for further information regarding our lease obligations.

Off-Balance Sheet Arrangements

As of December 31, 2010, we did not have any material off-balance sheet arrangements (as defined in Item 303(a)(4)(ii) of Regulation S-K).

Recent Accounting Pronouncements

In October 2009, the FASB issued ASU No. 2009-13, *Multiple Deliverable Revenue Arrangements*, impacting the determination of when the individual deliverables included in a multiple element arrangement may be treated as separate units of accounting. Additionally, ASU 2009-13 modifies the manner in which the transaction consideration is allocated across the separately identified deliverables by no longer permitting the residual method of allocating arrangement consideration. This ASU will be effective for periods beginning on or after June 15, 2010. Early application is permitted. Entities can apply this guidance prospectively to milestones achieved after adoption. However, retrospective application to all prior periods is also permitted. In the second quarter of 2010, we adopted ASU 2009-13 effective January 1, 2010 on a prospective basis for applicable transactions originating or materially modified after December 31, 2009. The new accounting standards for revenue recognition, if applied in the same manner to the year ended December 31, 2009, would not have had a material impact on our financial statements. In terms of the timing and pattern of revenue recognition, the new accounting guidance for revenue recognition had a significant effect on revenue in periods after the initial adoption, as we entered into a multiple element arrangement with Ono in September 2010. In accordance with ASU 2009-13, we identified the license in the exclusive license agreement entered into with Ono as a separate non-contingent deliverable and recognized $59.2 million of revenue allocated to the license in September 2010 when all related knowledge and data had been transferred. Refer to Note 3 in the Consolidated Financial Statements for further information.

In April 2010, the FASB issued ASU No. 2010-17, *Milestone Method of Revenue Recognition*, to (1) limit the scope of this ASU to research or development arrangements and (2) require that guidance in this ASU be met for an entity to apply the milestone method (record the milestone payment in its entirety in the period received). However, the FASB clarified that, even if the requirements in this ASU are met, entities would not be precluded from making an accounting policy election to apply another appropriate accounting policy that results in the deferral of some portion of the arrangement consideration. The ASU will be effective for periods beginning on or after June 15, 2010. Early application is permitted. Entities can apply this guidance prospectively to milestones achieved after adoption. However, retrospective application to all prior periods is also permitted. We adopted ASU 2010-17 effective January 1, 2010 and determined that the adoption did not have any impact on our financial statements.

Item 7A. Quantitative and Qualitative Disclosures about Market Risk

Interest Rate and Market 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. Under our 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 or decrease by 100 basis points, or 1%, as of December 31, 2010, the fair value of our portfolio would decline or increase, respectively, by approximately $1.7 million. Additionally, a hypothetical increase or decrease of 1% in market interest rates for the year ended December 31, 2010 would have resulted in a $4.6 million change in our investment income for the year ended December 31, 2010.

The table below presents the amounts and related weighted interest rates of our cash equivalents and marketable securities at December 31, 2010:

	2010			2009		
	Maturity	Fair Value (In millions)	Average Interest Rate	Maturity	Fair Value (In millions)	Average Interest Rate
Cash equivalents, fixed rate	0 — 3 months	$113.9	0.48%	0 — 3 months	$103.2	0.11%
Marketable securities, fixed rate	0 — 20 months	$351.5	0.57%	0 — 12 months	$479.6	0.53%

Our 2016 Notes, with a total par value of $230.0 million at December 31, 2010, bear interest at a fixed rate of 4.0%. Due to the fixed interest rate, we have no exposure to interest rate fluctuations. However, underlying market risk exists related to an increase in our stock price which may make the conversion of our 2016 Notes to common stock beneficial to the holders of such notes. Conversion of the 2016 Notes currently would have a dilutive effect on any future earnings and book value per common share.

Liquidity Risk

At December 31, 2010, our investment portfolio includes $32.7 million of AAA rated auction rate securities collateralized by student loans. In January 2011, $2.7 million in securities were redeemed at par and, accordingly, we classified these securities as current marketable securities in the accompanying Consolidated Balance Sheet at December 31, 2010. The remaining balance of $29.9 million of par value auction rate securities is currently outstanding in our investment portfolio. Since February 2008, securities of this type have experienced failures in the auction process. However, a limited number of these securities have been redeemed at par by the issuing agencies. As a result of the auction failures, interest rates on these securities reset at penalty rates linked to LIBOR or Treasury bill rates. The penalty rates are generally higher than interest rates set at auction. Based on the overall failure rate of these auctions, the frequency of the failures, the underlying maturities of the securities, a portion of which are greater than 30 years, and our belief that the market for these student loan collateralized instruments may take in excess of twelve months to fully recover, we have classified the auction rate securities with a par value of $29.9 million as non-current marketable securities on the accompanying Consolidated Balance Sheet. We have determined the fair value to be $28.6 million for these securities, based on a discounted cash flow model, and have reduced the carrying value of these marketable securities by $1.4 million through accumulated other comprehensive income (loss) instead of earnings because we have deemed the impairment of these securities to be temporary. We do not intend to sell the securities and we believe it is not more likely than not that we will be required to sell the securities prior to the recovery of their amortized cost bases.

Foreign Currency Exchange Rate Risk

A majority of Nexavar sales are generated outside of the United States, and a significant percentage of Nexavar commercial and development expenses are incurred outside of the United States. Our revenue from collaboration agreement is dependent on these foreign currency denominated activities. In addition, we incur research and development and general and administrative expenses outside of the United States. As a result of these underlying non-U.S. Dollar denominated activities, fluctuations in foreign currency exchange rates affect our operating results. Changes in exchange rates between these foreign currencies and the U.S. Dollar will affect the recorded levels of our assets and liabilities as foreign assets and liabilities are translated into U.S. Dollars for presentation in our financial statements, as well as our operating margins. The primary foreign currencies that we are exposed to are the Euro and the Japanese Yen. A hypothetical increase or decrease of 1% in exchange rates between the Euro versus the U.S. Dollar during the year ended December 31, 2010 would have resulted in a $1.0 million change in our net income based on our expected exposures. A hypothetical increase or decrease of 1% in exchange rates between the Japanese Yen versus the U.S. Dollar during the year ended December 31, 2010 would have resulted in a $0.1 million change in our net income based on our expected exposures. For these currencies, we utilize average exchange rates for the reporting period.

As we expand, we could be exposed to exchange rate fluctuation in other currencies. Exchange rates between foreign currencies and U.S. Dollars have fluctuated significantly in recent years and may do so in the future. Commencing in the third quarter of 2010, we established a foreign currency hedging program. The objective of the program is to mitigate the foreign exchange risk arising from transactions or cash flows that have a direct or underlying exposure in

non-U.S. Dollar denominated currencies in order to reduce volatility in our cash flow and earnings. Currently, we hedge a certain portion of our foreign currency exchange rate exposure with options, typically no more than one year into the future. These derivative instruments, which include derivative instruments that have been designated as hedges under ASC 815, *Derivatives and Hedging,* are intended to reduce the effects of variations in our cash flow resulting from fluctuations in foreign currency exchange rates. However, in certain circumstances, these derivative instruments may expose us to the risk of financial loss. Our cash flows are denominated in U.S. Dollars.

Item 8. Consolidated Financial Statements and Supplementary Data

Our Consolidated Financial Statements and notes thereto appear on pages 70 to 108 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 at the reasonable assurance level as of December 31, 2010 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, 2010. In making this assessment, management used the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission, or COSO in Internal Control-Integrated Framework. The Company's management has concluded that, as of December 31, 2010, the Company's internal control over financial reporting is effective at the reasonable assurance level based on these criteria.

The effectiveness of our internal control over financial reporting as of December 31, 2010 has been audited by Ernst & Young LLP, our independent registered public accounting firm, as stated in their attestation report, which is included 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, 2010 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. A control system, no matter how well conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met. 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. Accordingly, our disclosure controls and procedures are designed to provide reasonable, not absolute, assurance that the objectives of our disclosure control system are met and, as set forth above, our principal executive officer and principal financial officer have concluded, based on their evaluation as of the end of the period covered by this report, that our disclosure controls and procedures were effective at the reasonable assurance level to ensure that the objectives of our disclosure control system were met.

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

The Board of Directors and Stockholders of Onyx Pharmaceuticals, Inc.

We have audited Onyx Pharmaceuticals, Inc.'s internal control over financial reporting as of December 31, 2010, 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 included in the accompanying Management's Report on Internal Control over Financial Reporting. Our responsibility is to express an opinion on 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, assessing the risk that a material weakness exists, testing and evaluating the design and operating effectiveness of internal control based on the assessed risk, 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, Onyx Pharmaceuticals, Inc. maintained, in all material respects, effective internal control over financial reporting as of December 31, 2010, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the consolidated balance sheets of Onyx Pharmaceuticals, Inc. as of December 31, 2010 and 2009, and the related consolidated statements of operations, stockholders' equity, and cash flows for each of the three years in the period ended December 31, 2010 of Onyx Pharmaceuticals, Inc. and our report dated February 23, 2011 expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP

Palo Alto, California
February 23, 2011

Item 9B. Other information

Not applicable.

PART III.

Certain information required by Part III is omitted from this Annual Report on Form 10-K because the registrant will file with the U.S. Securities and Exchange Commission a definitive proxy statement pursuant to Regulation 14A in connection with the solicitation of proxies for the Company's Annual Meeting of Stockholders to be held on May 26, 2011, or the 2011 Definitive Proxy Statement, not later than 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K, and certain information included therein is incorporated herein by reference.

Item 10. Directors, Executive Officers and Corporate Governance

The information required under this Item 10 is incorporated by reference from our 2011 Definitive Proxy Statement.

Item 11. Executive Compensation

The information required under this Item 11 is incorporated by reference from our 2011 Definitive Proxy Statement.

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

The information required under this Item 12 with respect to security ownership of certain beneficial owners and management is incorporated by reference from our 2011 Definitive Proxy Statement.

Securities Authorized for Issuance Under Equity Compensation Plans as of December 31, 2010

Plan Category(1)	Number of securities to be issued upon exercise of outstanding options and rights Column a	Weighted-average exercise price of outstanding options 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	6,274,471	$29.48	6,566,178(2)

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

(2) This amount includes 355,336 shares that remain available for purchase under our Employee Stock Purchase Plan. Under the 2005 Equity Incentive Plan, as amended, shares available for issuance should be reduced by one and six tenths (1.6) shares for each share of common stock available for issuance pursuant to a stock purchase award, stock bonus award, stock unit award or other stock award granted. With this adjustment, the total amount available for future issuance would be reduced to 4,237,112 shares.

Item 13. Certain Relationships and Related Transactions, and Director Independence

The information required under this Item 13 is incorporated by reference from our 2011 Definitive Proxy Statement.

Item 14. Principal Accounting Fees and Services

The information required under this Item 14 is incorporated by reference from our 2011 Definitive Proxy Statement.

Consistent with Section 10A (i)(2) of the Securities Exchange Act of 1934, as amended, 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 independent registered public accounting firm. Non-audit services are defined as services other than those provided in connection with an audit or a review of our consolidated financial statements. Ernst & Young LLP did not provide any non-audit services related to the year ended December 31, 2010.

PART IV.

Item 15. Exhibits, Consolidated Financial Statement Schedules

(a) Documents filed as part of this report.

(1) Index to Consolidated Financial Statements

The Consolidated Financial Statements required by this item are submitted in a separate section beginning on page 73 of this Report.

Report of Independent Registered Public Accounting Firm

Consolidated Balance Sheets

Consolidated Statements of Operations

Consolidated Statement of Stockholders' Equity

Consolidated Statements of Cash Flows

Notes to Consolidated Financial Statements

(2) Consolidated Financial Statement Schedules

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

Exhibits

Exhibit Number	Description of Document
2.1(1)*	Agreement and Plan of Merger dated as of October 10, 2009 among the Company, Proteolix, Inc., Profiterole Acquisition Corp., and Shareholder Representative Services LLC.
3.1(2)	Restated Certificate of Incorporation of the Company.
3.2(3)	Amended and Restated Bylaws of the Company.
3.3(4)	Certificate of Amendment to Amended and Restated Certificate of Incorporation.
3.4(5)	Certificate of Amendment to Amended and Restated Certificate of Incorporation.
4.1	Reference is made to Exhibits 3.1, 3.2, 3.3 and 3.4.
4.2(2)	Specimen Stock Certificate.
4.3(6)	Indenture dated as of August 12, 2009 between the Company and Wells Fargo Bank, National Association.
4.4(6)	First Supplemental Indenture dated as of August 12, 2009 between the Company and Wells Fargo Bank, National Association.
4.5(6)	Form of 4.00% Convertible Senior Note due 2016.
10.1(i)(7)*	Collaboration Agreement between Bayer Corporation (formerly Miles, Inc.) and the Company dated April 22, 1994.
10.1(ii)(7)*	Amendment to Collaboration Agreement between Bayer Corporation and the Company dated April 24, 1996.
10.1(iii)(7)*	Amendment to Collaboration Agreement between Bayer Corporation and the Company dated February 1, 1999.
10.2(i)*	Amended and Restated Research, Development and Marketing Collaboration Agreement effective as of May 2, 1995 between the Company and Warner-Lambert Company.
10.2(ii)(8)*	Research, Development and Marketing Collaboration Agreement dated July 31, 1997 between the Company and Warner-Lambert Company.

Exhibit Number	Description of Document
10.2(iii)(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(iv)(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(v)(8)*	Second Amendment to Research, Development and Marketing Collaboration Agreement between Warner-Lambert and the Company dated July 31, 1997.
10.2(vi)(9)*	Amendment #3 to the Research, Development and Marketing Collaboration Agreement between the Company and Warner-Lambert dated August 6, 2001.
10.2(vii)(10)*	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(11)*	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(2)+	Letter Agreement between Dr. Gregory Giotta and the Company dated May 26, 1995.
10.5(2)+	1996 Equity Incentive Plan.
10.6(2)+	1996 Non-Employee Directors' Stock Option Plan.
10.7(12)+	1996 Employee Stock Purchase Plan.
10.8(2)+	Form of Indemnity Agreement to be signed by executive officers and directors of the Company.
10.9(13)+	Form of Executive Change in Control Severance Benefits Agreement.
10.10(i)(14)*	Collaboration Agreement between the Company and Warner-Lambert Company dated October 13, 1999.
10.10(ii)(9)*	Amendment #1 to the Collaboration Agreement between the Company and Warner-Lambert dated August 6, 2001.
10.10(ii)(15)*	Second Amendment to the Collaboration Agreement between the Company and Warner-Lambert Company dated September 16, 2002.
10.11(16)	Stock and Warrant Purchase Agreement between the Company and the investors dated May 6, 2002.
10.12(i)(17)	Sublease between the Company and Siebel Systems dated August 5, 2004.
10.12(ii)(18)	First Amendment to Sublease between the Company and Oracle USA Inc., dated November 3, 2006.
10.13(i)(19)+	2005 Equity Incentive Plan.
10.13(ii)(18)+	Form of Stock Option Agreement pursuant to the 2005 Equity Incentive Plan.
10.13(iii)(18)+	Form of Stock Option Agreement pursuant to the 2005 Equity Incentive Plan and the Non-Discretionary Grant Program for Directors.
10.13(iv)(20)+	Form of Stock Bonus Award Grant Notice and Agreement between the Company and certain award recipients.
10.14(7)*	United States Co-Promotion Agreement by and between the Company and Bayer Pharmaceuticals Corporation, dated March 6, 2006.
10.15(21)+	Letter Agreement between Laura A. Brege and the Company, dated May 19, 2006.
10.16	Reserved.
10.17(22)	Common Stock Purchase Agreement between the Company and Azimuth Opportunity Ltd., dated September 29, 2006.
10.18(32)+	Letter Agreement between Michael Kauffman, M.D., and the Company, dated October 10, 2009.
10.19(31)+	Base Salaries and Bonus Potential for Fiscal Year 2010, Cash Bonuses for Fiscal Year 2009 and 2010 Equity Compensation Awards for Named Executive Officers.
10.20(i)(24)+	Employment Agreement between the Company and N. Anthony Coles, M.D., dated as of February 22, 2008.

