

AVEO PHARMACEUTICALS INC  
Form 10-K  
March 30, 2012  
Table of Contents

**UNITED STATES**  
**SECURITIES AND EXCHANGE COMMISSION**

Washington, D.C. 20549

**FORM 10-K**

(Mark One)

**ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

**For the fiscal year ended: December 31, 2011**

Or

**TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

**For the transition period from** \_\_\_\_\_ **to** \_\_\_\_\_

**Commission file number: 001-34655**

**AVEO PHARMACEUTICALS, INC.**

Edgar Filing: AVEO PHARMACEUTICALS INC - Form 10-K

(Exact Name of Registrant as Specified in Its Charter)

Delaware  
(State or Other Jurisdiction of  
Incorporation or Organization)

04-3581650  
(I.R.S. Employer  
Identification No.)

75 Sidney Street

Cambridge, Massachusetts 02139

(Address of Principal Executive Offices) (zip code)

Registrant's telephone number, including area code: (617) 299-5000

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Name of each exchange on which registered
Common Stock, \$.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 Web site, 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 (§229.405) 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 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  (Do not check if a smaller reporting company) 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

## Edgar Filing: AVEO PHARMACEUTICALS INC - Form 10-K

The aggregate market value of the registrant's common stock, \$0.001 par value per share ( Common Stock ), held by non-affiliates of the registrant, based on the last reported sale price of the Common Stock on the NASDAQ Global Market at the close of business on June 30, 2011, was \$530,804,647. For purposes hereof, shares of Common Stock held by each executive officer and director of the registrant and entities affiliated with such executive officers and directors have been excluded from the foregoing calculation because such persons and entities may be deemed to be affiliates of the registrant. This determination of affiliate status is not necessarily a conclusive determination for other purposes.

The number of shares outstanding of the registrant's Common Stock as of February 29, 2012: 43,557,313

### **Documents incorporated by reference:**

Portions of our definitive proxy statement for our 2012 annual meeting of stockholders are incorporated by reference into Part III of this Annual Report on Form 10-K.

**Table of Contents**

## AVEO PHARMACEUTICALS, INC.

## TABLE OF CONTENTS

	<b>Page No.</b>
<b><u>PART I</u></b>	<b>1</b>
Item 1. <u>Business</u>	1
Item 1A. <u>Risk Factors</u>	47
Item 1B. <u>Unresolved Staff Comments</u>	74
Item 2. <u>Properties</u>	74
Item 3. <u>Legal Proceedings</u>	74
Item 4. <u>Mine Safety Disclosures</u>	74
<b><u>PART II</u></b>	<b>75</b>
Item 5. <u>Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities</u>	75
Item 6. <u>Selected Financial Data</u>	77
Item 7. <u>Management's Discussion and Analysis of Financial Condition and Results of Operations</u>	79
Item 7A. <u>Quantitative and Qualitative Disclosures about Market Risk</u>	107
Item 8. <u>Financial Statements and Supplementary Data</u>	109
Item 9. <u>Changes in and Disagreements with Accountants on Accounting and Financial Disclosure</u>	145
Item 9A. <u>Controls and Procedures</u>	145
Item 9B. <u>Other Information</u>	147
<b><u>PART III</u></b>	<b>148</b>
Item 10. <u>Director, Executive Officers and Corporate Governance</u>	148
Item 11. <u>Executive Compensation</u>	148
Item 12. <u>Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters</u>	148
Item 13. <u>Certain Relationships and Related Person Transactions and Director Independence</u>	148
Item 14. <u>Principal Accountant Fees and Services</u>	148
<b><u>PART IV</u></b>	<b>149</b>
Item 15. <u>Exhibits and Financial Statement Schedules</u>	149
<u>Signatures</u>	150

---

**Table of Contents**

**References to AVEO**

Throughout this Form 10-K, the words we, us, our and AVEO refer to AVEO Pharmaceuticals, Inc. and its consolidated subsidiaries, and board of directors refers to the board of directors of AVEO Pharmaceuticals, Inc.

**Forward-Looking Information**

This report contains forward-looking statements regarding our future discovery and development efforts, our collaborations, our future operating results and financial position, our business strategy, and other objectives for future operations. You can identify these forward-looking statements by their use of words such as anticipate, believe, estimate, expect, forecast, intend, plan, project, target, will a terms of similar meaning. You also can identify them by the fact that they do not relate strictly to historical or current facts. There are a number of important risks and uncertainties that could cause our actual results to differ materially from those indicated by forward-looking statements. These risks and uncertainties include those inherent in pharmaceutical research and development, such as adverse results in our drug discovery and clinical development activities, decisions made by the U.S. Food and Drug Administration and other regulatory authorities with respect to the development and commercialization of our drug candidates, our ability to obtain, maintain and enforce intellectual property rights for our drug candidates, our dependence on our strategic partners, our ability to obtain any necessary financing to conduct our planned activities, and other risk factors. Please refer to the section entitled Risk Factors in Part I of this report for a description of these risks and uncertainties. Unless required by law, we do not undertake any obligation to publicly update any forward-looking statements.

**PART I**

**ITEM 1. Business  
Overview**

We are a cancer therapeutics company committed to discovering, developing and commercializing targeted cancer therapies to impact patients lives. Our product candidates are directed against important mechanisms, or targets, known or believed to be involved in cancer. Our proprietary Human Response Platform, a novel method of building preclinical models of human cancer, provides us with unique insights into cancer biology and is being leveraged in the discovery and clinical development of our cancer therapeutics.