Exhibit Number	Description of Document
10.20(ii)(23)	Amendment to Executive Employment Agreement between the Company and N. Anthony Coles, M.D., effective as of March 12, 2009.
10.21(24)+	Executive Change in Control Severance Benefits Agreement between the Company and N. Anthony Coles, M.D., dated as of February 22, 2008.
10.22(32)**	License and Supply Agreement, dated October 12, 2005, by and between CyDex, Inc. and Proteolix, Inc., as amended.
10.23	Reserved.
10.24	Reserved.
10.25(3)+	Onyx Pharmaceuticals, Inc. Executive Severance Benefit Plan.
10.26(26)+	Letter Agreement between the Company and Matthew K. Fust, dated December 12, 2008.
10.27(27)*	Development and License Agreement between the Company and BTG International Limited, dated as of November 6, 2008.
10.28(i)(23)+	Letter Agreement between the Company and Juergen Lasowski, Ph.D., dated April 28, 2008.
10.28(ii)(23)+	Amendment to Letter Agreement between the Company and Juergen Lasowski, Ph.D., effective as of March 12, 2009.
10.29(28)+	Executive Employment Agreement between the Company and Suzanne M. Shema, effective as of August 31, 2009.
10.30(29)+	Letter Agreement between the Company and Ted Love, M.D., effective as of January 28, 2010.
10.31(29)+	Letter Agreement between the Company and Michael Kauffman, M.D., effective as of April 1, 2010.
10.32(30)+	Letter Agreement between the Company and Kaye Foster-Cheek, effective as of September 30, 2010.
10.33(30)+	Separation and Consulting Agreement between the Company and Judy Batlin, effective as of September 30, 2010.
10.34(30)	Lease Agreement between the Company and ARE-SAN FRANCISCO, No. 12, LLC, dated as of July 9, 2010, as amended by that certain Letter Agreement between the Company and ARE-SAN FRANCISCO No. 12, dated as of July 9, 2010.
10.35(30)	Sublease between the Company and Exelixis, Inc., dated as of July 9, 2010
10.36(30)*	License, Development and Commercialization Agreement between the Company and Ono Pharmaceutical Co., Ltd., dated as of September 7, 2010.
10.37+	Separation and Consulting Agreement between the Company and Michael Kauffman, effective as of December 31, 2010.
21.1	Subsidiaries of the Registrant.
23.1	Consent of Independent Registered Public Accounting Firm.
24.1	Power of Attorney. Reference is made to the signature page.
31.1	Certification of Principal Executive Officer required by Rule 13a-14(a) or Rule 15d-14(a).
31.2	Certification of Principal Financial Officer 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).

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

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

\+ Indicates management contract or compensatory plan or arrangement.

(1) Filed as an exhibit to Onyx's Current Report on Form 8-K filed on October 13, 2009.

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

(3) Filed as an exhibit to Onyx's Current Report on Form 8-K filed on December 5, 2008.

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

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

(6) Filed as an exhibit to Onyx's Current Report on Form 8-K filed on August 12, 2009.

(7) 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.

(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, 2001.

(10) 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.

(11) 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.

(12) Filed as an exhibit to Onyx's Current Report on Form 8-K filed on May 25, 2007.

(13) Filed as an exhibit to Onyx's Current Report on Form 8-K filed on June 10, 2008.

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

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

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

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

(18) Filed as an exhibit to Onyx's Annual Report on Form 10-K for the year ended December 31, 2006.

(19) Filed as an exhibit to Onyx's Current Report on Form 8-K filed on May 28, 2010

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

(21) Filed as an exhibit to Onyx's Current Report on Form 8-K filed on June 12, 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 March 31, 2009.

(24) Filed as an exhibit to Onyx's Current Report on Form 8-K filed on February 26, 2008.

(25) Filed as an exhibit to Onyx's Current Report on Form 8-K filed on June 23, 2008.

(26) Filed as an exhibit to Onyx's Current Report on Form 8-K filed on December 23, 2008.

(27) Filed as an exhibit to Onyx's Annual Report on Form 10-K for the year ended December 31, 2008.

(28) Filed as an exhibit to Onyx's Quarterly Report on Form 10-Q for the quarter ended September 30, 2009.

(29) Filed as an exhibit to Onyx's Quarterly Report on Form 10-Q for the quarter ended March 31, 2010.

(30) Filed as an exhibit to Onyx's Quarterly Report on Form 10-Q for the quarter ended September 30, 2010.

(31) Filed as an exhibit to Onyx's Current Report on Form 8-K filed on February 19, 2010.

(32) Filed as an exhibit to Onyx's Annual Report on Form 10-K for the year ended December 31, 2009.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange 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 23rd day of February, 2011.

ONYX PHARMACEUTICALS, INC.

By: /s/ N. ANTHONY COLES
N. Anthony Coles
President and Chief Executive Officer

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints N. Anthony Coles and Matthew K. Fust 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 connection 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/ N. ANTHONY COLES N. Anthony Coles	President and Chief Executive Officer (Principal Executive Officer)	February 23, 2011
/s/ MATTHEW K. FUST Matthew K. Fust	Executive Vice President and Chief Financial Officer (Principal Financial and Accounting Officer)	February 23, 2011
/s/ PAUL GODDARD Paul Goddard, Ph.D.	Director	February 23, 2011
/s/ ANTONIO GRILLO-LOPEZ Antonio Grillo-Lopez, M.D.	Director	February 23, 2011
/s/ MAGNUS LUNDBERG Magnus Lundberg	Director	February 23, 2011
/s/ CORINNE H. NEVINNY Corinne H. Nevinny	Director	February 23, 2011
/s/ WILLIAM R. RINGO William R. Ringo	Director	February 23, 2011
/s/ WENDELL WIERENGA Wendell Wierenga, Ph.D.	Director	February 23, 2011
/s/ THOMAS G. WIGGANS Thomas G. Wiggans	Director	February 23, 2011

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

The Board of Directors and Stockholders of Onyx Pharmaceuticals, Inc.

We have audited the accompanying consolidated balance sheets of Onyx Pharmaceuticals, Inc. as of December 31, 2010 and 2009, and the related consolidated statements of operations, stockholders' equity, and cash flows for each of the three years in the period ended December 31, 2010. These financial statements are the responsibility of the Company's 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 consolidated financial position of Onyx Pharmaceuticals, Inc. at December 31, 2010 and 2009, and the consolidated results of its operations and its cash flows for each of the three years in the period ended December 31, 2010, in conformity with U.S. generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), Onyx Pharmaceuticals, Inc.'s internal control over financial reporting as of December 31, 2010, 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 23, 2011 expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP

Palo Alto, California
February 23, 2011

ONYX PHARMACEUTICALS, INC.

CONSOLIDATED BALANCE SHEETS

	December 31, 2010	December 31, 2009
	(In thousands, except share and per share amounts)	
ASSETS		
Current assets:		
Cash and cash equivalents	$ 226,340	$ 107,668
Marketable securities, current	322,973	442,440
Restricted cash	31,910	27,600
Receivable from collaboration partners	51,412	51,418
Prepaid expenses and other current assets	12,549	9,597
Total current assets	645,184	638,723
Marketable securities, non-current	28,555	37,174
Property and equipment, net	10,822	7,473
Intangible assets — in-process research and development	438,800	438,800
Goodwill	193,675	193,675
Other assets	35,599	8,835
Total assets	$1,352,635	$1,324,680
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 16	$ 1,363
Accrued liabilities	16,866	11,852
Accrued clinical trials and related expenses	15,093	13,815
Accrued compensation	9,251	13,148
Liability for contingent consideration, current	-	40,000
Escrow account liability	31,634	27,600
Total current liabilities	72,860	107,778
Convertible senior notes due 2016	152,701	143,669
Liability for contingent consideration, non-current	253,458	160,528
Deferred tax liability	157,090	157,090
Other liabilities	18,952	5,059
Commitments and contingencies (Notes 5, 12 and 18)		
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; 62,855,376 and 62,260,183 shares issued and outstanding as of December 31, 2010 and 2009, respectively	63	62
Additional paid-in capital	1,238,204	1,207,010
Receivable from stock option exercises	(6)	(5)
Accumulated other comprehensive loss	(1,291)	(1,962)
Accumulated deficit	(539,396)	(454,549)
Total stockholders' equity	697,574	750,556
Total liabilities and stockholders' equity	$1,352,635	$1,324,680

See accompanying notes.

ONYX PHARMACEUTICALS, INC.

CONSOLIDATED STATEMENTS OF OPERATIONS

	Year Ended December 31,		
	2010	2009	2008
	(In thousands, except per share amounts)		
Revenue:			
Revenue from collaboration agreement	$265,350	$250,390	$194,343
License revenue	59,165	-	-
Contract revenue from collaborations	-	1,000	-
Total revenue	324,515	251,390	194,343
Operating expenses:			
Research and development	185,740	128,506	123,749
Selling, general and administrative	114,167	101,132	80,994
Contingent consideration	92,930	1,528	-
Total operating expenses	392,837	231,166	204,743
Income (loss) from operations	(68,322)	20,224	(10,400)
Investment income, net	2,829	4,028	12,695
Interest expense	(19,400)	(6,858)	-
Other expense	(773)	-	-
Income (loss) before provision for income taxes	(85,666)	17,394	2,295
Provision (benefit) for income taxes	(819)	1,233	347
Net income (loss)	$ (84,847)	$ 16,161	$ 1,948
Basic net income (loss) per share	$ (1.35)	$ 0.27	$ 0.03
Diluted net income (loss) per share	$ (1.35)	$ 0.27	$ 0.03
Shares used in computing basic net income (loss) per share	62,618	59,215	55,915
Shares used in computing diluted net income (loss) per share	62,618	59,507	56,765

See accompanying notes.

ONYX PHARMACEUTICALS, INC.

CONSOLIDATED STATEMENTS 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 shares and per share amounts)						
Balances at December 31, 2007	55,324,887	$56	$ 904,506	$ (23)	$ 356	$(472,658)	$432,237
Exercise of stock options	1,145,281	1	25,060	(432)	-	-	24,629
Stock-based compensation, related to stock option grants	-	-	16,779	-	-	-	16,779
Tax benefit associated with stock options	-	-	112	-	-	-	112
Issuance of common stock pursuant to employee stock purchase plan	37,631	-	1,386	-	-	-	1,386
Restricted stock awards issued, net of forfeitures	52,445	-	2,785	-	-	-	2,785
Comprehensive loss:							
Change in unrealized gain (loss) on investments	-	-	-	-	(4,676)	-	(4,676)
Net income	-	-	-	-	-	1,948	1,948
Comprehensive loss							(2,728)
Balances at December 31, 2008	56,560,244	57	950,628	(455)	(4,320)	(470,710)	475,200
Exercise of stock options	552,607	-	12,167	450	-	-	12,617
Issuance of common stock in connection with follow-on public offering	4,600,000	5	133,914	-	-	-	133,919
Warrant exercise	5,852	-	-	-	-	-	-
Stock-based compensation, related to stock option grants	-	-	16,669	-	-	-	16,669
Tax benefit associated with stock options	-	-	35	-	-	-	35
Issuance of common stock pursuant to employee stock purchase plan	45,435	-	1,647	-	-	-	1,647
Restricted stock awards issued, net of forfeitures	496,045	-	5,390	-	-		5,390
Equity component of convertible senior notes due 2016	-	-	86,560	-	-	-	86,560
Comprehensive income:							
Change in unrealized gain (loss) on investments	-	-	-	-	2,358	-	2,358
Net income	-	-	-	-	-	16,161	16,161
Comprehensive income							18,519
Balances at December 31, 2009	62,260,183	62	1,207,010	(5)	(1,962)	(454,549)	750,556
Exercise of stock options	323,436	1	6,863	(1)			6,863
Stock-based compensation, related to stock option grants	-	-	17,385	-	-	-	17,385
Issuance of common stock pursuant to employee stock purchase plan	78,991	-	2,129	-	-	-	2,129
Restricted stock awards issued, net of forfeitures	192,766	-	4,817	-	-	-	4,817
Comprehensive loss:							
Change in unrealized gain (loss) on investments	-	-	-	-	732	-	732
Change in unrealized gain (loss) on cash flow hedges	-	-	-	-	(61)	-	(61)
Net loss	-	-	-	-	-	(84,847)	(84,847)
Comprehensive loss							(84,176)
Balances at December 31, 2010	62,855,376	$63	$1,238,204	$ (6)	$(1,291)	$(539,396)	$697,574

See accompanying notes.

ONYX PHARMACEUTICALS, INC.

CONSOLIDATED STATEMENTS OF CASH FLOWS

	Year Ended December 31,		
	2010	2009	2008
		(In thousands)	
Cash flows from operating activities:			
Net income (loss)	$ (84,847)	$ 16,161	$ 1,948
Adjustments to reconcile net income (loss) to net cash provided by operating activities:			
Realized losses (gains) on sales of short-term marketable securities	(90)	32	(483)
Depreciation and amortization	3,641	1,625	1,333
Stock-based compensation	22,797	22,561	20,506
Excess tax benefit from stock-based awards	-	(35)	(112)
Amortization of convertible senior notes discount and debt issuance costs	9,655	3,371	-
Changes in fair value of liability for contingent consideration, non-current	92,930	1,528	-
Deferred income taxes	(11,860)	-	-
Changes in operating assets and liabilities:			
Restricted cash	(310)	-	-
Receivable from collaboration partners	6	(15,582)	(31,134)
Prepaid expenses and other current assets	(3,013)	(1,582)	(1,383)
Other assets	(15,527)	17	(4,442)
Accounts payable	(1,347)	843	(178)
Accrued liabilities	5,014	4,579	2,458
Accrued clinical trials and related expenses	1,278	(988)	2,718
Accrued compensation	(3,897)	2,925	232
Escrow liability	34	-	-
Other liabilities	13,893	(383)	92
Net cash provided by (used in) operating activities	28,357	35,072	(8,445)
Cash flows from investing activities:			
Acquisition of Proteolix, Inc., net of cash acquired	-	(252,514)	-
Purchases of marketable securities	(508,508)	(742,290)	(420,344)
Sales of marketable securities	277,891	106,846	96,839
Maturities of marketable securities	359,525	381,050	404,415
Capital expenditures	(6,990)	(1,300)	(1,550)
Transfers to restricted cash	(4,000)	-	-
Payment for liability for contingent consideration, current	(36,000)	-	-
Net cash provided by (used in) investing activities	81,918	(508,208)	79,360
Cash flows from financing activities:			
Repayment of notes payable	-	(8,160)	-
Repurchases of restricted stock awards	(78)	(18)	(577)
Payment to collaboration partner	-	(16,633)	(22,601)
Net proceeds from issuances of common stock	8,475	147,699	25,650
Proceeds from issuance of convertible senior notes	-	230,000	-
Convertible senior notes debt issuance costs	-	(7,271)	-
Excess tax benefit from stock-based awards	-	35	112
Net cash provided by financing activities	8,397	345,652	2,584
Net increase (decrease) in cash and cash equivalents	118,672	(127,484)	73,499
Cash and cash equivalents at beginning of period	107,668	235,152	161,653
Cash and cash equivalents at end of period	$ 226,340	$ 107,668	$ 235,152
Supplemental cash flow data			
Cash paid during the period for income taxes	$ 537	$ 506	$ 641
Cash paid during the period for interest	9,277	-	-

See accompanying notes.

Note 1. Overview and Summary of Significant Accounting Policies

Overview

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 dedicated to developing innovative therapies that target the molecular mechanisms that cause cancer. Through the Company's internal research programs and in conjunction with its collaborators, the Company is applying its expertise to develop and commercialize therapies designed to exploit the genetic and molecular differences between cancer cells and normal cells.

The Company's first commercially available product, Nexavar® (sorafenib) tablets, being developed with the Company's collaborator Bayer HealthCare Pharmaceuticals, Inc., or Bayer, is approved by the United States Food and Drug Administration, or FDA, for the treatment of patients with unresectable liver cancer and advanced kidney cancer.

The Company has broadened its pipeline through its acquisition of anti-cancer compounds, including carfilzomib, a selective proteasome inhibitor the Company is developing for the potential treatment of patients with multiple myeloma and solid tumors, and through the acquisition of rights to development-stage and novel anti-cancer agents.

Basis of Presentation

The consolidated financial statements include the accounts of Onyx and its wholly owned subsidiaries. All intercompany balances and transactions have been eliminated in consolidation.

Business Combinations

The Company accounted for the acquisition of Proteolix Inc., or Proteolix, in accordance with Accounting Standards Codification ("ASC") Topic 805, *Business Combinations*. ASC Topic 805 establishes principles and requirements for recognizing and measuring the total consideration transferred to and the assets acquired, liabilities assumed and any non-controlling interests in the acquired target in a business combination. ASC Topic 805 also provides guidance for recognizing and measuring goodwill acquired in a business combination; requires purchased in-process research and development to be capitalized at fair value as intangible assets at the time of acquisition; requires acquisition-related expenses and restructuring costs to be recognized separately from the business combination; expands the definition of what constitutes a business; and requires the acquirer to disclose information that users may need to evaluate and understand the financial effect of the business combination.

Significant Accounting Policies, Estimates and Judgments

The preparation of these Consolidated Financial Statements in conformity with United States generally accepted accounting principles requires the Company to make estimates and judgments that affect the reported amounts of assets, liabilities, revenues and expenses, and related disclosures. On an ongoing basis, management evaluates its estimates, including critical accounting policies or estimates related to revenue from collaboration agreement, the effect of business combinations, fair value measurements of tangible and intangible assets and liabilities, goodwill and other intangible assets, income taxes, stock-based compensation and research and development expenses. The Company bases its estimates on historical experience and on various other market specific and other relevant assumptions that management believes to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results may differ significantly from these estimates.