Tivozanib, our lead product candidate, which we partnered with Astellas Pharma Inc., or Astellas, in 2011, is a potent, selective, long half-life inhibitor of all three vascular endothelial growth factor, or VEGF, receptors that is designed to optimize VEGF blockade while minimizing off-target toxicities. Our clinical trials of tivozanib to date have demonstrated a favorable safety and efficacy profile for tivozanib. In January 2012, we announced top-line data from our global, phase 3 clinical trial comparing the efficacy and safety of tivozanib with Nexavar® (sorafenib), an approved therapy, for first-line treatment in renal cell carcinoma, or RCC, which we refer to as the TIVO-1 study. The TIVO-1 study is being conducted in patients with advanced clear cell RCC who have undergone a prior nephrectomy (kidney removal) and who have not received any prior VEGF- and mTOR-targeted therapy. In this trial, we measured, among other things, each patient s progression-free survival, or PFS, which refers to the period of time that began when a patient entered the clinical trial and ended when either the patient died or the patient s cancer had grown by a specified percentage or spread to a new location in the body. PFS is the primary endpoint in the TIVO-1 study. In the TIVO-1 study, tivozanib demonstrated a statistically significant improvement in PFS over Nexavar with a median PFS of 11.9 months for tivozanib compared to a median PFS of 9.1 months for Nexavar in the overall study population. Tivozanib also demonstrated a statistically significant improvement in PFS with a median PFS of 12.7 months compared to a median PFS of 9.1 months for Nexavar in the pre-specified subpopulation of patients who received no prior

---

**Table of Contents**

systemic anti-cancer therapy for metastatic disease a subpopulation that comprised approximately 70% of the total study population. In the TIVO-1 study, tivozanib demonstrated a well-tolerated safety profile consistent with the results from our tivozanib phase 2 clinical trial in patients with advanced RCC; the most commonly reported side effect was hypertension, a well established on-target and manageable effect of VEGF receptor inhibitors. The most common treatment-related side effects seen in the phase 2 clinical trial were hypertension (44.9%) and dysphonia, or hoarseness of voice (21.7%). Additionally, the incidence of other side effects in the phase 2 clinical trial that are commonly associated with other VEGF receptor inhibitors, such as diarrhea, rash, mucositis, stomatitis, fatigue, and hand-foot syndrome, was relatively low.

In addition to the TIVO-1 study, we are evaluating tivozanib in multiple phase 1 and phase 2 clinical trials including our BATON (Biomarker Assessment of Tivozanib in ONcology) program, a series of clinical trials assessing tivozanib biomarkers in solid tumors. The BATON trials include BATON-RCC, a phase 2 exploratory biomarker study in patients with advanced RCC, which completed enrollment in early 2012. The second BATON study underway is BATON-CRC, a phase 2 clinical trial evaluating tivozanib in combination with modified FOLFOX6 (mFOLFOX6) compared to Avastin® (bevacizumab) in combination with mFOLFOX6 as first-line therapy in patients with advanced metastatic colorectal cancer, or CRC. Additionally, we expect to initiate further clinical evaluation of tivozanib in breast cancer in 2012 as part of our BATON program.

We expect that the results of all of our phase 1 and phase 2 trials will help to inform our clinical development plans for tivozanib as a monotherapy and in combination with other anti-cancer therapies in multiple cancer indications.

We acquired exclusive rights to develop and commercialize tivozanib worldwide outside of Asia pursuant to a license agreement we entered into with Kirin Brewery Co. Ltd. (now Kyowa Hakko Kirin), or KHK, in 2006. Under the license agreement, we obtained an exclusive license to research, develop, manufacture and commercialize tivozanib, pharmaceutical compositions thereof and associated biomarkers for the diagnosis, prevention and treatment of any and all human diseases and conditions outside of Asia. KHK has retained all rights to tivozanib in Asia. We have obligations to make milestone and royalty payments to KHK. The royalty rates range from the low to mid-teens as a percentage of our net sales of tivozanib. We are also obligated to pay a specified percentage of certain amounts we receive from any third party sublicensees, including Astellas. As discussed below under the heading Strategic Partnerships, we entered into a strategic collaboration with Astellas in which we have agreed to share responsibility, including all profits and losses, with Astellas for continued development and commercialization of tivozanib in North America and Europe. Throughout the rest of the world, outside of North America, Europe and Asia, we granted Astellas an exclusive, royalty-bearing license to develop and commercialize tivozanib.

In addition to tivozanib, we have a pipeline of monoclonal antibodies derived from our proprietary Human Response Platform. Ficlatusumab, our next most advanced product candidate, is an antibody which binds to hepatocyte growth factor, or HGF, thereby blocking its function. We have completed two phase 1 clinical trials of ficlatusumab demonstrating the ability to combine ficlatusumab with epidermal growth factor receptor, or EGFR, inhibitors Tarceva® and Iressa®. In May 2010, we initiated a phase 2 clinical trial evaluating ficlatusumab in patients with non-small cell lung cancer. This is a first-line study comparing ficlatusumab in combination with Iressa versus Iressa monotherapy. We anticipate announcing data from the ficlatusumab phase 2 trial in the second half of 2012.

We have also identified a number of other promising targets for the development of novel cancer therapeutics using our Human Response Platform. We have preclinical and discovery antibody programs underway focused on targets that appear to be important drivers of tumor growth, including our third clinical candidate AV-203, which targets the ErbB3 receptor (partnered with Biogen Idec, Inc., or Biogen Idec), as well as programs directed toward the RON receptor (Recepteur d Origine Nantais) (partnered with Centocor Ortho Biotech Inc., or Centocor). We expect to initiate clinical development with AV-203 in the first half of 2012.