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 have been rendered; (3) the fee is fixed or determinable; and (4) collectability 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 collectability 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 earned. If the Company has continuing obligations to perform, such fees are recognized over the period of continuing performance obligation.

Revenue from Multiple Element Arrangements. The Company accounts for multiple element arrangements, such as license and development agreements in which a customer may purchase several deliverables, in accordance with Accounting Standard Update ("ASU") No. 2009-13, *Multiple Deliverable Revenue Arrangements*. ASU 2009-13 was issued in October 2009 to:

- provide updated guidance on whether multiple deliverables exist, how the deliverables in an arrangement should be separated, and how the consideration should be allocated;
- require an entity to allocate revenue in an arrangement using the best estimated selling price ("BESP") of deliverables if a vendor does not have vendor-specific objective evidence ("VSOE") of selling price or third-party evidence ("TPE") of selling price; and
- eliminate the use of the residual method and require an entity to allocate revenue using the relative selling price method.

In the second quarter of 2010, the Company elected to early adopt this accounting guidance as of January 1, 2010 on a prospective basis for applicable transactions originating or materially modified after December 31, 2009. The new accounting standards for revenue recognition, if applied in the same manner to the year ended December 31, 2009, would not have had a material impact on the Company's Consolidated Financial Statements. In terms of the timing and pattern of revenue recognition, the new accounting guidance for revenue recognition had a significant effect on revenue in periods after the initial adoption, as the Company entered into a multiple element arrangement in September 2010. Refer to Note 3 for further details.

The Company may continue to enter into multiple element arrangements, such as license and development agreements, in which a customer may purchase several deliverables. For these multiple element arrangements, the Company allocates revenue to each non-contingent element based upon the relative selling price of each element. When applying the relative selling price method, the Company determines the selling price for each deliverable using VSOE of selling price or TPE of selling price, if either exists. If neither VSOE nor TPE of selling price exist for a deliverable, the Company uses BESP for that deliverable. Revenue allocated to each element is then recognized based on when the basic four revenue recognition criteria are met for each element.

Revenue from Collaboration Agreement

In accordance with ASC Subtopic 808-10, *Collaborative Arrangements,* the Company records its share of the pre-tax commercial profit generated from the collaboration with Bayer, reimbursement of its shared marketing costs related to Nexavar and royalty revenue in one line item, "Revenue from collaboration agreement." The Company's portion of shared collaboration research and development expenses is not included in the line item "Revenue from collaboration agreement," but is reflected under operating expenses. According to the terms of the collaboration agreement, the companies share all research and development, marketing, and non-U.S. sales expenses. The Company and Bayer each bear their own U.S. sales force and medical science liaison expenses. These costs, which are related to the Company's U.S. sales force and medical science liaisons, are recorded in selling, general and administrative expenses. Bayer recognizes all revenue under the Nexavar collaboration and incurs the majority of expenses relating to the development and marketing of Nexavar. The Company is highly dependent on Bayer for timely and accurate information regarding any revenues realized from sales of Nexavar and the costs incurred in

developing and selling it, in order to accurately report its results of operations. For the periods covered in the financial statements presented, there have been no significant or material changes to prior period estimates of revenues and expenses. However, if the Company does not receive timely and accurate information or incorrectly estimates activity levels associated with the collaboration of Nexavar at a given point in time, the Company could be required to record adjustments in future periods and may be required to restate its results for prior 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, preclinical study expenses, 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. Preclinical study expenses include, but are not limited to, costs incurred for the laboratory evaluation of a product candidate's chemistry and its biological activities and costs incurred to assess the potential safety and efficacy of a product candidate and its formulations. Clinical trial expenses include, but are not limited to, investigator fees, site costs, comparator drug costs, clinical research organization costs. In the normal course of business, the Company contracts with third parties to perform various clinical trial activities in the on-going development of potential products. The financial terms of these agreements are subject to negotiation and variation from contract to contract and may result in uneven payment flows. Payments under the contracts depend on factors such as the achievement of certain events, the successful enrollment of patients and the completion of portions of the clinical trial or similar conditions. The 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, cooperative groups and clinical research organizations. The objective of the Company's accrual policy is to match the recording of expenses in its Consolidated Financial Statements to the actual services received and efforts expended. As such, expense accruals related to clinical trials are recognized based on the Company's estimate of the degree of completion of the event or events specified in the specific clinical study or trial contract. The Company monitors service provider activities to the extent possible; however, if the Company incorrectly estimates activity levels associated with various studies at a given point in time, the Company could be required to record adjustments to its research and development expenses in future periods.

In instances where the Company enters into agreements with third parties for clinical trials and other consulting activities, up-front payment amounts are capitalized and expensed as services are performed or as the underlying goods are delivered. If the Company does not expect the services to be rendered or goods to be delivered, any remaining capitalized amounts for non-refundable up-front payments are charged to expense immediately. 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.

Non-refundable option payments, including those made under the Company's agreement with S*BIO, that do not have any future alternative use are recorded as research and development expense. Not all research and development costs are incurred by the Company. A significant portion of the Company's total research and development expenses, approximately 49% in 2010, 63% in 2009 and 55% in 2008, relates to the Company's cost sharing arrangement with Bayer and represents the Company's share of the research and development costs incurred by Bayer. As a result of the cost sharing arrangement between the Company and Bayer, there was a net reimbursable amount of $78.8 million, $63.7 million and $50.7 million to Bayer for the years ended December 31, 2010, 2009 and 2008, respectively. Such amounts were recorded based on invoices and estimates the Company receives from Bayer. When such invoices have not been received, the Company must estimate the amounts owed to Bayer based on discussions with Bayer. For the periods covered in the financial statements presented, there have been no significant or material differences between actual amounts and estimates. However, if the Company underestimates or overestimates the amounts owed to Bayer, the Company may need to adjust these amounts in a future period, which could have an effect on earnings in the period of adjustment.

Stock-Based Compensation

The Company accounts for stock-based compensation of stock options granted to employees and directors and of employee stock purchase plan shares by estimating the fair value of stock-based awards using the Black-Scholes option-pricing model and amortizing the fair value of the stock-based awards granted over the applicable vesting

period. The Black-Scholes option pricing model includes assumptions regarding dividend yields, expected volatility, expected option term and risk-free interest rates. The Company estimates expected volatility based upon a combination of historical and implied stock prices. The risk-free interest rate is based on the U.S. treasury yield curve in effect at the time of grant. The expected option term calculation incorporates historical employee exercise behavior and post-vesting employee termination rates. The Company accounts for stock-based compensation of restricted stock award grants by amortizing the fair value of the restricted stock award grants, which is the grant date market price, over the applicable vesting period.

The net loss for the year ended December 31, 2010 includes employee stock-based compensation expense of $22.1 million, or $0.35 per diluted share. The net income for the years ended December 31, 2009 and December 31, 2008 includes employee stock-based compensation expense of $21.1 million, or $0.35 per diluted share, and $18.8 million, or $0.33 per diluted share, respectively. As of December 31, 2010, the total unrecorded stock-based compensation expense for unvested stock options, net of expected forfeitures, was $37.5 million, which is expected to be amortized over a weighted-average period of 2.7 years. As of December 31, 2010, the total unrecorded stock-based compensation expense for unvested restricted stock awards, net of expected forfeitures, was $6.8 million, which is expected to be amortized over a weighted-average period of 1.6 years.

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. 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 $0.7 million, $1.5 million and $1.7 million for the years ended December 31, 2010, 2009 and 2008, respectively.

The assumptions used in computing the fair value of stock-based awards reflect the Company's best estimates, but involve uncertainties relating to market and other conditions, many of which are outside of the Company's control. In addition, the Company's estimate of future stock-based compensation expense will be affected by a number of items including the Company's stock price, the number of stock options the Company's board of directors may grant in future periods, as well as a number of complex and subjective valuation adjustments and the related tax effect. As a result, if other assumptions or estimates had been used, the stock-based compensation expense that was recorded for the years ended December 31, 2010, 2009 and 2008 could have been materially different. Furthermore, if different assumptions are used in future periods, stock-based compensation expense could be materially impacted in the future.

Net Income (Loss) Per Share

Basic net income (loss) per share amounts for each period presented were computed by dividing net income (loss) by the weighted-average number of shares of common stock outstanding. Diluted net income (loss) per share for each period presented was computed by dividing net income (loss) plus interest on dilutive convertible senior notes by the weighted-average number of shares of common stock outstanding during each period plus all additional common shares that would have been outstanding assuming dilutive potential common shares had been issued for dilutive convertible senior notes and other dilutive securities.

Dilutive potential common shares for dilutive convertible senior notes are calculated based on the "if-converted" method. Under the "if-converted" method, when computing the dilutive effect of convertible senior notes, the numerator is adjusted to add back the amount of interest and debt issuance costs recognized in the period and the denominator is adjusted to add back the amount of shares that would be issued if the entire obligation is settled in shares. As of December 31, 2010, the Company's outstanding indebtedness consisted of its 4.0% convertible senior notes due 2016, or the 2016 Notes.

Dilutive potential common shares also include the dilutive effect of the common stock underlying in-the-money stock options and are calculated based on the average share price for each period using the treasury stock method. Under the treasury stock method, the exercise price of an option, the average amount of compensation cost, if any, for future service that the Company has not yet recognized when the option is exercised, are assumed to be used to repurchase shares in the current period. Dilutive potential common shares also reflect the dilutive effect of unvested restricted stock units.

The computations for basic and diluted net income (loss) per share were as follows:

	Year Ended December 31,		
	2010	2009	2008
	(In thousands, except per share amounts)		
Numerator:			
Net income (loss) — basic	$(84,847)	$16,161	$ 1,948
Add: interest and issuance costs related to convertible senior notes	-	-	-
Net income (loss) — diluted	$(84,847)	$16,161	$ 1,948
Denominator:			
Weighted average common shares outstanding — basic	62,618	59,215	55,915
Dilutive effect of stock options	-	292	850
Weighted average common shares outstanding and dilutive potential common shares — diluted	62,618	59,507	56,765
Net income (loss) per share:			
Basic	$ (1.35)	$ 0.27	$ 0.03
Diluted	$ (1.35)	$ 0.27	$ 0.03

Under the "if-converted" method, 5.8 million potential common shares relating to the 2016 Notes were not included in diluted net income (loss) per share for the years ended December 31, 2010 and 2009 because their effect would be anti-dilutive. Diluted net income (loss) per share does not include the effect of 5.1 million, 4.0 million and 1.8 million stock-based awards that were outstanding during the years ended December 31, 2010, 2009 and 2008. These stock-based awards were not included in the computation of diluted net income (loss) per share because the proceeds received, if any, from such stock-based awards combined with the average unamortized compensation costs were greater than the average market price of the Company's common stock, and, therefore, their effect would have been antidilutive.

Income Taxes

The Company uses the asset and liability method to account for income taxes in accordance with ASC 740, *Income Taxes*. Under this method, deferred tax assets and liabilities are determined based on differences between the financial reporting and tax bases of assets and liabilities. At each balance sheet date, the Company evaluates the available evidence about future taxable income and other possible sources of realization of deferred tax assets, and records a valuation allowance that reduces the deferred tax assets to an amount that represents management's best estimate of the amount of such deferred tax assets that more likely than not will be realized. Deferred tax assets and liabilities are measured using the enacted tax rates and laws that will be in effect when the differences are expected to reverse. The effect on deferred tax assets and liabilities of a change in tax rates is recognized in income in the period that includes the enactment date.

On January 1, 2007 the Company adopted authoritative guidance under ASC 740, formerly *FASB Interpretation No. 48 ("FIN 48")* which clarifies the accounting for uncertainty in tax positions recognized in the financial statements. FIN 48 provides that a tax benefit from an uncertain tax position may be recognized when it is more likely than not that the position will be sustained upon examination, including resolutions of any related appeals or litigation processes, based on the technical merits. Income tax positions must meet a more-likely-than-not recognition threshold at the effective date to be recognized upon the adoption of FIN 48 and in subsequent periods. This interpretation also provides guidance on measurement, derecognition, classification, interest and penalties, accounting in interim periods, disclosure and transition.

The Company's policy for classifying interest and penalties associated with unrecognized income tax benefits is to include such items as tax expense.

Cash and Cash Equivalents

The Company considers all highly liquid investments with a maturity from the date of purchase of three months or less to be cash equivalents. Cash equivalents are carried at cost, which approximates fair value.

With the acquisition of Proteolix in November 2009 under the Agreement and Plan of Merger, or the Merger Agreement, the Company was required to set aside funds to be placed in an escrow account until December 31, 2010 to secure the indemnification rights of Onyx and other indemnitees with respect to certain matters. However, in December 2010, the Company filed a claim notice in good faith describing circumstances that the Company believed entitled it to indemnification, compensation and/or reimbursement. This escrow amount was paid to the former Proteolix stockholders in February 2011 after the settlement of the claim through the Amendment of the original Merger Agreement in January 2011. Refer to Note 5 for further detail.

Marketable Securities

Marketable securities consist primarily of corporate debt securities, corporate commercial paper, debt securities of United States government agencies, auction rate notes and money market funds and are classified as available-for-sale securities. Concentration of risk is limited by diversifying investments among a variety of industries and issuers. 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). For securities with unobservable quoted market prices, such as the AAA rated auction rate securities collateralized by student loans that are included in the Company's investment portfolio, the fair value is determined using a discounted cash flow analysis. The discounted cash flow model used to value these securities is based on a specific term and liquidity assumptions. Unrealized losses are charged against "investment income" when a decline in fair value is determined to be other-than-temporary. The Company reviews several factors to determine whether a loss is other-than-temporary. These factors include but are not limited to: (i) the extent to which the fair value is less than cost and the cause for the fair value decline, (ii) the financial condition and near-term prospects of the issuer, (iii) the length of time a security is in an unrealized loss position and (iv) the Company's ability to hold the security for a period of time sufficient to allow for any anticipated recovery in fair value. The Company does not intend to sell its marketable securities and it is not more likely than not that the Company will be required to sell its securities prior to the recovery of their amortized cost bases. Available-for-sale securities with remaining maturities of greater than one year are classified as long-term. 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. The cost of securities sold or the amount reclassified out of accumulated other comprehensive income into earnings is based on the specific identification method. Realized gains and losses and declines in value judged to be other than temporary are included in the statements of operations. Interest and dividends on securities classified as available-for-sale are included in investment income.

Fair Value Measurements

In accordance with ASC Subtopic 820-10, *Fair Value Measurements and Disclosures*, the carrying amounts of certain financial instruments of the Company, including cash equivalents, marketable securities and liabilities for contingent consideration, continue to be valued at fair value. ASC Subtopic 820-10 defines fair value and provides guidance for using fair value to measure assets and liabilities and is applicable whenever assets or liabilities are required or permitted to be measured at fair value,

The fair value estimates presented in this report reflect the information available to the Company as of December 31, 2010. See Note 7, "Fair Value Measurements."

Concentration of Credit Risk

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

The Company's investment portfolio includes $32.7 million of AAA rated securities with an auction reset feature, or auction rate securities, that are collateralized by student loans. In January 2011, $2.7 million in securities were redeemed at par and, accordingly, the Company classified these securities as current marketable securities in the accompanying Consolidated Balance Sheet at December 31, 2010. The remaining balance of $29.9 million of par value auction rate securities is currently outstanding in the Company's investment portfolio. Since February 2008, these types of securities have experienced failures in the auction process. However, a limited number of these securities have been redeemed at par by the issuing agencies. As a result of the auction failures, interest rates on these securities reset at penalty rates linked to LIBOR or Treasury bill rates. The penalty rates are generally higher than interest rates set at auction. Based on the overall failure rate of these auctions, the frequency of the failures, the underlying maturities of the securities, a portion of which are greater than 30 years, and the Company's belief that the market for these student loan collateralized instruments may take in excess of twelve months to fully recover, the Company has classified the auction rate securities with a par value of $29.9 million as non-current marketable securities on the accompanying Consolidated Balance Sheet. The Company has determined the fair value to be $28.6 million for these securities, based on a discounted cash flow model, and have reduced the carrying value of these marketable securities by $1.4 million through accumulated other comprehensive income (loss) instead of earnings because the Company has deemed the impairment of these securities to be temporary. Further adverse developments in the credit market could result in an impairment charge through earnings in the future. The Company does not intend to sell these securities and management believes it is not more likely than not that the Company will be required to sell these securities prior to the recovery of their amortized cost bases.

Derivative Instruments

The Company has established a foreign currency hedging program beginning in 2010. The objective of the program is to mitigate the foreign exchange risk arising from transactions or cash flows that have a direct or underlying exposure in non-U.S. Dollar denominated currencies in order to reduce volatility in the Company's cash flow and earnings. The Company hedges a certain portion of anticipated Nexavar-related cash flows owed to the Company with options, typically no more than one year into the future. The underlying exposures, both revenue and expenses, in the Nexavar program are denominated in currencies other than the U.S. Dollar, primarily the Euro and Japanese Yen. For purposes of calculating the cash flows due to or due from the Company each quarter, the foreign currencies are converted into U.S. dollars based on average exchange rates for the reporting period. The Company does not enter into derivative financial contracts for speculative purposes.