**Table of Contents**

Our proprietary Human Response Platform was designed to overcome many of the limitations of traditional approaches to modeling human cancer. The traditional method of modeling human cancer uses a model referred to as a xenograft. A xenograft model is created by adapting cells from a human tumor to grow in a petri dish, and then injecting these cells in a mouse, where they grow into tumors. However, the resulting tumors differ from the original tumor in important respects, and, accordingly, xenograft models are often poor predictors of the success of cancer drugs in human clinical trials. In our Human Response Platform, we use patented genetic engineering techniques to grow populations of spontaneous tumors in animals containing human-relevant, cancer-causing mutations and tumor variation akin to what is seen in populations of human tumors. Because we believe that these populations of tumors better replicate what is seen in human cancer, we believe that our Human Response Platform provides us with unique insights into cancer biology and mechanisms of drug response and resistance, and represents a significant improvement over traditional approaches. We are utilizing this Human Response Platform alone and with our strategic partners to (i) identify and validate target genes which drive tumor growth, (ii) evaluate drugs which can block the function of these targets and (iii) identify biomarkers, which are indicators of drug response and resistance in patients, in an effort to evaluate which patients are most likely to respond favorably to treatment with such drugs. The potential identification and development of relevant biomarkers through our Human Response Platform is a core component of our oncology drug development efforts. Our goal is to utilize the biomarker data from BATON-CRC and other BATON clinical trials to further inform our clinical development strategy.

## **Table of Contents**

### **Product Pipeline**

We are seeking to develop multiple new drugs that target important mechanisms known or believed to be involved in cancer. These drugs include our lead drug candidate, tivozanib, a small molecule oral cancer drug designed to prevent tumor growth by inhibiting angiogenesis, as well as monoclonal antibodies against HGF and ErbB3. We also are developing a pipeline of earlier stage, novel antibodies that are designed to target mechanisms which we believe to be important in cancer. Our drug discovery and development activities are supported by our Human Response Platform.

The chart below summarizes our current product candidates and their stages of development and planned development.

### ***Tivozanib: Triple VEGF Receptor Inhibitor***

#### *VEGF Pathway Inhibitors in Tumor Angiogenesis*

The formation of new blood vessels, known as angiogenesis, is required to support certain important natural processes such as embryonic development, reproduction and wound healing. Angiogenesis also plays an important role in cancer progression and the spread of tumors within the body, or metastasis. Tumors cannot grow beyond a small size in the absence of the formation of new blood vessels. Tumors use these vessels to obtain oxygen and nutrients, both of which are required to sustain tumor growth, and to remove toxic waste products that result from rapid metabolism. In addition, new vessels in the tumor provide a way for tumor cells to enter the circulation and to spread to other organs.



---

**Table of Contents**

Cancer cells and associated tumor tissue secrete a variety of protein activators, or growth factors, that bind to receptors and promote angiogenesis. Growth factors that bind to specific receptors are known as ligands for those receptors. Vascular endothelial growth factor, or VEGF, stimulates angiogenesis and is required for the maintenance of new blood vessels. Most tumors produce various forms of VEGF and other ligands which bind to the three VEGF receptors, VEGF receptors 1, 2 and 3. The VEGF receptors are found predominantly on the surface of normal vascular endothelial cells. The secretion of these ligands attracts normal endothelial cells to the tumor site where they are stimulated to proliferate and form new blood vessels that feed the tumor.

Each of the three VEGF receptors has been shown to play a distinct and critical role in angiogenesis. Drugs designed to inhibit the VEGF pathway may be directed either to one or more ligands of the receptors, or to the VEGF receptors themselves. Because there are multiple ligands that can bind to the three VEGF receptors and stimulate angiogenesis, products that block only one of these ligands may result in an incomplete blockade of the VEGF pathway. Similarly, receptor-targeted drugs that fail to effectively block all three of the VEGF receptors may also result in an incomplete blockade of the VEGF pathway.

Because essentially all solid tumors require angiogenesis to progress beyond microscopic size, anti-angiogenesis drugs have demonstrated benefit in a wide variety of tumor types. Current therapies targeting the VEGF pathway have been approved in many tumor types, including colon, lung, breast, kidney, liver and brain cancers. In many of these cancers, other than kidney, liver and brain cancers, VEGF pathway inhibitors have demonstrated meaningful efficacy only when given in combination with other drugs; therefore, the opportunity for VEGF pathway inhibitors is most significant for those agents that can be safely combined with other anti-cancer agents.

We believe that the optimal approach to inhibiting the VEGF pathway is through an oral drug that provides optimal blockage of the VEGF pathway by potently and selectively inhibiting all three VEGF receptors. Each of the currently approved VEGF receptor inhibitors has significant side effects when administered alone, and studies have shown that it is challenging to administer these drugs in combination with other anti-cancer agents at their full dose and schedule due to overlapping toxicities. Each of the currently available VEGF receptor inhibitors has one or more drawbacks, including: (i) a lack of adequate potency, which may necessitate high dosage levels in order to sufficiently block all three VEGF receptors; (ii) a lack of selectivity, which may result in off-target side effects due to an unintended impact on other biological targets; and (iii) a short duration of inhibition, which may necessitate dosing more than once per day and may not ensure continuous inhibition of the VEGF pathway.