In accordance with ASC 815, *Derivatives and Hedging*, all derivative instruments, such as foreign currency option contracts, are recognized on the Consolidated Balance Sheet at fair value. Changes to the fair value of derivative instruments are recorded in current earnings or accumulated other comprehensive gain (loss) each period, depending on whether or not the derivative instrument is designated as part of a hedging transaction and, if it is, the type of hedging transaction. For a derivative to qualify as a hedge at inception and throughout the hedged period, the Company formally documents the nature and relationships between the hedging instruments and hedged item. The Company assesses, both at inception and on an on-going basis, whether the derivative instruments that are used in cash flow hedging transactions are highly effective in offsetting the changes in cash flows of hedged items. The Company assesses hedge ineffectiveness on a quarterly basis and records the gain or loss related to the ineffective portion of derivative instruments, if any, to current earnings. If the Company determines that a forecasted transaction is no longer probable of occurring, it discontinues hedge accounting and any related unrealized gain or loss on the derivative instrument is recognized in current earnings. Changes in the fair value of derivative instruments that are not designated as part of a hedging transaction are recognized in current earnings. Refer to Note 6 for further information.

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 seven years.

Deferred Rent and Lease Incentives

Deferred rent and lease incentives consists of the difference between cash payments and the recognition of rent expense on a straight-line basis for the buildings the Company occupies. The leases provide for fixed increases in minimum annual rental payments, as well as rent free periods. The total amount of rental payments due over the lease terms are being charged to rent expense ratably over the life of the leases. Tenant improvement allowances are recorded as a deferred rent liability and are amortized over the term of the lease as a reduction to rent expense.

Intangible Assets — In-process Research and Development

Intangible assets related to in-process research and development costs, or IPR&D, are considered to be indefinite-lived until the completion or abandonment of the associated research and development efforts. During the period the assets are considered indefinite-lived, they will not be amortized but will be tested for impairment on an annual basis and between annual tests if the Company becomes aware of any events occurring or changes in circumstances that would indicate a reduction in the fair value of the IPR&D projects below their respective carrying amounts. If and when development is complete, which generally occurs if and when regulatory approval to market a product is obtained, the associated assets would be deemed finite-lived and would then be amortized based on their respective estimated useful lives at that point in time.

Intangible Assets — Goodwill

Goodwill represents the excess of the consideration transferred over the estimated fair values of assets acquired and liabilities assumed in a business combination and is considered to be indefinite-lived. Goodwill is not amortized but is tested for impairment on an annual basis and between annual tests if the Company becomes aware of any events occurring or changes in circumstances that would indicate a reduction in the fair value of the goodwill below its carrying amount.

Liability for Contingent Consideration

In addition to the initial cash consideration paid to former Proteolix stockholders and the first earn-out payment made in April 2010 of $40.0 million, the Company may be required to pay up to an additional $535.0 million in earn-out payments upon the receipt of certain regulatory approvals and the satisfaction of other milestones. These earn-out payments will become payable in up to four additional installments, upon the achievement of regulatory approvals in the U.S. and Europe within pre-specified timeframes for carfilzomib. In accordance with ASC Topic 805, *Business Combinations*, the Company determined the fair value of this liability for contingent consideration on the acquisition date using a probability weighted income approach. Future changes to the fair value of the contingent consideration will be determined each period and charged to expense in the "Contingent consideration" expense line item in the Consolidated Statements of Operations under operating expenses. Refer to *Liability for Contingent Consideration* in Note 5 for further information.

Convertible Senior Notes

In August 2009, the Company issued, through an underwritten public offering, $230.0 million aggregate principal amount of 4.0% convertible senior notes due 2016. The 2016 Notes are accounted for in accordance with ASC Subtopic 470-20, *Debt with Conversion and Other Options*. Under ASC Subtopic 470-20, issuers of certain convertible debt instruments that have a net settlement feature and may be settled in cash upon conversion, including partial cash settlement, are required to separately account for the liability (debt) and equity (conversion option) components of the instrument. The carrying amount of the liability component of the 2016 Notes, as of the issuance date, was computed by estimating the fair value of a similar liability issued at 12.5% effective interest rate, which was determined by considering the rate of return investors would require in the Company's capital structure as well as taking into consideration effective interest rates derived by comparable companies. The amount of the equity component was calculated by deducting the fair value of the liability component from the principal amount of the 2016 Notes and resulted in a corresponding increase to debt discount. Subsequently, the debt discount is being amortized as interest expense through the maturity date of the 2016 Notes.

Segment Reporting

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

Recent Accounting Pronouncements

In October 2009, the FASB issued Accounting Standard Update ("ASU") No. 2009-13, *Multiple Deliverable Revenue Arrangements*, impacting the determination of when the individual deliverables included in a multiple element arrangement may be treated as separate units of accounting. Additionally, ASU 2009-13 modifies the manner in which the transaction consideration is allocated across the separately identified deliverables by no longer permitting the residual method of allocating arrangement consideration. This ASU will be effective for periods beginning on or after June 15, 2010. Early application is permitted. Entities can apply this guidance prospectively to milestones achieved after adoption. However, retrospective application to all prior periods is also permitted. During the second quarter of 2010, the Company adopted ASU 2009-13 effective January 1, 2010 on a prospective basis for applicable transactions originating or materially modified after December 31, 2009. The new accounting standards for revenue recognition, if applied in the same manner to the year ended December 31, 2009, would not have had a material impact on the Company's financial statements. In terms of the timing and pattern of revenue recognition, the new accounting guidance for revenue recognition had a significant effect on revenue in periods after the initial adoption, as the Company entered into a multiple element arrangement with Ono Pharmaceutical Co., Ltd., or Ono, in September 2010. In accordance with ASU 2009-13, the Company identified the license in the exclusive license agreement entered into with Ono as a separate non-contingent deliverable and recognized $59.2 million of revenue allocated to the license in September 2010 when all related knowledge and data had been transferred. Refer to Note 3 for further information.

In April 2010, the FASB issued ASU No. 2010-17, *Milestone Method of Revenue Recognition*, to (1) limit the scope of this ASU to research or development arrangements and (2) require that guidance in this ASU be met for an entity to apply the milestone method (record the milestone payment in its entirety in the period received). However, the FASB clarified that, even if the requirements in this ASU are met, entities would not be precluded from making an accounting policy election to apply another appropriate accounting policy that results in the deferral of some portion of the arrangement consideration. The ASU is effective for periods beginning on or after June 15, 2010. Early application is permitted. Entities can apply this guidance prospectively to milestones achieved after adoption. However, retrospective application to all prior periods is also permitted. During the second quarter of 2010, the Company adopted ASU 2010-17 effective January 1, 2010 and determined that the adoption did not have any impact on the Company's financial statements.

Note 2. Revenue from Collaboration Agreement

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. Together with Bayer, the Company 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 Company's collaboration agreement with Bayer, the Company is currently funding 50% of mutually agreed development costs worldwide, excluding Japan. Bayer is funding 100% of development costs in Japan and pays the Company a royalty on sales in 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 the Company does not continue to bear 50% of product development costs, Bayer would retain exclusive, worldwide rights to this product candidate and would pay royalties to the Company based on net sales.

In March 2006, the Company and Bayer entered into a co-promotion agreement to co-promote Nexavar in the United States. This agreement amends and generally supersedes those provisions of the collaboration 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, the Company and Bayer share equally in the profits or losses of Nexavar, if any, in the

United States. If for any reason the Company does not continue to co-promote in the United States, but continue to co-fund development worldwide (excluding Japan), 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 in the United States.

The Company's collaboration agreement with Bayer will terminate when patents expire that were issued in connection with product candidates discovered under the agreement, or at the time when neither we nor Bayer are entitled to profit sharing under the agreement, whichever is latest. The Company's co-promotion agreement with Bayer will terminate upon the earlier of the termination of the Company's collaboration agreement with Bayer or the date products subject to the co-promotion agreement are no longer sold by either party in the United States due to a permanent product withdrawal or recall or a voluntary decision by the parties to abandon the co-promotion of such products in the United States. Either party may also terminate the co-promotion agreement upon failure to cure a material breach of the agreement within a specified cure period.

In addition, the Company's collaboration agreement with Bayer provides that if the Company were acquired by another entity by reason of merger, consolidation or sale of all or substantially all of the Company's assets, or if a single entity other than Bayer or its affiliate acquires ownership of a majority of the Company's outstanding voting stock, and Bayer does not consent to the transaction, then for 60 days following the transaction, Bayer may elect to terminate the co-development and co-promotion rights under the collaboration agreement and convert the Company's profit sharing interest under that agreement into a royalty based on any sales of Nexavar and other collaboration products. The applicable royalty rate would be a function of expected profitability of Nexavar for the remaining patent life of Nexavar. Also, either party may terminate the agreement upon 30 days' notice within 60 days of specified events relating to insolvency of the other party.

Nexavar is currently marketed and sold primarily in the United States and the European Union for the treatment of advanced kidney cancer and unresectable liver cancer. Nexavar also has regulatory applications pending in other territories internationally. Outside of the United States, excluding Japan, Bayer incurs all of the sales and marketing expenditures, and the Company reimburses Bayer for half of those expenditures. In addition, for sales generated outside of the United States, excluding Japan, the Company reimburses Bayer a fixed percentage of sales for their marketing infrastructure. Research and development expenditures on a worldwide basis, excluding Japan, are equally shared by both companies regardless of whether the Company or Bayer incurs the expense. In Japan, Bayer is responsible for all development and marketing costs, and the Company receives a royalty on net sales of Nexavar.

In the United States, Bayer provides all product distribution and all marketing support services for Nexavar, 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. The companies share equally in any other out-of-pocket marketing expenses (other than expenses for sales force and medical science liaisons) that the Company 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, the Company 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. The Company 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.

Revenue from collaboration agreement consists of the Company's share of the pre-tax commercial profit generated from its collaboration with Bayer, reimbursement of the Company's shared marketing costs related to Nexavar and royalty revenue. Under the collaboration, Bayer recognizes all sales of Nexavar worldwide. The Company records revenue from collaboration agreement on a quarterly basis. Revenue from collaboration agreement 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 and allocable overhead costs. Reimbursement by Bayer of the Company's shared marketing costs related to Nexavar and royalty revenue is also included in the revenue from collaboration agreement line item.

The Company's portion of shared collaboration research and development expenses is not included in this line item, but is reflected under operating expenses. According to the terms of the collaboration agreement, the companies share all research and development, marketing and non-U.S. sales expenses. 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 used to derive the revenue from collaboration agreement 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.

Revenue from collaboration agreement was $265.4 million, $250.4 million and $194.3 million for the years ended December 31, 2010, 2009 and 2008, respectively, calculated as follows:

	Year Ended December 31,		
	2010	2009	2008
		(In thousands)	
Onyx's share of collaboration commercial profit	$232,494	$220,567	$169,334
Reimbursement of Onyx's shared marketing expenses	23,122	23,514	22,185
Royalty revenue	9,734	6,309	2,824
Revenue from collaboration agreement	$265,350	$250,390	$194,343

Through December 31, 2010, 2009 and 2008, the Company has invested $596.5 million, $493.5 million and $392.1 million, respectively, in the development of Nexavar, representing its share of the costs incurred to date under the collaboration.

Note 3. Agreement with Ono Pharmaceutical Co., Ltd.

In September 2010, the Company entered into an exclusive license agreement with Ono, granting Ono the right to develop and commercialize both carfilzomib and ONX 0912 for all oncology indications in Japan. The Company retains all development and commercialization rights for other countries in the Asia Pacific region, as well as in all other regions of the world, including the United States and Europe. The Company agreed to provide Ono with development and commercial supply of carfilzomib and ONX 0912 on a cost-plus basis. Ono agreed to pay the Company development and commercial milestone payments based on the achievement of pre-specified criteria. In addition, Ono agreed to share a percentage of costs incurred by the Company for the global development of carfilzomib and ONX 0912 that may support filings for regulatory approval in Japan. Ono is responsible for all development costs in support of regulatory filings in Japan as well as commercialization costs it incurs. If regulatory approval for carfilzomib and/or ONX 0912 is achieved in Japan, Ono is obligated to pay the Company double-digit royalties on net sales of the licensed compounds in Japan.

In accordance with ASU 2009-13, the Company identified the license and certain amounts of development supply to be provided in 2011 as separate non-contingent deliverables under this agreement. The Company determined that the delivered license has stand-alone value based on Ono's internal product development capabilities. The Company identified the reimbursement of global development costs by Ono, and the future development and commercial supply arrangements, subject to future negotiation, as contingent deliverables. Contingent deliverables will be evaluated separately as the related contingency is resolved. The Company allocated consideration relating to non-contingent deliverables on the basis of their relative selling price, which is BESP because VSOE or TPE are unavailable for these elements. The objective of BESP is to determine the price at which the Company would transact a sale if the product were sold on a stand-alone basis. BESP for the license is based on discounted future projected cash flows relating to the licensed territory. Revenue allocated to the license of $59.2 million was recognized in September 2010 when all related knowledge and data had been transferred. BESP for the development supply shipments is based on an estimated cost to produce supply plus a mark-up consistent with similar agreements. Revenue allocated to the clinical material to be delivered in 2011 will be recognized upon delivery of the bulk drug product to Ono.

A percentage of costs incurred by the Company for the global development of carfilzomib and ONX 0912 are required to be reimbursed by Ono at cost. Global development work is conducted by Onyx at Onyx's discretion. These reimbursements will be recorded as a reduction of operating expenses by the Company. For the year ended

December 31, 2010, the reimbursement of global development costs was $8.5 million, which reduced the "Research and development expenses" line item in the Consolidated Statement of Operations. In addition, because the development and commercial milestone payments are solely dependent on Ono's performance and not on any performance obligations of the Company, revenue from the milestone payments will be recognized as the milestones are achieved. The milestone and global development support payments could total approximately $283.5 million at current exchange rates. If regulatory approval for carfilzomib and/or ONX 0912 is achieved in Japan, royalty revenue to be received from Ono will be recognized by the Company based upon the net sales of the products by Ono.

The agreement will terminate upon the expiration of the royalty terms specified for each product. In addition, Ono may terminate this agreement for certain scientific or commercial reasons with advance written notice, and either party may terminate this agreement for the other party's uncured material breach or bankruptcy.

Note 4. Agreements with Other Companies

Pfizer

In May 1995, the Company entered into a research and development collaboration agreement with Warner-Lambert Company, now a subsidiary of Pfizer, Inc., or 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, the Company developed screening tests, or assays, for jointly selected targets and transferred these assays to Pfizer for screening of their compound library to identify active compounds. The discovery research term under the agreement ended in August 2001. Pfizer is responsible for subsequent medicinal chemistry and preclinical investigations on the active compounds. In addition, Pfizer is obligated to conduct and fund all clinical development, make regulatory filings and manufacture for sale any approved collaboration compounds. The Company is entitled to receive payments upon achievement of certain clinical development milestones and upon registration of any resulting products, and is entitled to receive royalties on worldwide sales of the products. Pfizer has identified a small molecule lead compound, PD 0332991, an inhibitor of cyclin-dependent kinase 4/6, or CDK 4/6, and began clinical testing with this drug candidate in 2004. In accordance with the Company's collaboration agreement, it earned a $1.0 million milestone payment from Pfizer in December 2009 upon the initiation of a Phase 2 trial. To date, the Company has earned $1.5 million in milestone fees from Pfizer relating to this drug candidate.

The May 1995 collaboration agreement with Pfizer will remain in effect until the expiration of all licenses granted pursuant to the agreement. Either party may terminate the agreement for the uncured material breach of the other party. Under this agreement, remaining additional potential milestones payable by Pfizer to the Company are, in aggregate, up to approximately $15.5 million and royalty payments will be based on a single digit percentage of net sales, if any.

BTG

In November 2008, the Company licensed a novel targeted oncology compound, ONX 0801, from BTG. Under the terms of the agreement, the Company obtained a worldwide license for ONX 0801 and all of its related patents. The Company received exclusive worldwide marketing rights and is responsible for all product development and commercialization activities. The Company paid BTG a $13.0 million upfront payment, a $7.0 million milestone payment in 2009 and may be required to make additional payments of up to $65.0 million upon the attainment of certain global development and regulatory milestones, plus additional milestone payments upon the achievement of certain marketing approvals and commercial milestones. The Company is also required to pay royalties to BTG on any future product sales.