Despite the various challenges encountered with the approved VEGF receptor inhibitors, sales of VEGF pathway inhibitor drugs have been estimated to exceed over \$8.0 billion worldwide in 2011, based on quarterly and annual reports made publicly available by companies marketing such drugs. According to EvaluatePharma<sup>®</sup> consensus forecasts from equity research analysts, drugs targeting angiogenesis are projected to have sales of more than \$14 billion by 2014. Currently approved VEGF pathway inhibitors include Avastin, an antibody that blocks only one of the ligands for the VEGF receptors, and Nexavar, Sutent<sup>®</sup> (sunitinib), Inlyta<sup>®</sup> (axitinib) and Votrient<sup>®</sup> (pazopanib), each of which are small molecule drugs that target the VEGF receptors, but that also bind to a number of other targets with varying potency.

We believe there is a significant unmet need for a new, oral VEGF pathway inhibitor that is designed to provide optimal blockade of all three VEGF receptors, which is more tolerable, which can be more easily combined with other anti-cancer drugs and which can maintain continuous inhibition of the pathway with a convenient dosing regimen.

*Potential Advantages of Tivozanib*

We believe that the top-line efficacy and safety data on tivozanib reported from the TIVO-1 trial could position tivozanib as a first-line treatment for patients with RCC. The potential advantages of tivozanib, which we believe are the basis for the favorable efficacy and safety profile observed in the clinical trials of tivozanib to

---

**Table of Contents**

date, are its potency, selectivity and long half-life inhibition of all three VEGF receptors. We believe that this favorable profile may allow tivozanib to be successfully used as a monotherapy and to be more readily combined with other anti-cancer agents in multiple tumor types. These advantages, along with tivozanib's one capsule, once-daily dosing regimen, may differentiate tivozanib from currently marketed and in-development VEGF receptor inhibitors, and may allow tivozanib to fulfill an unmet need in the anti-angiogenesis market.

The high potency of tivozanib across VEGF receptors 1, 2 and 3 provides a comprehensive blockade of the VEGF pathway, while its high level of selectivity for all three VEGF receptors is designed to minimize unintended side effects, referred to as off-target toxicities. In the clinical trials of tivozanib to date, hypertension and dysphonia have been the most commonly reported side effects in patients. The occurrence of hypertension and dysphonia are driven by inhibition of the VEGF pathway, and suggest that the pathway has been substantially inhibited. Hypertension associated with tivozanib can usually be managed using standard anti-hypertensive drugs, and both hypertension and dysphonia have been manageable and reversible in our clinical trials.

In contrast, many of the existing drugs that act by inhibiting the VEGF pathway also inhibit targets in other pathways, which can cause off-target toxicities. The most commonly reported toxicities for Sutent and Inlyta are fatigue and diarrhea, for Nexavar are fatigue, rash and diarrhea, and for Votrient is diarrhea. Votrient has also been associated with severe, and sometimes fatal, liver toxicity. Sutent, Nexavar and Votrient can also cause myelosuppression, which refers to a decrease in the production of blood cells, resulting in both anemia and neutropenia. Anemia is a decrease in the number of red blood cells, which carry oxygen, and neutropenia is a decrease in the number of certain white blood cells, which fight infection. None of these side effects are believed to be associated with inhibition of the VEGF pathway and, therefore, are considered off-target toxicities.

In clinical trials, levels of tivozanib in a patient's blood have been maintained for a prolonged period following a single dose, which allows for convenient, once-a-day dosing. Tivozanib has demonstrated an approximate four and a half day half-life, meaning the time it takes for the concentration of a drug in circulation to be reduced by one-half. Drugs with a short half-life may not sufficiently inhibit their intended therapeutic targets. In RCC, we believe that drugs that do not maintain blockade of the VEGF receptors throughout the course of therapy may result in a loss of efficacy or the occurrence of adverse events due to spikes in drug exposure. For this reason, it is important to maintain sufficient levels of drug in the patient throughout the course of therapy. Because tivozanib has demonstrated a long half-life, we believe it maintains a more consistent blockade of the relevant receptors and, accordingly, tivozanib is dosed on a one-capsule, once-per-day schedule.

***Renal Cell Cancer***

*Market Opportunity.* Based on the World Health Organization GLOBOCAN data (published in 2008), in the United States it is estimated that over 56,000 patients are diagnosed with RCC and that almost 14,000 die from the disease each year. In Europe it is estimated that over 73,000 patients are diagnosed with RCC and that over 31,000 die from the disease each year. According to the American Cancer Society, RCC accounts for approximately 90% of all kidney cancer. We estimate, based on publicly-available information for the 12 months ending in December of 2011, including quarterly and annual reports made available by companies that market drugs approved for RCC and secondary published sources, that the current worldwide RCC market is over \$2 billion, with agents targeting the VEGF pathway representing over 70% of sales. The market is expected to expand significantly over the next ten years, driven by an increased incidence of RCC, an increased use of frontline therapy as more tolerable agents are developed and an increased use of later-stage therapy as more treatment options become available.

*Current Diagnosis and Treatments.* The diagnosis of RCC is generally made by examination of a tumor biopsy under a microscope. Evaluation of the visual appearance of the tumor cells by a pathologist allows classification of RCC into clear cell or non-clear cell types. In general, patients with clear cell RCC, approximately 80% of all RCC diagnoses according to a 2006 article by N. Nakaigawa et al, in Cancer Research,

---

**Table of Contents**

tend to have a more favorable prognosis than patients with non-clear cell RCC. The initial treatment for most patients with both clear cell and non-clear cell RCC is surgical removal of the tumor, usually requiring removal of the affected kidney, or nephrectomy, if that is technically feasible. Patients who undergo a nephrectomy tend to have a better prognosis than patients who do not undergo a nephrectomy. Patients whose tumors have metastasized to other organs or whose tumors cannot be removed surgically are considered to have advanced RCC. Advanced RCC is highly resistant to chemotherapy. The standard of care for advanced RCC is treatment with one of the approved drugs that inhibit the VEGF pathway, including the oral drugs Sutent, Nexavar and Votrient as well as the injectable product Avastin. Although none of these drugs have been compared head-to-head in phase 3 clinical trials, Sutent, Nexavar, Votrient and Avastin (when administered in combination with alpha interferon) have all demonstrated improvements in progression-free survival in clear cell RCC patients compared to placebo or interferon. Inlyta, an oral VEGF inhibitor, has also recently been approved for the treatment of RCC after failure of one prior systemic therapy. Torisel and Afinitor, drugs which target mTOR, have also been approved in RCC.

Despite the efficacy of the approved oral VEGF pathway inhibitors, drugs such as Sutent, Nexavar and Votrient are also associated with significant side effects such as neutropenia, fatigue, diarrhea, hand-foot syndrome, mucositis, stomatitis and abnormalities in liver function. A significant number of patients in the phase 3 clinical trials for each of these drugs required a reduction or discontinuation of their therapy due to these side effects. Although these drugs were not tested head-to-head in their respective phase 3 clinical trials, the reported frequency of dose reductions of these drugs in patients with advanced RCC is 52% for Sutent, 13% for Nexavar and 36% for Votrient. The reported frequency of dose interruptions due to adverse events in the phase 3 clinical trials of these drugs in patients with advanced RCC is 54% for Sutent, 21% for Nexavar and 42% for Votrient.

*The Tivozanib Opportunity.* We believe there is unmet need for an RCC therapy that demonstrates significant efficacy while having a safety profile that will allow patients to remain on drug while maintaining a good quality of life. Added potential may exist for a selective VEGF pathway inhibitor that could be combined with other anti-cancer agents having a different mechanism of action, as VEGF pathway inhibitors are often most effective when administered in combination with other anti-cancer agents.

***Clinical Trials***

*Certain Terminology.* Standard Response Evaluation Criteria in Solid Tumors (version 1.0), or RECIST, defines disease progression and tumor response based on changes in a set of target tumor lesions identified when the patient enters the trial, which we refer to as baseline. A 20% or greater increase in the sum of the longest diameters in the target lesions compared to the smallest sum of the longest diameter recorded since the treatment started, unequivocal progression in non-target lesions or the appearance of a new lesion, is defined as disease progression. A reduction of at least 30% in the sum of the longest diameters of the target lesion as compared to baseline is defined as a partial response. A complete disappearance of target and non-target lesions, and the normalization of any tumor markers, constitutes a complete response. Both partial and complete responses must be confirmed by repeat assessments at least four weeks after the partial or complete response was first documented. Stable disease refers to patients who exhibit neither response nor disease progression. Objective response rate is typically defined as the sum of the partial and complete response rates.

*Phase 3 Clinical Trial.* Based on the results of the phase 2 clinical trial of tivozanib and following discussions we have had with the U.S. Food and Drug Administration, or FDA, and European Medicines Agency, or EMA, we initiated a phase 3 clinical trial, which we refer to as the TIVO-1 study, in patients with advanced clear cell RCC who have undergone a prior nephrectomy, and who are treatment-naïve or have received no more than one prior regimen of immunotherapy or chemotherapy with no prior VEGF or mTOR-targeted therapy. The TIVO-1 study enrolled 517 patients at 76 sites in 15 countries, including the United States, Canada, Europe, South America and India. The TIVO-1 study is a global, phase 3, randomized clinical trial comparing the efficacy and safety of tivozanib with Nexavar for first-line treatment in RCC. Nexavar was approved in the United States in December 2005 as the first VEGF receptor inhibitor for the treatment of

---

**Table of Contents**

advanced RCC. Following discussions with both the FDA and EMA, both agencies indicated that Nexavar is an acceptable choice as the active comparator in the TIVO-1 study. The primary endpoint for the trial is PFS based on independent radiology review. Secondary endpoints include overall survival, objective response rate, duration of response, which is a measure of the time from when a patient's tumors have shrunk until they resume their growth in size, and quality of life, as measured from questionnaires completed by the patient that provide information about symptoms and the impact of the cancer on a patient's daily life activities. Disease progression and tumor response rates were determined in accordance with RECIST.

In the TIVO-1 study, patients were randomized in approximately equal numbers to treatment with tivozanib or Nexavar. Patients randomized to the tivozanib treatment arm received tivozanib on the same dose and schedule that was well tolerated in our phase 2 clinical trial of tivozanib. Patients randomized to the Nexavar treatment arm received the approved dose of Nexavar, which is 400 mg twice a day. Patients randomized to the tivozanib treatment arm who developed documented disease progression were discontinued from the clinical trial. Patients randomized to the Nexavar treatment arm who developed documented disease progression were discontinued from the clinical trial and were given the option to receive tivozanib by enrolling in a separate long-term treatment protocol. In order to meet FDA standards for assessing results in phase 3 trials, all radiology scans were assessed by a single, centralized group of independent radiology reviewers in the United States who were blinded to the assigned treatment.