The Company's development and license agreement with BTG will expire 10 years after the first commercial sale of the licensed product or until patent coverage expires, whichever is later. The Company may terminate the agreement at any time without cause by giving BTG prior written notice, and either party may terminate the agreement upon failure to cure a material breach in certain cases. BTG may terminate the agreement by written notice upon the occurrence of certain specified events, including the Company's failure to pay BTG payments due under the agreement after demand for such payments, the Company challenging the licensed rights under the agreement, the Company's failure to conduct material development activity in relation to a licensed product for a specified period,

the Company's decision to cease development of licensed products, or specified events relating to insolvency of the Company. Upon any termination of the agreement, rights to the licensed compounds will revert to BTG. Except in the case of termination for the Company's breach at an early stage of development, the Company will receive a portion of any compensation received by BTG from the sale of the reverted compounds.

*S*BIO*

In December 2008, the Company entered into a development collaboration, option and license agreement with S*BIO pursuant to which the Company acquired options to license rights to each of ONX 0803 and ONX 0805. Under the terms of the agreement, the Company has obtained options, which if the Company exercises, would give it rights to exclusively develop and commercialize ONX 0803 and ONX 0805 for all potential indications in the United States, Canada and Europe. S*BIO retains responsibility for all development costs prior to the option exercise, after which the Company will assume development costs for the U.S., Canada and Europe, subject to S*BIO's option to fund a portion of the development costs in return for enhanced royalties on any future product sales. Upon the exercise of the Company's option of either compound, S*BIO is entitled to receive a one-time fee, milestones upon achievement of certain development and sales levels and royalties on future product sales. Under the terms of the agreement, in December 2008 the Company made a $25.0 million payment to S*BIO, including an up-front payment and an equity investment in S*BIO.

In May 2010, the Company announced the expansion of its development collaboration, option and license agreement with S*BIO. The Company provided an additional $20.0 million in funding to S*BIO to broaden and accelerate the existing development program for ONX 0803 and ONX 0805. S*BIO agreed to utilize the funding to continue to perform the clinical development of ONX 0803 and preclinical through clinical development of ONX 0805. The Company capitalized the $20.0 million as prepaid research and development expense and is amortizing a portion of this amount as research and development expense each period based on the actual expenses incurred by S*BIO for the development of ONX 0803 and ONX 0805.

The Company's development collaboration, option and license agreement with S*BIO will remain in effect until the expiration of all payment obligations. Because the Company has not exercised its option in the agreement, the Company may terminate the agreement at any time without cause by giving S*BIO prior written notice. In addition, either party may terminate the agreement for the uncured material breach of the other party.

Note 5. Acquisition of Proteolix

On November 16, 2009, or the Acquisition Date, the Company acquired Proteolix under the terms of an Agreement and Plan of Merger, or the Merger Agreement, entered into in October 2009. Proteolix was a privately-held biopharmaceutical company located in South San Francisco, California. Proteolix focused primarily on the discovery and development of novel therapies that target the proteasome for the treatment of hematological malignancies, solid tumors and autoimmune disorders. Proteolix's lead compound, carfilzomib, is a proteasome inhibitor currently in multiple clinical trials, including an advanced Phase 2b clinical trial for patients with relapsed and refractory multiple myeloma. This acquisition provided the Company with an opportunity to expand into the hematological malignancies market.

Under the Merger agreement, the aggregate consideration payable by the Company to former Proteolix stockholders at closing consisted of $276.0 million in cash, less $27.6 million that was temporarily held in an escrow account subject to the terms described below under *Escrow Account Liability.* In addition, a $40.0 million earn-out payment, less $4.0 million that was temporarily held in the escrow account, was made in April 2010, 180 days after the completion of enrollment in an ongoing pivotal Phase 2b clinical study involving relapsed and refractory multiple myeloma patients, known as the "003-A1" trial. The escrow amounts were paid to the former Proteolix stockholders in February 2011. The Company may be required to pay up to an additional $535.0 million in earn-out payments as outlined below under *Liability for Contingent Consideration.*

Intangible Assets — IPR&D

Intangible assets for IPR&D consist of Proteolix's IPR&D programs resulting from the Company's acquisition of Proteolix, including their lead compound, carfilzomib and two other product candidates (ONX 0912 and ONX

0914). The Company determined that the combined estimated Acquisition Date fair values of carfilzomib, ONX 0912 and ONX 0914 was $438.8 million. The Company used an income approach, which is a measurement of the present value of the net economic benefit or cost expected to be derived from an asset or liability, to measure the fair value of carfilzomib and a cost approach to measure the fair values of ONX 0912 and ONX 0914. Under the income approach, an intangible asset's fair value is equal to the present value of the incremental after-tax cash flows (excess earnings) attributable solely to the intangible asset over its remaining useful life. Under the cost approach, an intangible asset's fair value is equal to the costs incurred to-date to develop the asset to its current stage.

To calculate fair value of carfilzomib under the income approach, the Company used probability-weighted cash flows discounted at a rate considered appropriate given the inherent risks associated with this type of asset. The Company estimated the fair value of this asset using a present value discount rate based on the estimated weighted-average cost of capital for companies with profiles substantially similar to that of Proteolix. This is comparable to the estimated internal rate of return for Proteolix's operations and represents the rate that market participants would use to value this asset. Cash flows were generally assumed to extend either through or beyond the patent life of the asset, depending on the circumstances particular to the asset. In addition, the Company compensated for the phase of development for this program by probability-adjusting the Company's estimation of the expected future cash flows. The Company believes that the level and timing of cash flows appropriately reflect market participant assumptions. The projected cash flows from this project was based on key assumptions such as estimates of revenues and operating profits related to the project considering its stage of development; the time and resources needed to complete the development and approval of the related product candidate; the life of the potential commercialized product and associated risks, including the inherent difficulties and uncertainties in developing a drug compound such as obtaining marketing approval from the FDA and other regulatory agencies; and risks related to the viability of and potential alternative treatments in any future target markets. The resultant probability-weighted cash flows were then discounted using a rate the Company believes is appropriate and representative of a market participant assumption.

For the other two intangible assets acquired, ONX 0912 and 0914, the Company used the costs incurred to-date by Proteolix to develop these assets to their current stage as their fair value as result of the lack of financial projections for these assets in their current development stages.

These IPR&D programs represent Proteolix's incomplete research and development projects, which had not yet reached technological feasibility at the Acquisition Date. A summary of these programs and estimated fair values at the Acquisition Date is as follows:

Product Candidates	Description	Estimated Acquisition Date Fair Value
		(In thousands)
Carfilzomib	First in a new class of selective and irreversible proteasome inhibitors associated with prolonged target suppression, improved antitumor activity and low neurotoxicity for treatment against multiple myeloma and solid tumors.	$435,000
ONX 0912	Oral proteasome inhibitor for treatment against hematologic and solid tumors.	3,500
ONX 0914	Immunoproteasome inhibitor for treatment against rheumatoid arthritis and inflammatory bowel disease.	300
		$438,800

Goodwill

The excess of the consideration transferred over the fair values assigned to the assets acquired and liabilities assumed was $193.7 million, which represents the goodwill amount resulting from the acquisition. None of the goodwill is expected to be deductible for income tax purposes. The Company tests goodwill for impairment on an annual basis on October 1 or sooner, if deemed necessary. As of December 31, 2010, there were no changes in the recognized amount of goodwill resulting from the acquisition of Proteolix.

Liability for Contingent Consideration

Under the terms of the Merger Agreement, the aggregate cash consideration paid to former Proteolix stockholders at closing was $276.0 million and an additional $40.0 million earn-out payment was made in April 2010, 180 days after completion of enrollment in an ongoing pivotal Phase 2b clinical study involving relapsed and refractory multiple myeloma patients, known as the "003-A1" trial. The Company may also be required to pay up to an additional $535.0 million in earn-out payments payable in up to four installments upon the achievement of certain regulatory approvals for carfilzomib in the United States and Europe within pre-specified timeframes. In January 2011, the Company entered into Amendment No. 1 to the Merger Agreement, or the Amendment. Under the original Merger Agreement, the first of these additional earn-out payments would be in the amount of $170.0 million if achieved by the date originally contemplated, and would be triggered by accelerated marketing approval for carfilzomib in the United States for relapsed/refractory multiple myeloma. This obligation is unchanged in the Amendment. The Amendment modifies this payment if the milestone is not achieved by the date originally contemplated on a sliding scale basis, as follows:

- if accelerated marketing approval in the United States for relapsed/refractory multiple myeloma is achieved after the date originally contemplated, but within six months of the original date, subject to extension under certain circumstances, then the amount payable will be reduced to $130.0 million; and
- if accelerated marketing approval in the United States for relapsed/refractory multiple myeloma is achieved more than six months after the date originally contemplated, but within 12 months of the original date, subject to extension under certain circumstances, then the amount payable will be reduced to $80.0 million.

The remaining earnout payments will continue to become payable in up to three additional installments as follows:

- $65.0 million would be triggered by marketing approval in the European Union for relapsed/refractory multiple myeloma;
- $150.0 million would be triggered by marketing approval in the United States for relapsed multiple myeloma; and
- $150.0 million would be triggered by marketing approval for relapsed multiple myeloma in the European Union.

The range of the undiscounted amounts the Company could be required to pay for these earn-out payments is between zero and $535.0 million. The fair value of the liability for the contingent consideration recognized on the acquisition date was $199.0 million, of which $40.0 million related to the first milestone payment that was paid in full in April 2010 and the remaining balance of $159.0 million was classified as a non-current liability in the Consolidated Balance Sheet. The Company determined the fair value of the liability for the non-current liability contingent consideration based on a probability-weighted discounted cash flow analysis. This fair value measurement is based on significant inputs not observable in the market and thus represents a Level 3 measurement within the fair value hierarchy. The fair value of the contingent consideration liability associated with those future earn-out payments was based several factors including:

- estimated cash flows projected from the success of unapproved product candidates;
- the probability of technical and regulatory success ("PTRS") for unapproved product candidates considering their stages of development;
- the time and resources needed to complete the development and approval of product candidates;
- the life of the potential commercialized products and associated risks, including the inherent difficulties and uncertainties in developing a product candidate such as obtaining FDA and other regulatory approvals; and
- risk associated with uncertainty, achievement and payment of the milestone events.

The resultant probability-weighted cash flows were then discounted using a rate that reflects the uncertainty surrounding the expected outcomes, which the Company believes is appropriate and representative of a market participant assumption. During the year ended December 31, 2010, the fair value of the non-current liability for contingent consideration increased by $92.9 million, of which $74.6 million was primarily due to an increase in the

PTRS, partially offset by a benefit recorded as a result of the Amendment. In June 2010, positive data was presented for the 006 carfilzomib trial, a phase 1b multicenter dose escalation study of carfilzomib plus lenalidomide and low-dose dexamethasone in relapsed and refractory multiple myeloma patients. In July 2010, positive data was also presented for the 003-A1 carfilzomib trial, an open label, single-arm phase 2b study of single-agent carfilzomib in relapsed and refractory multiple myeloma patients. The data from the 006 and 003-A1 trials positively impacted the PTRS. The remaining increase in the fair value of the non-current liability for contingent consideration of $18.4 million was due to the passage of time.

Escrow Account Liability

In accordance with the Merger Agreement, 10% of each of the total cash consideration payment in November 2009 and the first earn-out payment made to former Proteolix stockholders in April 2010 was placed in an escrow account and was to be held until December 31, 2010 to secure the indemnification rights of the Company and other indemnitees with respect to certain matters, including breaches of representations, warranties and covenants of Proteolix included in the Merger Agreement. However, in December 2010, the Company filed a claim notice in good faith describing circumstances that the Company believed entitled it to indemnification, compensation and/or reimbursement under the Merger Agreement. This amount was reported as restricted cash on the Company's Consolidated Balance Sheet at December 31, 2010 and was paid to former Proteolix stockholders in February 2011 after the settlement of the claim through the Amendment of the original Merger Agreement in January 2011.

Deferred Tax Liabilities

The $157.1 million of deferred tax liabilities resulting from the acquisition was related to the difference between the book basis and tax basis of the intangible assets related to the IPR&D projects.

Note 6. Derivative Instruments

In the third quarter of 2010, the Company established a foreign currency hedging program. The objective of the program is to mitigate the foreign exchange risk arising from transactions or cash flows that have a direct or underlying exposure in non-U.S. Dollar denominated currencies in order to reduce volatility in the Company's cash flow and earnings. The Company hedges a certain portion of anticipated Nexavar-related cash flows owed to the Company with options, typically no more than one year into the future. The Company's underlying exposures, both revenue and expenses, in the Nexavar program are denominated in currencies other than the U.S. Dollar, primarily the Euro and the Japanese Yen. For purposes of calculating the cash flows due to or due from the Company each quarter, the foreign currencies are converted into U.S. Dollars based on average exchange rates for the reporting period. The Company does not enter into derivative financial instruments for speculative purposes.

The fair values of the Company's derivative instruments are estimated as described in Note 7, taking into consideration current market rates and the current creditworthiness of the counterparties or the Company, as applicable. The Company's foreign currency options to hedge anticipated cash flows, where the underlying exposure of revenues and expenses from the Nexavar program are denominated in the Euro, have not been designated as hedging instruments under ASC 815. The changes in the fair value of these foreign currency options are included in the "Other expense" line item in the Consolidated Statements of Operations. The foreign currency options used to hedge anticipated cash flows, where the underlying exposure of royalty income from the Nexavar program is denominated in the Japanese Yen, are designated as cash flow hedges. At the inception of the hedge, the Company documents the risk management objectives and the nature of the risk being hedged, the hedged instrument and hedged item, as well as the manner in which hedge effectiveness and ineffectiveness will be assessed. On a prospective and retrospective basis, at least quarterly, the Company will assess hedge effectiveness based on the total changes in the option's cash flow. During the life of the hedge, the Company will periodically verify that the critical terms of the hedging instrument continue to match the forecasted transaction, the forecasted transaction is still probable in occurring at the same time as originally projected based on the most recent forecasts, and the counterparties are still able to honor their obligations under the hedge contract. Hedge ineffectiveness, both prospective and retrospective, will be assessed by evaluating the dollar offset ratio of the dollar change in fair value or cash flows of the hedging instrument with the amount of the dollar change in fair value or cash flows of the "perfectly effective" hypothetical hedging instrument that has the terms that meet the currency, notional amount,

timing and credit criteria. The change in the fair value of the hypothetical hedging instrument will be regarded as a proxy for the present value of the cumulative change in the expected future cash flows on the hedged transaction. The portion of hedge ineffectiveness will be recognized in earnings. The amount of ineffectiveness would be equal to the excess of the cumulative change in the fair value of the actual derivative over the cumulative change in the fair value of the "perfect" hypothetical hedging instrument.

The effective component of the hedge is recorded in accumulated other comprehensive income (OCI) within stockholders' equity as an unrealized gain or loss on the hedging instrument. When the hedged forecasted transactions occur and the hedge instrument matures, the hedges are de-designated and the unrealized gains and losses are reclassified into the "Other expense" line item in the Consolidated Statement of Operations. The majority of the gains and losses related to the hedged forecasted transactions reported in accumulated OCI at December 31, 2010 are expected to be reclassified to other income (expense) within 9 months. At December 31, 2010, the Company had outstanding foreign currency option contracts with maturity dates ranging from December 31, 2010 to September 30, 2011 and U.S. Dollar notional amounts ranging from $2.1 million to $13.3 million.

At December 31, 2010, the fair value carrying amount of the Company's derivative instruments were recorded as follows:

	Asset Derivatives December 31, 2010		Liability Derivatives December 31, 2010	
	Balance Sheet Location	Fair Value (In thousands)	Balance Sheet Location	Fair Value (In thousands)
Derivatives designated as hedges:				
Foreign currency option contracts	Other current assets	$ 89	Accrued liabilities	$ -
Total derivatives designated as hedges		89		-
Derivatives not designated as hedges:				
Foreign currency option contracts	Other current assets	$ 188	Accrued liabilities	$ -
Total derivatives not designated as hedges		188		-
Total derivatives		$ 277		$ -

The effect of derivative instruments on the Consolidated Balance Sheet and Consolidated Statements of Operations for the year ended December 31, 2010 was as follows:

	Foreign Currency Option Contracts Year Ended December 31, 2010 (In thousands)
Derivatives designated as hedges:	
Net gain (loss) recognized in accumulated other comprehensive income (loss) (effective portion)	$ (61)
Net gain (loss) reclassified from accumulated other comprehensive income to net income (loss) (effective portion)(1)	(10)
Net gain (loss) recognized in net income (loss) (ineffective portion)(1)	-
Derivatives not designated as hedges:	
Net gain (loss) recognized in net income (loss)(1)	(763)

(1) Classified in "Other expense" on the Consolidated Statement of Operations

The Company is exposed to counterparty credit risk on all of its derivative financial instruments. The Company has established and maintained strict counterparty credit guidelines and enters into derivative instruments only with

financial institutions that are investment grade or better to minimize the Company's exposure to potential defaults. The Company does not generally require collateral to be pledged under these agreements. Refer to Note 7 for further information.