Based on the top-line analysis of events in the TIVO-1 study, determined by an independent radiology review committee, tivozanib demonstrated a statistically significant improvement in PFS with a median PFS of 11.9 months compared to a median PFS of 9.1 months for Nexavar in the overall study population. Tivozanib also demonstrated a statistically significant improvement in PFS with a median PFS of 12.7 months compared to a median PFS of 9.1 months for Nexavar in the pre-specified subpopulation of patients who received no prior systemic anti-cancer therapy for metastatic disease, a subpopulation that comprised approximately 70% of the total study population. Tivozanib demonstrated a well-tolerated safety profile consistent with the safety profile seen in the phase 2 clinical trial; the most commonly reported side effect was hypertension, a well established on-target and manageable effect of VEGF receptor inhibitors. Detailed findings with respect to both efficacy and safety from the TIVO-1 study have been submitted for presentation at the American Society of Clinical Oncology, or ASCO, Annual Meeting in June 2012.

Results from the TIVO-1 study, together with results from our already completed phase 2 clinical trial, will form the basis for registration applications to be submitted to the U.S. and European regulatory agencies for tivozanib's approval in advanced RCC, which we estimate will be submitted in the second half of 2012. AVEO is responsible for submission of the New Drug Application, or NDA, to the FDA which we expect completing in the third quarter of 2012.

*Phase 2 Clinical Trial.* In 2007, we began a phase 2 clinical trial of tivozanib in patients with advanced RCC. This clinical trial was conducted under an Investigational New Drug application submitted to the FDA, and 272 patients were enrolled between October 2007 and July 2008 at sites in Russia, the Ukraine and India. To be eligible for the clinical trial, patients could not have received any prior VEGF-targeted therapies. Results from the prior phase 1 clinical trial showed that patients were able to tolerate tivozanib at a dose of 1.5 mg/day given continuously for four weeks followed by a two week rest period, but in order to minimize the rest period during which patients are off treatment, the dosing regimen for the phase 2 clinical trial was changed to three weeks continuous dosing followed by a one week rest period. The trial included patients with both clear cell RCC (83%) and non-clear cell RCC (17%), and 27% of patients had not had a prior nephrectomy. Approximately 54% of patients had not received any other drug treatment for their disease, while the remainder had received one or more prior therapies, but no VEGF pathway inhibitors.

All patients received tivozanib for the first 16 weeks, at which time, based on investigator assessment, patients with  $\geq 25\%$  tumor regression continued on tivozanib for the next 12 weeks while patients with  $< 25\%$  change from baseline were randomly assigned to tivozanib or placebo in a double-blinded manner for the next 12 weeks. Patients with  $\geq 25\%$  increase in tumor size discontinued tivozanib treatment.

---

**Table of Contents**

The primary endpoints of the trial were (i) the percentage of patients remaining progression-free 12 weeks following random assignment to tivozanib or placebo, (ii) objective response rate after the initial 16 week treatment period and (iii) safety. Secondary endpoints included overall progression-free survival from start of treatment and progression-free survival after random assignment to tivozanib or placebo.

All radiology scans from the study were reviewed, retrospectively, by a single, centralized group of independent radiologists in the United States who were blinded to treatment assignment. All laboratory tests were conducted at a central lab in the United Kingdom. Disease progression and tumor response rates were determined in accordance with RECIST.

Based on final data from the tivozanib phase 2 clinical trial, the overall median progression-free survival of patients in the phase 2 clinical trial was 11.7 months. Progression-free survival was significantly higher among patients with clear cell RCC (12.4 months) compared to patients with non clear cell RCC (6.7 months). Within the group of 176 patients with clear cell histology and prior nephrectomy, progression-free survival was similar between those patients who were treatment naïve (14.3 months), and those who had received prior therapy with cytokines and/or chemotherapy (15.9 months). There were 51 patients who remained on tivozanib therapy for more than 2 years.

A significantly higher percentage of patients on tivozanib remained progression-free 12 weeks following random assignment as compared to placebo. As assessed by the study investigators, 57% of patients randomized to tivozanib were progression-free compared to 28% of patients randomized to placebo. This difference was statistically significant ( $p=0.001$ ). The median progression-free survival of patients from the 12-week double-blind period was 3.3 months for patients randomized to the placebo treatment arm and 10.3 months for patients randomized to the tivozanib treatment arm. The median was calculated based on data from the phase 2 clinical trial using a standard statistical procedure known as a Kaplan-Meier analysis.

Approximately 84% of patients who received tivozanib therapy and had at least one post-baseline CT scan in the phase 2 clinical trial experienced some degree of tumor shrinkage while on therapy. By independent radiological assessment, 24.3% of patients who received tivozanib demonstrated a confirmed objective response. There was one (0.4%) confirmed complete response, and 65 (23.9%) confirmed partial responses as measured by independent radiological assessment. In patients with clear cell RCC who had undergone a prior nephrectomy, 29.5% had a confirmed objective response as measured by independent radiological assessment. The confirmed responses include one confirmed complete response and 51 confirmed partial responses. Per RECIST, confirmed responses are defined as responses that are confirmed by a repeat assessment that is performed at least four weeks after the criteria for response are first met.

Of the 272 patients enrolled in the clinical trial, 25 patients discontinued tivozanib due to an adverse event, 22 patients had a dose reduction due to an adverse event, and 11 patients had a dose interruption due to an adverse event.