Note 7. Fair Value Measurements

In accordance with ASC Subtopic 820-10, *Fair Value Measurements and Disclosures*, the Company measures certain assets and liabilities at fair value on a recurring basis using the three-tier fair value hierarchy, which prioritizes the inputs used in measuring fair value. The three tiers include:

- Level 1, defined as observable inputs such as quoted prices for identical assets in active markets;
- Level 2, defined as inputs other than quoted prices in active markets that are either directly or indirectly observable; and
- Level 3, defined as unobservable inputs in which little or no market data exists, therefore requiring management to develop its own assumptions based on best estimates of what market participants would use in pricing an asset or liability at the reporting date.

The Company's fair value hierarchies for its financial assets and liabilities (cash equivalents, current and non-current marketable securities, current and non-current liability from contingent consideration, foreign currency option contracts and convertible senior notes), which require fair value measurement on a recurring basis are as follows:

	As of December 31, 2010				
	As reflected on the balance sheet	Level 1	Level 2	Level 3	Total
			(In thousands)		
Assets:					
Money market funds	$ 20,932	$20,932	$ -	$ -	$ 20,932
Corporate and financial institutions debt	197,813	-	197,813	-	197,813
Auction rate securities	31,280	-	2,725	28,555	31,280
U.S. government agencies	99,294	-	99,294	-	99,294
U.S. treasury bills	78,916	78,916	-	-	78,916
Municipal bonds	37,160	-	37,160	-	37,160
Foreign currency option contracts designated as hedges	89	-	89	-	89
Foreign currency option contracts not designated as hedges	188	-	188	-	188
Total	$465,672	$99,848	$337,269	$ 28,555	$465,672
Liabilities:					
Liability for contingent consideration, current and non-current	$253,548	$ -	$ -	$253,548	$253,548
Convertible senior notes due 2016 (face value $230,000)	152,701	-	271,768	-	$271,768
Total	$406,249	$ -	$271,768	$253,548	$525,316

	As of December 31, 2009				
	As reflected on the balance sheet	Level 1	Level 2	Level 3	Total
			(In thousands)		
Assets:					
Money market funds	$ 83,115	$ 83,115	$ -	$ -	$ 83,115
Corporate and financial institutions debt	110,644	-	110,644	-	110,644
Auction rate securities	37,274	-	100	37,174	37,274
U.S. government agencies	168,692	-	168,692	-	168,692
U.S. treasury bills	183,090	183,090	-	-	183,090
Total	$582,815	$266,205	$279,436	$ 37,174	$582,815
Liabilities:					
Liability for contingent consideration, current and non-current	$200,528	$ -	$ -	$200,528	$200,528
Convertible senior notes due 2016 (face value $230,000)	143,669	-	242,098	-	242,098
Total	$344,197	$ -	$242,098	$200,528	$442,626

Auction Rate Securities

Auction rate securities are Level 3 assets classified as available for sale securities and are reflected at fair value. In February 2008, auctions began to fail for the auction rate securities and each auction for the majority of these securities since then has failed. As of December 31, 2010, the fair value of each of these securities is estimated utilizing a discounted cash flow analysis that considers interest rates, the timing and amount of cash flows, credit and liquidity premiums, and the expected holding periods of these securities. The following table provides a summary of changes in fair value of the Company's auction rate securities:

	Auction Rate Securities Year Ended December 31,	
	2010	2009
	(In thousands)	
Fair value at beginning of period	$37,174	$39,622
Redemptions	(6,550)	(5,600)
Transfer to Level 2	(2,725)	100
Change in valuation	656	3,052
Fair value at end of period	$28,555	$37,174

Transfers of auction rate securities from Level 3 to Level 2 are recognized when the Company becomes aware of actual redemptions of such securities. As a result of the decline in the fair value of the Company's auction rate securities, which the Company believes is temporary and attributes to liquidity rather than credit issues, the Company has recorded an unrealized loss of $1.4 million and $2.0 million for the years ended December 31, 2010 and 2009, respectively, included in the accumulated other comprehensive income (loss) line of stockholders' equity. All of the auction rate securities held by the Company at December 31, 2010, consist of securities collateralized by student loan portfolios, which are substantially guaranteed by the United States government. Any future fluctuation in fair value related to the non-current marketable securities that the Company deems to be temporary, including any recoveries of previous write-downs, will be recorded in accumulated other comprehensive income (loss). If the Company determines that any decline in fair value is other than temporary, it will record a charge to earnings as

appropriate. The Company does not intend to sell these securities and it is not more likely than not that the Company will be required to sell these securities prior to the recovery of their amortized cost bases.

Foreign Currency Option Contracts

Foreign currency option contracts are Level 2 assets and liabilities that are reflected at fair value. The Company has established a foreign currency hedging program to manage the economic risk of its exposure to fluctuations in foreign currency exchange rates from the Nexavar program. Refer to Note 6 for further information.

The Company has elected to use the income approach to value the derivatives, using observable Level 2 market expectations at the measurement date and standard valuation techniques to convert future amounts to a single present amount assuming that participants are motivated, but not compelled to transact. Level 2 inputs for the valuations are limited to quoted prices for similar assets or liabilities in active markets and inputs other than quoted prices that are observable for the asset or liability (specifically LIBOR cash, credit risk at commonly quoted intervals, spot and forward rates). Mid-market pricing is used as a practical expedient for fair value measurements. ASC 820 states that the fair value measurement of an asset or liability must reflect the non-performance risk of the entity and the counterparty. Therefore, the impact of the counterparty's creditworthiness, when in an asset position, and the Company's creditworthiness, when in a liability position, has also been factored into the fair value measurement of the derivative instruments and did not have a material impact on the fair value of these derivative instruments. Both the counterparty and the Company are expected to continue to perform under the contractual terms of the instruments.

Liability for Contingent Consideration

The Company initially recorded acquisition-related liabilities at the acquisition date for contingent consideration representing the amounts payable to former Proteolix stockholders, as outlined under the terms of the Merger Agreement, upon the achievement of specified regulatory approvals within pre-specified timeframes for carfilzomib. The fair values of these Level 3 liabilities are estimated using a probability-weighted discounted cash flow analysis. Subsequent changes in the fair value of these contingent consideration liabilities are recorded to the "Contingent consideration" expense line item in the Consolidated Statements of Operations under operating expenses. For the year ended December 31, 2010, the recognized amount of the liability for contingent consideration increased by $92.9 million primarily as the result of the change in the PTRS, a significant input in the discounted cash flow analysis used to calculate the fair value of the non-current liability and also, the passage of time, partially offset by a benefit recorded as a result of the Amendment. Refer to *Liability for Contingent Consideration* in Note 5 for further details.

	Liability for Contingent Consideration Year Ended December 31,	
	2010	2009
	(In thousands)	
Fair value at beginning of period	$200,528	$199,000
Payments	(40,000)	-
Change in valuation	92,930	1,528
Fair value at end of period	$253,458	$200,528

Convertible Senior Notes due 2016

The fair value of the Company's 2016 Notes as of December 31, 2010 is estimated by computing the fair value of a similar liability without the conversion option in accordance with ASC Subtopic 825-10, *Financial Instruments*. The Company's 2016 Notes are not marked-to-market and are shown in the accompanying consolidated balance sheet at their original issuance value net of amortized discount. The portion of the value allocated to the conversion option is included in stockholders' equity in the accompanying Consolidated Balance Sheet at December 31, 2010.

Note 8. Marketable Securities

The Company limits the amount of investment exposure as to institution, maturity, and investment type. Marketable securities consist of investments that are subject to concentration of credit risk that are classified as "available for sale." To mitigate credit risk, the Company invests in marketable debt securities, primarily United States government securities, agency bonds and corporate bonds and notes, with investment grade ratings. Such securities are reported at fair value, with unrealized gains and losses excluded from earnings and shown separately as a component of accumulated other comprehensive income (loss) within stockholders' equity. The Company may pay a premium or receive a discount upon the purchase of marketable securities. Interest earned and gains realized on marketable securities and amortization of discounts received and accretion of premiums paid on the purchase of marketable securities are included in investment income. There was a realized gain of $90,000 for the year ended December 31, 2010, a realized loss of $32,000 for the year ended December 31, 2009 and a realized gain of $483,000 for the year ended December 31, 2008. The weighted average maturity of the Company's marketable securities as of December 31, 2010 was six months.

Available-for-sale marketable securities consisted of the following:

	December 31, 2010			
	Adjusted Cost	Unrealized Gains	Unrealized Losses	Estimated Fair Value
		(In thousands)		
Agency bond investments:				
Current	$178,221	$ 18	$ (29)	$178,210
Total agency bond investments	178,221	18	(29)	178,210
Corporate debt investments:				
Current	237,547	175	(24)	237,698
Non-current	29,925	-	(1,370)	28,555
Total corporate investments	267,472	175	(1,394)	266,253
Total available-for-sale marketable securities	$445,693	$193	$(1,423)	$444,463

	December 31, 2009			
	Adjusted Cost	Unrealized Gains	Unrealized Losses	Estimated Fair Value
		(In thousands)		
Agency bond investments:				
Current	$349,254	$162	$ (156)	$349,260
Total agency bond investments	349,254	162	(156)	349,260
Corporate debt investments:				
Current	93,119	92	(31)	93,180
Non-current	39,200	-	(2,026)	37,174
Total corporate investments	132,319	92	(2,057)	130,354
Total available-for-sale marketable securities	$481,573	$254	$(2,213)	$479,614

The Company's investment portfolio includes $32.7 million of AAA rated auction rate securities that are collateralized by student loans. Since February 2008, these types of securities have experienced failures in the auction process. However, a limited number of these securities have been redeemed at par by the issuing agencies. As a result of the auction failures, interest rates on these securities reset at penalty rates linked to LIBOR or Treasury bill rates. The penalty rates are generally higher than interest rates set at auction. Due to the failures in the auction process, these securities are not currently liquid. Of the $32.7 million of par value auction rate securities, $2.7 million in securities were redeemed at par in January 2011. Therefore, the Company has classified a portion of the auction rate securities with a fair value of $2.7 million, based on the amount redeemed in January 2011, as

current marketable securities and the remaining auction rate securities with an estimated fair value of $28.6 million, based on a discounted cash flow model, as non-current marketable securities on the accompanying unaudited balance sheet at December 31, 2010. The Company has reduced the carrying value of the marketable securities classified as non-current by $1.4 million through accumulated other comprehensive income or loss instead of earnings because the Company has deemed the impairment of these securities to be temporary. The Company does not intend to sell these securities and management believes it is not more likely than not that the Company will be required to sell these securities prior to the recovery of their amortized cost bases.

Note 9. Property and Equipment

Property and equipment consist of the following:

	December 31,	
	2010	2009
	(In thousands)	
Computers, machinery and equipment	$ 7,634	$ 6,323
Furniture and fixtures	1,171	1,056
Leasehold and tenant improvements	6,074	6,078
Construction in progress	4,789	-
	19,668	13,457
Less accumulated depreciation and amortization	(8,846)	(5,984)
	$10,822	$ 7,473

Construction in progress relates to the construction of facilities in South San Francisco, California that the Company leased and subleased beginning in July 2010, which will serve as the Company's new corporate headquarters in 2011. Depreciation expense was $3.6 million, $1.6 million and $1.3 million for the years ended December 31, 2010, 2009 and 2008, respectively.

Note 10. Other Long-Term Assets

In December 2008, the Company entered into a development collaboration, option and license agreement with S*BIO. Under the terms of the agreement, in December 2008, the Company made a $25.0 million payment to S*BIO, of which the Company expensed $20.7 million as an up-front payment and recognized the remaining amount of $4.3 million as an equity investment. As a result, the accompanying Consolidated Balance Sheet at December 31, 2010 includes $4.3 million for this long-term private equity investment in other long-term assets. The equity investment is accounted for using the cost method of accounting. At December 31, 2010, there has been no impairment of the carrying value of the Company's investment and there have been no events or changes in circumstances identified by the Company that would adversely impact the fair value of this investment.

S*BIO qualifies as a variable interest entity, or VIE. However, the Company does not have the power to direct the activities that most significantly impact the performance of S*BIO because S*BIO has other compounds in development and has the decision making authority and the power to control the clinical research of these compounds. Therefore, the Company is not considered the primary beneficiary and consolidation is not required. The equity investment in S*BIO could result in the Company absorbing losses up to the amount of its investment.

In May 2010, the Company announced the expansion of its development collaboration, option and license agreement with S*BIO related to its novel JAK inhibitors, ONX 0803 and ONX 0805. The expanded agreement builds upon the development and commercialization collaboration between the two companies announced in January 2009. The Company provided an additional $20.0 million in funding to S*BIO to broaden and accelerate the existing development program for both compounds. S*BIO agreed to utilize the funding to continue to perform the clinical development of ONX 0803 and preclinical through clinical development of ONX 0805. The Company capitalized the $20.0 million as prepaid research and development expense and is amortizing a portion of this amount as research and development expense each period based on the actual expenses incurred by S*BIO for the development of ONX 0803 and ONX 0805.

The development collaboration, option and licensing agreement with S*BIO will remain in effect until the expiration of all payment obligations. Because the Company has not exercised its option in the agreement, the Company may terminate the agreement at any time without cause by giving S*BIO prior written notice. In addition, either party may terminate the agreement for the uncured material breach of the other party.

Note 11. Convertible Senior Notes due 2016

In August 2009, the Company issued $230.0 million aggregate principal amount of 4.0% convertible senior notes due 2016, or the 2016 Notes. The 2016 Notes will mature on August 15, 2016 unless earlier redeemed or repurchased by the Company or converted. The 2016 Notes bear interest at a rate of 4.0% per year, payable semi-annually in arrears on February 15 and August 15 of each year, commencing on February 15, 2010.

The 2016 Notes are general unsecured senior obligations of the Company and rank equally in right of payment with all of the Company's future senior unsecured indebtedness, if any, and senior in right of payment to the Company's future subordinated debt, if any.

On or after May 15, 2016, the 2016 Notes will be convertible, under certain circumstances and during certain periods, at an initial conversion rate of 25.2207 shares of common stock per $1,000 principal amount of the 2016 Notes, which is equivalent to an initial conversion price of approximately $39.65 per share of common stock. The conversion rate is subject to adjustment in certain circumstances. Upon conversion of a 2016 Note, the Company will deliver, at its election, shares of common stock, cash or a combination of cash and shares of common stock.

Upon the occurrence of certain fundamental changes involving the Company, holders of the 2016 Notes may require the Company to repurchase all or a portion of their 2016 Notes for cash at a price equal to 100% of the principal amount of the 2016 Notes to be purchased, plus accrued and unpaid interest to, but excluding, the fundamental change repurchase date.

Beginning August 20, 2013, the Company may redeem all or part of the outstanding 2016 Notes, provided that the last reported sale price of the common stock for 20 or more trading days in a period of 30 consecutive trading days ending on the trading day prior to the date the Company provides the notice of redemption to holders of the 2016 Notes exceeds 130% of the conversion price in effect on each such trading day. The redemption price will equal 100% of the principal amount of the 2016 Notes to be redeemed, plus all accrued and unpaid interest, plus a "make-whole premium" payment. The Company must make the make-whole premium payments on all 2016 Notes called for redemption prior to August 15, 2016, including the 2016 Notes converted after the date the Company delivered the notice of redemption.

The 2016 Notes are accounted for in accordance with ASC Subtopic 470-20, *Debt with Conversion and Other Options*. Under ASC Subtopic 470-20, issuers of certain convertible debt instruments that have a net settlement feature and may be settled in cash upon conversion, including partial cash settlement, are required to separately account for the liability (debt) and equity (conversion option) components of the instrument. The carrying amount of the liability component of any outstanding debt instrument is computed by estimating the fair value of a similar liability without the conversion option. The amount of the equity component is then calculated by deducting the fair value of the liability component from the principal amount of the convertible debt instrument.

The following is a summary of the equity and liability components of the 2016 Notes, its net carrying amount and its unamortized discount:

	December 31, 2010	
	2010	2009
	(In thousands)	
Carrying amount of the equity component	$89,468	$89,468
Net carrying amount of the liability component	$63,233	$54,201
Unamortized discount of the liability component	$77,299	$86,331

The effective interest rate used in determining the liability component of the 2016 Notes was 12.5%. The application of ASC Subtopic 470-20 resulted in an initial recognition of $89.5 million as the debt discount with a corresponding increase to paid-in capital, the equity component, for the 2016 Notes. The debt discount and debt

issuance costs are amortized as interest expense through August 2016. The cash interest expense for the years ended December 31, 2010 and 2009 for the 2016 Notes was $9.3 million and $3.5 million, respectively, relating to the 4.0% stated coupon rate. The non-cash interest expense relating to the amortization of the debt discount for the 2016 Notes for the years ended December 31, 2010 and 2009 was $9.0 million and $3.1 million, respectively.

Note 12. 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 current corporate headquarters. 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. In 2008, the Company entered into another operating lease for an additional 23,000 square feet of office space in Emeryville, California. This lease expires on November 30, 2013.