Table 1 lists treatment-related adverse events (defined as any adverse event which first occurs or increases in severity after the first dose of study drug and is considered by the investigator to be related to the use of the study drug) seen in >10% of patients in our phase 2 clinical trial of tivozanib. These were combined hypertension, which includes the adverse events of hypertension, blood pressure increased, essential hypertension, and hypertensive crisis (122 subjects, 44.9%), dysphonia (59 subjects, 21.7%), diarrhea (33 subjects, 12.1%), and asthenia or weakness (28 subjects, 10.3%). Hypertension is well established as an effect of inhibition of the VEGF pathway. Dysphonia has been associated with a variety of VEGF inhibitors but the causal mechanism is not as well established as it is with respect to hypertension.

Table 1 also lists treatment emergent (defined as any adverse event which first occurs or increases in severity after the first dose of study drug, regardless of whether it is considered to be related to the use of the study drug) seen in >10% of patients. It includes the total number of patients experiencing an adverse event as well as the number of patients that experienced a Grade 3 or higher events, Grade 3 adverse events are severe, Grade 4 adverse events are life-threatening, and Grade 5 adverse events are fatal.

**Table of Contents**

In the phase 2 clinical trial, the incidence of mucositis, stomatitis and hand-foot syndrome that were considered treatment-related were less than 5%, with less than 1% Grade 3 or Grade 4 events reported. No Grade 5 events occurred.

**Table 1: Treatment Emergent Adverse Events & Treatment Related Adverse Events Occurring in >10% of Patients in the Phase 2 Trial**

Adverse Event Term	Treatment Emergent Adverse Events (All causality)		Treatment Related Adverse Events	
	Total	Grade 3	Total	Grade 3
Combined Hypertension <sup>1</sup>	125 (46%)	32 (12%)	122 (45%)	32 (12%)
Dysphonia	62 (23%)	0	59 (22%)	0
Asthenia	61 (22%)	23 (9%)	28 (10%)	<5%
Dyspnea	51 (19%)	16 (6%)	16 (6%)	<5%
Fatigue	46 (17%)	<5%	22 (8%)	<5%
Cough	42 (15%)	<5%	13 (5%)	0
Diarrhea	39 (14%)	<5%	33 (12%)	<5%
Back pain	35 (13%)	<5%	<5%	0

- (1) Combined hypertension includes the following: hypertension, blood pressure increased, essential hypertension, and hypertensive crisis. Subjects could be counted more than once if they had more than one of these side effects, but were counted only one time for the total combined hypertension class.

*Other RCC Monotherapy Trials.* In February 2011, we initiated a phase 2 clinical trial in the US and Canada, which we refer to as BATON-RCC, evaluating tivozanib in patients with advanced RCC who have undergone a prior nephrectomy, and who are treatment-naïve or have received no more than one prior regimen of immunotherapy or chemotherapy, with no prior VEGF or mTOR -targeted therapy. In this phase 2 clinical trial, we will evaluate biomarkers and their correlation with clinical activity and/or tumor related toxicity and conduct an expanded assessment of safety and activity in this patient population. Enrollment in BATON-RCC was completed in early 2012. We have also completed a mass balance study, a food effect study, a QTc study and drug-drug interaction studies for tivozanib. We plan to conduct, or will seek waivers from conducting, a variety of other clinical trials that would support a NDA for tivozanib including special population studies and a pediatric study. We are also conducting additional toxicology studies in rodents, which will be included in our registration application.

#### *Tivozanib Combination Therapy*

We believe tivozanib's favorable efficacy and safety profile increases its potential to be combined with other anti-cancer agents in a manner that may produce better clinical outcomes. As a result, we have a number of clinical trials underway that are designed to test tivozanib in combination with other drugs and chemotherapies in multiple solid tumor types. We are also utilizing our Human Response Platform to help identify rational drug combinations and patient populations most likely to be responsive to these combination therapies. We expect that the results of these clinical trials, together with the results of our ongoing research efforts, will help to inform our clinical development plans for tivozanib in additional indications.

*Renal Cell Cancer.* We completed a phase 1b clinical trial of tivozanib in combination with Torisel, an injectable mTOR inhibitor, in patients with advanced clear cell RCC who have failed up to one prior VEGF-targeted therapy. Torisel was approved by the FDA in 2007 for the treatment of advanced RCC, and is considered a standard of care for treatment of patients with a poor prognosis.

## **Table of Contents**

Clinical trials have shown that Sutent and Nexavar cannot be used in combination with Torisel due to severe toxicities. The only approved VEGF pathway inhibitor that we are aware of that is currently being developed in combination with Torisel at full doses is Avastin. The preliminary data using this combination showed a high rate of tumor shrinkage in patients with RCC; however, the results of this study showed substantial toxicity with this combination.

While no other oral VEGF receptor inhibitor has demonstrated that it can be safely combined with Torisel at full dose, our completed phase 1b clinical trial indicates that tivozanib may be able to be used safely in combination with Torisel at full recommended dose and schedule. Final data from the clinical trial indicate that the combination has been well-tolerated and resulted in disease control in 22 out of 28 evaluable patients (79%), with eight patients (29%) experiencing partial responses as assessed by RECIST.

*Colorectal Cancer.* We believe that tivozanib has the potential to improve the treatment of colorectal cancer when used in combination with standard of care chemotherapy or other targeted drugs. According to the American Cancer Society, in the United States in 2011, more than 140,000 patients have been diagnosed with colorectal cancer, or CRC, and nearly 50,000 patients have died from this disease. Based on the World Health Organization GLOBOCAN data (published in 2008), in Europe it is estimated that approximately 333,000 patients are diagnosed with CRC and that nearly 148,000 die from the disease each year. Despite recent advances in chemotherapy, the American Cancer Society reports that less than 10% of patients with metastatic colorectal cancer survive beyond 5 years. Therefore, there is a need for new and more effective treatments for colorectal cancer. Based on recent clinical trials, Avastin in combination with chemotherapy has become the standard of care for metastatic colorectal cancer. These studies have demonstrated that the VEGF pathway is important in colorectal cancer. We believe more potent inhibitors of the pathway, such as tivozanib, have the potential to improve therapy for this disease.