In 2009, the Company acquired an operating lease in South San Francisco, California through its acquisition of Proteolix. The lease, which expires October 2014, includes 67,000 square feet of office and laboratory space and has options to extend the lease for two additional one-year terms after the initial lease expiration. The lease provides for fixed increases in minimum annual rental payments, as well as rent free periods. As a result of the Company determining that the estimated fair value of the operating lease was less than the rent obligations, the Company recorded a liability for the difference between the rent obligations and the estimated fair value. This liability will be amortized over the life of the lease using the effective interest rate method.

The Company also had a lease for 9,000 square feet of space in a secondary facility in Richmond, California. In September 2002, the Company entered into a sublease agreement for this space through September 2010. The lease for this facility expired in September 2010.

In July 2010, the Company entered into an operating lease and sublease for approximately 126,493 square feet located at 249 East Grand Avenue, South San Francisco, California, which will serve as the Company's new corporate headquarters in 2011. The lease and the sublease expire in 2021 and 2015, respectively. Upon expiration of the sublease, the lease will be automatically expanded to include the premises subject to the sublease. The lease includes two successive five-year options to extend the term of the lease. The lease also includes a one-time option exercisable until 2014 to lease additional premises that will be constructed after the exercise of the option. If the option is exercised, the term of the lease will be automatically extended by ten years.

Minimum annual rental commitments, net of sublease income, under all operating leases at December 31, 2010 are as follows (in thousands):

Year ending December 31:	
2011	$ 7,345
2012	8,144
2013	7,464
2014	6,205
2015	3,831
Thereafter	28,505
	$61,494

Rent expense, net of sublease income, for the years ended December 31, 2010, 2009 and 2008 was approximately $4.3 million, $1.8 million and $1.0 million, respectively. Sublease income was $66,000, $54,000 and $72,000 for the years ended December 31, 2010, 2009 and 2008, respectively.

Note 13. 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 $16,500 of their eligible compensation, subject to certain Internal Revenue Service restrictions. Historically, the Company did not match employee contributions in the 401(k) Plan. Beginning in fiscal

year 2008, the Company provided a discretionary company match to employee contributions of $0.50 per dollar contributed, up to a maximum match of $3,500 in any calendar year. Effective January 1, 2011, the company match was increased to a maximum match of $4,500 in any calendar year. The Company incurred total expenses of $914,000, $683,000 and $548,000 related to 401(k) contribution matching for the years ended December 31, 2010, 2009 and 2008, respectively.

Note 14. 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, or the "2005 Plan." Prior to adoption of the 2005 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 prior plans:

1) The 1996 Equity Incentive Plan, or the "1996 Plan," which amended and restated the 1992 Incentive Stock Plan in March 1996. The Company's Board of Directors reserved 1,725,000 shares of common stock for issuance under the 1996 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 1996 Plan. The 1996 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. Stock options may be granted with an exercise price not less than 100% of the fair market value of the common stock on the date of grant. Stock options are generally granted with terms of up to ten years and vest over a period of four years.

2) The 1996 Non-Employee Directors' Stock Option Plan, or 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. Stock options may be granted with an exercise price not less than 100% of the fair market value of the common stock on the date of grant. Stock options are generally granted with terms of up to ten years and vest over a period of four years.

The 2005 Plan was approved at the Company's annual meeting of stockholders to supersede and replace both the 1996 Plan and the Directors' Plan 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 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 Plan. All outstanding stock awards granted under the two prior plans remain subject to the terms of those plans. Subsequently, at annual meetings of stockholders, a total of 9,700,000 shares were approved to be added to the 2005 Plan reserve for a total of 17,260,045 shares available for issuance.

In March 1996, the Board of Directors adopted the Employee Stock Purchase Plan, or ESPP. The number of shares available for issuance over the term of the ESPP was limited to 400,000 shares. At the May 2007 Annual Meeting of Stockholders an additional 500,000 shares were added to the ESPP for a total of 900,000 shares available for issuance over the term of the ESPP. 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% 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 78,991 shares in 2010, 45,435 shares in 2009 and 37,631 shares in 2008. Since inception, a total of 544,664 shares have been issued under the ESPP, leaving a total of 355,336 shares available for issuance.

In December 2010, stock options were exercised that were not settled prior to December 31, 2010. The Company recorded a receivable from stock option exercises of $6,000 at December 31, 2010 related to these stock options, which is included in the caption "Receivable from stock option exercises" in the accompanying Consolidated Balance Sheets and Consolidated Statements of Stockholders' Equity as of December 31, 2010. The Company

recorded a receivable from stock option exercises of $5,000 at December 31, 2009, related to stock options exercised that had not settled prior to December 31, 2009.

Common Stock Offering

In August 2009, the Company sold 4,600,000 shares of its common stock at a price to the public of $30.50 per share in an underwritten public offering pursuant to an effective registration statement previously filed with the Securities and Exchange Commission. The Company received cash proceeds, net of underwriting discounts and commissions, of approximately $134.0 million from this public offering.

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, 2010, 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. In May 2009, the Company issued an aggregate of 5,852 shares of its common stock pursuant to a cashless net exercise of 9,259 warrants. As of December 31, 2009 and 2010, no warrants remained outstanding.

Note 15. Stock-Based Compensation

The Company accounts for stock-based compensation of stock options granted to employees and directors and of employee stock purchase plan shares by estimating the fair value of stock-based awards using the Black-Scholes option-pricing model and amortizing the fair value of the stock-based awards granted over the applicable vesting period. The Black-Scholes option pricing model includes assumptions regarding dividend yields, expected volatility, expected option term and risk-free interest rates. The Company estimates expected volatility based upon a combination of historical and implied stock prices. The risk-free interest rate is based on the U.S. treasury yield curve in effect at the time of grant. The expected option term calculation incorporates historical employee exercise behavior and post-vesting employee termination rates. The Company accounts for stock-based compensation of restricted stock award grants by amortizing the fair value of the restricted stock award grants, which is the grant date market price, over the applicable vesting period.

Employee stock-based compensation for the years ended December 31, 2010, 2009 and 2008, was as follows:

	Year Ended December 31,		
	2010	2009	2008
	(In thousands except per share data)		
Research and development	$ 4,252	$ 3,574	$ 3,166
Selling, general and administrative	17,865	17,506	15,630
Total share-based compensation expense	$22,117	$21,080	$18,796
Impact on basic net income (loss) per share	$ 0.35	$ 0.36	$ 0.34
Impact on diluted net income (loss) per share	$ 0.35	$ 0.35	$ 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. 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 $0.7 million, $1.5 million and $1.7 million for the years ended December 31, 2010, 2009 and 2008, respectively.

As of December 31, 2010, the total unrecorded stock-based compensation expense for unvested stock options shares, net of expected forfeitures, was $37.5 million, which is expected to be amortized over a weighted-average period of 2.7 years. As of December 31, 2010, the total unrecorded stock-based compensation expense for unvested restricted stock awards, net of expected forfeitures, was $6.8 million, which is expected to be amortized over a weighted-average period of 1.6 years. Cash received during the year ended December 31, 2010, for stock options exercised under all stock-based compensation arrangements was $6.9 million.

For the years ended December 31, 2010, 2009 and 2008, the total fair value of restricted stock awards vested was $5.0 million, $3.6 million and $1.8 million, respectively, based on weighted average grant date per share fair values of $28.74, $28.49 and $24.89 for the years ended December 31, 2010, 2009 and 2008, respectively.

Valuation Assumptions

As of December 31, 2010, 2009 and 2008, the fair value of stock-based awards for employee stock option awards, restricted stock 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,		
	2010	2009	2008
Stock Option Plans:			
Risk-free interest rate	2.06%	1.95%	2.86%
Expected life	4.4 years	4.3 years	4.4 years
Expected volatility	55%	64%	64%
Expected dividends	None	None	None
Weighted average option fair value	$13.12	$15.15	$17.32
Restricted stock awards:			
Expected life	3 years	3 years	3 years
Expected dividends	None	None	None
Weighted average fair value per share	$29.92	$29.05	$30.80
ESPP:			
Risk-free interest rate	0.18%	0.29%	2.69%
Expected life	6 months	6 months	6 months
Expected volatility	46%	60%	59%
Expected dividends	None	None	None
Weighted average fair value per share	$6.25	$9.16	$13.56

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, 2007, the expected stock price volatility assumption was determined using a combination of historical and implied volatility for the Company's stock. The Company has determined that the combined method of determining volatility is more reflective of market conditions and a better indicator of expected volatility than historical volatility. The Company considers several factors in estimating the expected life of its options granted, including the expected lives used by a peer group of companies and the historical option exercise behavior of its employees, which it believes 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, 2010, 2009 and 2008:

	Shares Available for Grant	Number of Shares Outstanding	Weighted Average Exercise Price
Employee stock options:			
Balance at December 31, 2007	2,753,688	4,437,906	$25.39
Shares authorized	3,100,000	-	-
Granted	(1,624,036)	1,624,036	$32.81
Exercised	-	(1,145,281)	$21.90
Expired	13,642	(13,642)	$35.71
Forfeited	336,345	(336,345)	$26.88
Balance at December 31, 2008	4,579,639	4,566,674	$28.76
Shares authorized	2,000,000	-	-
Granted	(1,476,972)	1,476,972	$29.47
Exercised	-	(552,607)	$22.02
Expired	181,043	(181,043)	$37.92
Forfeited	241,886	(241,886)	$26.50
Balance at December 31, 2009	5,525,596	5,068,110	$29.48
Shares authorized	3,000,000	-	-
Granted	(2,013,989)	2,013,989	$28.57
Exercised	-	(323,436)	$21.22
Expired	98,172	(98,172)	$34.69
Forfeited	386,020	(386,020)	$30.36
Balance at December 31, 2010	6,995,799	6,274,471	

	Shares	Weighted Average Grant Date Fair Value
Restricted stock awards:		
Balance at December 31, 2007	180,023	$24.42
Granted	223,015	$30.72
Vested	(72,551)	$24.89
Cancelled	(34,645)	$26.51
Balance at December 31, 2008	295,842	$28.81
Granted	233,934	$28.92
Vested	(128,014)	$28.49
Cancelled	(33,121)	$27.39
Balance at December 31, 2009	368,641	$29.12
Granted	250,464	$29.68
Vested	(172,870)	$28.74
Cancelled	(54,713)	$28.94
Balance at December 31, 2010	391,522	$28.91

The options outstanding and exercisable for stock-based payment awards as of December 31, 2010 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
$ 4.20 - $26.21	1,298,804	6.1	$22.45	838,756	$21.39
$26.26 - $28.62	1,674,304	7.7	$28.11	802,740	$28.36
$28.66 - $30.28	1,978,264	8.0	$29.66	748,490	$29.33
$30.50 - $54.83	1,261,599	6.6	$36.97	877,334	$37.60
$55.06 - $56.21	61,500	7.0	$55.79	47,553	$55.75
Total	6,274,471	7.2	$29.48	3,314,873	$29.65

As of December 31, 2010, weighted average contractual life remaining for exercisable shares is 6.2 years. The total number of in-the-money options exercisable as of December 31, 2010 was 3,314,873 shares. The aggregate intrinsic values of options exercised were $3.0 million and $6.1 million for the years ended December 31, 2010 and 2009, respectively. The aggregate intrinsic values of in-the-money outstanding and exercisable options were $50.2 million and $27.0 million, respectively, as of December 31, 2010. The aggregate intrinsic value of options represents the total pre-tax intrinsic value, based on the Company's closing stock price of $36.87 at December 31, 2010, which would have been received by option holders had all option holders exercised their options that were in-the-money as of that date.

As of December 31, 2009, 2,525,317 outstanding options were exercisable, at a weighted average price of $28.93. As of December 31, 2008, 1,956,714 outstanding options were exercisable, at a weighted average price of $28.20.

Note 16. Comprehensive Income (Loss)

Comprehensive income (loss) is comprised of net income (loss) and other comprehensive income (loss). Other comprehensive income (loss) is comprised of unrealized holding gains and losses on the Company's available-for-sale securities that are excluded from net income (loss) and reported separately in stockholders' equity and

changes in the fair value of the Company's outstanding derivative instruments that have been designated as hedging instruments. Comprehensive income (loss) and its components are as follows:

	Year Ended December 31,		
	2010	2009	2008
	(In thousands)		
Net income (loss)	$(84,847)	$16,161	$ 1,948
Other comprehensive income (loss):			
Change in unrealized gain (loss) on available-for-sale securities	732	2,358	(4,676)
Change in unrealized gain (loss) on derivatives designated as hedges	(61)	-	-
Comprehensive income (loss)	$(84,176)	$18,519	$(2,728)

The activities in other comprehensive income (loss) are as follows:

	Year Ended December 31,		
	2010	2009	2008
	(In thousands)		
Available-for-sale securities:			
Increase (decrease) in unrealized gain (loss) on available-for-sale securities	$642	$2,390	$(5,159)
Reclassification adjustment for net gains (losses) on available-for-sale securities included in net income	90	(32)	483
Change in unrealized gain (loss) on available-for-sale securities	$732	$2,358	$(4,676)
Derivatives:			
Increase (decrease) in unrealized gain (loss) on derivatives designated as hedges	$(61)	$ -	$ -
Realized gain (loss) reclassified from accumulated other comprehensive income to net income (loss)	(10)	-	-
Change in unrealized gain (loss) on derivatives designated as hedges	$(71)	$ -	$ -

Note 17. Income Taxes

Income from continuing operations before taxes for the years ended December 31, 2010, 2009 and 2008 consists of the following:

	Year Ended December 31,		
	2010	2009	2008
	(In thousands)		
U.S. operations	$ 83,834	$17,394	$2,295
Foreign operations	(169,500)	-	-
Income (loss) before income tax expense	$ (85,666)	$17,394	$2,295

For the years ended December 31, 2010, 2009 and 2008, the Company recorded a benefit for income taxes of $0.8 million and a provision for income taxes of $1.2 million and $0.3 million, respectively, related to income from continuing operations. The components of the (benefit) provision for income taxes were as follows:

	Year Ended December 31,		
	2010	2009	2008
	(In thousands)		
Current:			
Federal	$(767)	$ 624	$226
State	(52)	609	121
Total current	(819)	1,233	347
Deferred:			
Federal	-	-	-
State	-	-	-
Total deferred	-	-	-
Total (benefit) provision for income taxes	$(819)	$1,233	$347

The Company's federal tax benefit in 2010 principally related to its election to carryback net operating losses under the Worker, Homeownership and Business Association Act of 2009. The election enabled the Company to eliminate all federal Alternative Minimum Taxes (AMT) previously recorded in 2009. The Company's federal tax provision in 2009 and 2008 was principally related to U.S. alternative minimum tax based on the Company's ability to fully offset current regular federal taxable income with its federal net operating loss carryforwards. The 2009 and 2008 state tax liability was greater than might otherwise be expected due to the State of California suspending the utilization of California net operating losses for those years.

Reconciliation between the Company's effective tax rate and the U.S. statutory tax rate for the years ended December 31, 2010, 2009 and 2008 is as follows:

	Year Ended December 31,		
	2010	2009	2008
Federal income tax at statutory rate	35%	35%	34%
State income tax, net of federal benefit	0%	2%	3%
Federal minimum tax	0%	4%	10%
Foreign rate differential	(69)%	0%	0%
Stock compensation expense	(3)%	11%	55%
Research credits expense add-back	(8)%	5%	51%
Non-deductible meals and entertainment expense	(1)%	2%	17%
Other non-deductible expenses	0%	1%	6%
Capitalized acquisition costs	0%	11%	0%
Contingent consideration	(32)%	3%	0%
Other	1%	0%	0%
Change in valuation allowance	78%	(67)%	(161)%
Income tax expense	1%	7%	15%

Deferred income taxes reflect the net tax effects of temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes. Significant components of the Company's deferred tax assets and liabilities as of December 31, 2010 and 2009 are as follows:

	December 31,	
	2010	2009
	(In thousands)	
Deferred tax assets:		
Net operating loss carryforwards	$ 107,435	$ 182,228
Tax credit carryforwards	76,986	52,431
Capitalized research and development	84	160
Accrued expenses	3,721	5,238
Stock options	12,874	9,753
Property and equipment	609	1,192
Intangible assets	61,751	11,964
Other long-term assets	2,521	2,991
Contingent consideration	14,406	11,518
Capitalized costs	9,791	11,870
Other	17	-
Total deferred tax assets	290,195	289,345
Valuation allowance	(250,662)	(258,439)
Total deferred tax assets after valuation allowance	39,533	30,906
Deferred tax liabilities:		
Discount on debt offering	(27,673)	(30,906)
Intangible assets — in-process research and development	(157,090)	(157,090)
Total deferred tax liabilities	(184,763)	(187,996)
Net deferred tax assets (liabilities)	$(145,230)	$(157,090)

As part of accounting for the acquisition of Proteolix, the Company recorded goodwill and intangible assets. Amortization expenses associated with acquired intangible assets are generally not tax deductible. Intangible assets acquired for use in a particular research and development project are considered indefinite-lived intangible assets until the completion or abandonment of the associated research and development efforts. Deferred taxes will continue to be recognized for the difference between the book and tax bases of indefinite-lived intangible assets as well as amortizable intangible assets. As a result, a deferred tax liability was established for the IPR&D of $157.1 million as a part of the business combination accounting.

Realization of deferred tax assets is dependent upon future earnings, if any, the timing and the amount of which are uncertain. Accordingly, the net deferred tax assets, not including the deferred tax liability related to IPR&D, have been fully offset by a valuation allowance. The valuation allowance decreased by $7.8 million in 2010, increased by $45.3 million in 2009 and decreased by $6.8 million in 2008. The Company continues to maintain a full valuation allowance against most of its net operating loss carryforwards and other deferred tax assets because the Company does not believe it is more likely than not that they will be realized. On a quarterly basis, the Company reassesses its valuation allowance for deferred income taxes. The Company will consider reducing the valuation allowance when it becomes more likely than not the benefit of those assets will be realized.

At December 31, 2010, the Company has net operating loss carryforwards for federal and state income tax purposes of approximately $271.2 million and $434.6 million, respectively. These net operating losses may be available to reduce future taxable income, if any. Approximately $28.8 million of the federal and $27.1 million of the state valuation allowance for deferred tax assets related to net operating loss carryforwards represents 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. The federal net operating loss carryforwards expire beginning in 2025 through 2029,

and the state net operating loss carryforwards begin to expire in 2014 through 2031 and may be subject to certain limitations. As of December 31, 2010, the Company has research and development credit and orphan drug credit carryforwards of approximately $68.8 million for federal income tax purposes that expire beginning in 2011 through 2030, and $12.1 million for California income tax purposes, which do not expire.

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

The Company adopted authoritative guidance under ASC 740 on January 1, 2007, which clarifies the accounting for uncertainty in tax positions recognized in the financial statements. As of December 31, 2010, the Company recognized $11.9 million of unrecognized tax benefits. The Company had no unrecognized income tax benefits during the years ended December 31, 2009 and 2008. The Company is in process of completing an analysis of its tax credit carryforwards. Any uncertain tax positions identified in the course of this analysis will not impact the consolidated financial statements due to the full valuation allowance.

A reconciliation of the beginning and ending amount of unrecognized tax benefits is as follows:

	Year Ended December 31,		
	2010	2009	2008
	(In thousands)		
Balance at January 1	$ -	$-	$-
Additions based on tax positions related to the current year	11,860	-	-
Additions/ Reductions for tax positions of prior years	-	-	-
Reductions for tax positions of prior years	-	-	-
Settlement	-	-	-
Balance at December 31	$11,860	$-	$-

At December 31, 2010, all unrecognized tax benefits are subject to full valuation allowance and, if recognized, will not affect the annual effective tax rate.

The Company's policy for classifying interest and penalties associated with unrecognized income tax benefits is to include such items as tax expense. No interest or penalties have been recorded during the years ended December 31, 2010, 2009 and 2008.

The Company does not expect to have any significant changes to unrecognized tax benefits over the next twelve months other than potentially an adjustment resulting from our tax credit analysis mentioned above. The tax years from 1993 and forward remain open to examination by federal and California authorities due to net operating loss and credit carryforwards. The Company is currently not under examination by the Internal Revenue Service or any other taxing authorities.

Note 18. 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 to 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, 2010 or 2009 as the value of the indemnification obligations, if any, are 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 19. 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.

	2010 Quarter Ended			
	December 31	September 30	June 30	March 31
	(In thousands, except per share data)			
Revenue:				
Revenue from collaboration agreement	$ 69,978	$ 63,696	$ 68,773	$ 62,903
License revenue	-	59,165	-	-
Total revenue	69,978	122,861	68,773	62,903
Operating expenses:				
Research and development expenses	54,346	44,568	43,251	43,575
Selling, general and administrative expenses	36,875	25,924	26,647	24,721
Contingent consideration	(8,177)	5,622	92,037	3,448
Income (loss) from operations	(13,066)	46,747	(93,162)	(8,841)
Investment income, net	632	628	780	789
Interest expense	(4,933)	(4,943)	(4,800)	(4,724)
Other income (expense)	89	(862)	-	-
Provision (benefit) for income taxes	(157)	70	-	(732)
Net income (loss)	$(17,121)	$ 41,500	$(97,182)	$(12,044)
Basic net income (loss) per share	$ (0.27)	$ 0.66	$ (1.55)	$ 0.19
Diluted net income (loss) per share	$ (0.27)	$ 0.66	$ (1.55)	$ 0.19

	2009 Quarter Ended			
	December 31	September 30	June 30	March 31
	(In thousands, except per share data)			
Revenue:				
Revenue from collaboration agreement	$67,317	$69,137	$60,219	$53,717
Contract revenue	1,000	-	-	-
Total revenue	68,317	69,137	60,219	53,717
Operating expenses:				
Research and development expenses	36,028	35,635	28,022	28,820
Selling, general and administrative expenses	32,232	23,440	23,507	21,953
Contingent consideration	1,528	-	-	-
Income (loss) from operations	(1,471)	10,062	8,690	2,944
Investment income, net	920	1,015	972	1,121
Interest expense	(4,603)	(2,255)	-	-
Provision for income taxes	(355)	(589)	(288)	-
Net income (loss)	$ (5,509)	$ 8,233	$ 9,374	$ 4,065
Basic net income (loss) per share	$ (0.09)	$ 0.14	$ 0.16	$ 0.07
Diluted net income (loss) per share	$ (0.09)	$ 0.14	$ 0.16	$ 0.07

Note 20. Subsequent Events

In January 2011, the Company entered into an Amendment No. 1 to the Agreement and Plan of Merger, or the Amendment, with Shareholder Representative Services LLC (SRS). The Amendment amended the Merger Agreement entered into in October 2009 among the Company, Proteolix, SRS, and Profiterole Acquisition Corp., pursuant to which the Company had acquired Proteolix in November 2009.

Under the original Merger Agreement, the aggregate cash consideration paid to former Proteolix stockholders at closing was $276.0 million and an additional $40.0 million earn-out payment was made in April 2010. The Company may be required to pay up to an additional $535.0 million in up to four earn-out payments, upon the achievement of regulatory approvals for carfilzomib in the United States and Europe within pre-specified timeframes. Under the original Merger Agreement, the first of these additional earn-out payments would be in the amount of $170.0 million (the "Accelerated Approval Earn-Out"), if achieved by the date originally contemplated, and would be triggered by accelerated marketing approval for carfilzomib in the United States for relapsed/refractory multiple myeloma (the "Accelerated Approval Milestone"). This obligation is unchanged in the Amendment.

The Amendment modifies the amount of the Accelerated Approval Earn-Out if the Accelerated Approval Milestone is not achieved by the date originally contemplated on a sliding scale basis, as follows:

- if the Accelerated Approval Milestone is achieved after the date originally contemplated, but within six months of the original date, subject to extension under certain circumstances, then the amount payable will be reduced to $130.0 million; and
- if the Accelerated Approval Milestone is achieved more than six months after the date originally contemplated, but within twelve months of the original date, subject to extension under certain circumstances, then the amount payable will be reduced to $80.0 million.

In addition, funds held in the escrow account to secure the indemnification rights of the Company and other indemnitees with respect to certain matters, including breaches of representations, warranties and covenants of Proteolix under the Merger Agreement were paid to former Proteolix stockholders in February 2011.

Exhibits

Exhibit Number	Description of Document
2.1(1)*	Agreement and Plan of Merger dated as of October 10, 2009 among the Company, Proteolix, Inc., Profiterole Acquisition Corp., and Shareholder Representative Services LLC.
3.1(2)	Restated Certificate of Incorporation of the Company.
3.2(3)	Amended and Restated Bylaws of the Company.
3.3(4)	Certificate of Amendment to Amended and Restated Certificate of Incorporation.
3.4(5)	Certificate of Amendment to Amended and Restated Certificate of Incorporation.
4.1	Reference is made to Exhibits 3.1, 3.2, 3.3 and 3.4.
4.2(2)	Specimen Stock Certificate.
4.3(6)	Indenture dated as of August 12, 2009 between the Company and Wells Fargo Bank, National Association.
4.4(6)	First Supplemental Indenture dated as of August 12, 2009 between the Company and Wells Fargo Bank, National Association.
4.5(6)	Form of 4.00% Convertible Senior Note due 2016.
10.1(i)(7)*	Collaboration Agreement between Bayer Corporation (formerly Miles, Inc.) and the Company dated April 22, 1994.
10.1(ii)(7)*	Amendment to Collaboration Agreement between Bayer Corporation and the Company dated April 24, 1996.
10.1(iii)(7)*	Amendment to Collaboration Agreement between Bayer Corporation and the Company dated February 1, 1999.
10.2(i)*	Amended and Restated Research, Development and Marketing Collaboration Agreement effective as of May 2, 1995 between the Company and Warner-Lambert Company.
10.2(ii)(8)*	Research, Development and Marketing Collaboration Agreement dated July 31, 1997 between the Company and Warner-Lambert Company.
10.2(iii)(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(iv)(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(v)(8)*	Second Amendment to Research, Development and Marketing Collaboration Agreement between Warner-Lambert and the Company dated July 31, 1997.
10.2(vi)(9)*	Amendment #3 to the Research, Development and Marketing Collaboration Agreement between the Company and Warner-Lambert dated August 6, 2001.
10.2(vii)(10)*	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(11)*	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(2)+	Letter Agreement between Dr. Gregory Giotta and the Company dated May 26, 1995.
10.5(2)+	1996 Equity Incentive Plan.
10.6(2)+	1996 Non-Employee Directors' Stock Option Plan.
10.7(12)+	1996 Employee Stock Purchase Plan.
10.8(2)+	Form of Indemnity Agreement to be signed by executive officers and directors of the Company.
10.9(13)+	Form of Executive Change in Control Severance Benefits Agreement.
10.10(i)(14)*	Collaboration Agreement between the Company and Warner-Lambert Company dated October 13, 1999.
10.10(ii)(9)*	Amendment #1 to the Collaboration Agreement between the Company and Warner-Lambert dated August 6, 2001.
10.10(ii)(15)*	Second Amendment to the Collaboration Agreement between the Company and Warner-Lambert Company dated September 16, 2002.

Exhibit Number	Description of Document
10.11(16)	Stock and Warrant Purchase Agreement between the Company and the investors dated May 6, 2002.
10.12(i)(17)	Sublease between the Company and Siebel Systems dated August 5, 2004.
10.12(ii)(18)	First Amendment to Sublease between the Company and Oracle USA Inc., dated November 3, 2006.
10.13(i)(19)+	2005 Equity Incentive Plan.
10.13(ii)(18)+	Form of Stock Option Agreement pursuant to the 2005 Equity Incentive Plan.
10.13(iii)(18)+	Form of Stock Option Agreement pursuant to the 2005 Equity Incentive Plan and the Non-Discretionary Grant Program for Directors.
10.13(iv)(20)+	Form of Stock Bonus Award Grant Notice and Agreement between the Company and certain award recipients.
10.14(7)*	United States Co-Promotion Agreement by and between the Company and Bayer Pharmaceuticals Corporation, dated March 6, 2006.
10.15(21)+	Letter Agreement between Laura A. Brege and the Company, dated May 19, 2006.
10.16	Reserved.
10.17(22)	Common Stock Purchase Agreement between the Company and Azimuth Opportunity Ltd., dated September 29, 2006.
10.18(32)+	Letter Agreement between Michael Kauffman, M.D., and the Company, dated October 10, 2009.
10.19(31)+	Base Salaries and Bonus Potential for Fiscal Year 2010, Cash Bonuses for Fiscal Year 2009 and 2010 Equity Compensation Awards for Named Executive Officers.
10.20(i)(24)+	Employment Agreement between the Company and N. Anthony Coles, M.D., dated as of February 22, 2008.
10.20(ii)(23)	Amendment to Executive Employment Agreement between the Company and N. Anthony Coles, M.D., effective as of March 12, 2009.
10.21(24)+	Executive Change in Control Severance Benefits Agreement between the Company and N. Anthony Coles, M.D., dated as of February 22, 2008.
10.22(32)**	License and Supply Agreement, dated October 12, 2005, by and between CyDex, Inc. and Proteolix, Inc., as amended.
10.23	Reserved.
10.24	Reserved.
10.25(3)+	Onyx Pharmaceuticals, Inc. Executive Severance Benefit Plan.
10.26(26)+	Letter Agreement between the Company and Matthew K. Fust, dated December 12, 2008.
10.27(27)*	Development and License Agreement between the Company and BTG International Limited, dated as of November 6, 2008.
10.28(i)(23)+	Letter Agreement between the Company and Juergen Lasowski, Ph.D., dated April 28, 2008.
10.28(ii)(23)+	Amendment to Letter Agreement between the Company and Juergen Lasowski, Ph.D., effective as of March 12, 2009.
10.29(28)+	Executive Employment Agreement between the Company and Suzanne M. Shema, effective as of August 31, 2009.
10.30(29)+	Letter Agreement between the Company and Ted Love, M.D., effective as of January 28, 2010.
10.31(29)+	Letter Agreement between the Company and Michael Kauffman, M.D., effective as of April 1, 2010.
10.32(30)+	Letter Agreement between the Company and Kaye Foster-Cheek, effective as of September 30, 2010.
10.33(30)+	Separation and Consulting Agreement between the Company and Judy Batlin, effective as of September 30, 2010.
10.34(30)	Lease Agreement between the Company and ARE-SAN FRANCISCO, No. 12, LLC, dated as of July 9, 2010, as amended by that certain Letter Agreement between the Company and ARE-SAN FRANCISCO No. 12, dated as of July 9, 2010.
10.35(30)	Sublease between the Company and Exelixis, Inc., dated as of July 9, 2010.

Exhibit Number	Description of Document
10.36(30)*	License, Development and Commercialization Agreement between the Company and Ono Pharmaceutical Co., Ltd., dated as of September 7, 2010.
10.37+	Separation and Consulting Agreement between the Company and Michael Kauffman, effective as of December 31, 2010.
21.1	Subsidiaries of the Registrant.
23.1	Consent of Independent Registered Public Accounting Firm.
24.1	Power of Attorney. Reference is made to the signature page.
31.1	Certification of Principal Executive Officer required by Rule 13a-14(a) or Rule 15d-14(a).
31.2	Certification of Principal Financial Officer 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).

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

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

\+ Indicates management contract or compensatory plan or arrangement.

(1) Filed as an exhibit to Onyx's Current Report on Form 8-K filed on October 13, 2009.

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

(3) Filed as an exhibit to Onyx's Current Report on Form 8-K filed on December 5, 2008.

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

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

(6) Filed as an exhibit to Onyx's Current Report on Form 8-K filed on August 12, 2009.

(7) 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.

(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, 2001.

(10) 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.

(11) 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.

(12) Filed as an exhibit to Onyx's Current Report on Form 8-K filed on May 25, 2007.

(13) Filed as an exhibit to Onyx's Current Report on Form 8-K filed on June 10, 2008.

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

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

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

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

(18) Filed as an exhibit to Onyx's Annual Report on Form 10-K for the year ended December 31, 2006.

(19) Filed as an exhibit to Onyx's Current Report on Form 8-K filed on May 28, 2010.
(20) Filed as an exhibit to Onyx's Current Report on Form 8-K filed on July 12, 2006.
(21) Filed as an exhibit to Onyx's Current Report on Form 8-K filed on June 12, 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 March 31, 2009.
(24) Filed as an exhibit to Onyx's Current Report on Form 8-K filed on February 26, 2008.
(25) Filed as an exhibit to Onyx's Current Report on Form 8-K filed on June 23, 2008.
(26) Filed as an exhibit to Onyx's Current Report on Form 8-K filed on December 23, 2008.
(27) Filed as an exhibit to Onyx's Annual Report on Form 10-K for the year ended December 31, 2008.
(28) Filed as an exhibit to Onyx's Quarterly Report on Form 10-Q for the quarter ended September 30, 2009.
(29) Filed as an exhibit to Onyx's Quarterly Report on Form 10-Q for the quarter ended March 31, 2010.
(30) Filed as an exhibit to Onyx's Quarterly Report on Form 10-Q for the quarter ended September 30, 2010.
(31) Filed as an exhibit to Onyx's Current Report on Form 8-K filed on February 19, 2010.
(32) Filed as an exhibit to Onyx's Annual Report on Form 10-K for the year ended December 31, 2009.

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ONYX PHARMACEUTICALS, INC. 249 EAST GRAND AVENUE SOUTH SAN FRANCISCO, CA 94080 (650) 266-0000 TEL (650) 266-0100 FAX WWW.ONYX-PHARM.COM