We initiated a phase 1b clinical trial of tivozanib in combination with FOLFOX6, a standard chemotherapy regimen, in patients with gastrointestinal cancers, including colorectal cancer. This clinical trial has shown that tivozanib can be safely administered at full dose (1.5 mg) and schedule in combination with full dose FOLFOX6 chemotherapy. Preliminary data from the clinical trial reported in January 2011 indicate that the combination has been well-tolerated and resulted in disease control in 14 of the 22 enrolled patients (63%), with six of the 22 enrolled patients (27%) experiencing partial responses as assessed by RECIST. This clinical trial has completed enrollment and final analysis is being conducted.

In December 2011, we initiated an open-label, multicenter, randomized phase 2 clinical trial, called BATON-CRC, evaluating tivozanib in combination with modified FOLFOX6 (mFOLFOX6) compared to Avastin in combination with mFOLFOX6 as first-line therapy in patients with advanced metastatic CRC. BATON-CRC, which is being led by AVEO's collaborator Astellas, will enroll approximately 252 patients with no prior VEGF-targeted therapy at approximately 80 centers in the U.S., Canada, Australia and Europe. Patients will be randomized to one of the two treatments arms in a 2:1 ratio (168 patients in the tivozanib arm and 84 patients in the Avastin arm). One component of BATON-CRC is the assessment of biomarker relationships that may be predictive of response, including VEGF-A, VEGF-C and lactate dehydrogenase (LDH). LDH is a protein that normally appears throughout the body in small amounts and can be elevated in patients with certain cancers, including colorectal cancer. Measuring LDH levels can be helpful in monitoring cancer treatment and determining patients' response to therapy.

In November 2010, we initiated a phase 1b clinical trial evaluating an all-oral combination of tivozanib with Xeloda in patients with advanced solid tumors. In the next component of this trial, we plan to enroll patients with locally advanced or metastatic breast or colorectal cancer to further evaluate safety and activity of this combination in these tumor types.

Building on the safety data generated to date in the phase 1 Torisel combination clinical trial in RCC, we are also interested in exploring the safety and activity of tivozanib in combination with an mTOR inhibitor in colorectal cancer. A phase 1 investigator sponsored clinical trial was completed evaluating the combination of

---

**Table of Contents**

tivozanib with Afinitor, an oral mTOR inhibitor approved for the treatment of RCC, in twelve patients with advanced colorectal cancer. The phase 2 portion of this all-oral clinical trial combining tivozanib and Afinitor commenced in February 2011 and enrolled 40 patients with refractory metastatic colorectal cancer. Preliminary data presented in January 2012 showed tivozanib (1.0 mg) in combination with Afinitor (10 mg) can be safely administered to patients with refractory metastatic CRC. Thrombocytopenia was the most common toxicity and necessitated dose delays and/or reductions in some patients. Thrombocytopenia is commonly associated with Afinitor therapy and is reflected in that drug's label. Preliminary results from this phase 2 clinical trial showed that 50% of patients had stable disease as best response and median PFS was 3.0 months. A previous trial of single-agent Afinitor given weekly noted 25.3% with stable disease as best response and median PFS of 1.7 months.

*Breast Cancer.* We believe that tivozanib can provide an improved therapy for women diagnosed with breast cancer. In 2011, approximately 230,000 women were diagnosed with invasive breast cancer, and approximately 40,000 women will have died from breast cancer, in the United States, according to the American Cancer Society. Based on the World Health Organization GLOBOCAN data (published in 2008), in Europe it is estimated that approximately 300,000 patients are diagnosed with breast cancer and that nearly 90,000 die from the disease each year. Currently available chemotherapy and hormonal therapies have significantly enhanced the survival of women diagnosed with breast cancer; however metastatic breast cancer remains an incurable disease.

Avastin was approved by the FDA and EMA in 2008 for the treatment of metastatic breast cancer. In November 2011, the FDA withdrew the accelerated approval of Avastin for use with Taxol® (paclitaxel) in the treatment of metastatic breast cancer and revoked Avastin's approval in this indication based on recent clinical trial data indicating that the benefits of Avastin may be outweighed by dangerous side effects. Despite the recent data, European regulators have decided to retain the approval of Avastin for advanced breast cancer when used in combination with Taxol.

We completed a phase 1b clinical trial of tivozanib in combination with a standard dose of Taxol in patients with metastatic breast cancer. Final data from the clinical trial reported in June 2011 indicate that the combination has been well-tolerated and resulted in an objective response rate of 38%, with 5 of the 13 patients evaluable for efficacy experiencing partial response and 7 of the 13 patients (54%), evaluable for efficacy, experiencing stable disease with five patients (31%) experiencing stable disease for at least 24 weeks.

We expect to initiate a clinical trial of tivozanib in patients with breast cancer in 2012, in which a core component will be biomarker analysis that may provide us the opportunity to identify the breast cancer patients who are most likely to benefit from tivozanib in combination with chemotherapy.

*Non-small Cell Lung Cancer.* Lung cancer is the most deadly cancer in men and women, with approximately 221,000 new cases and 157,000 deaths in the United States in 2011, according to the American Cancer Society. Based on the World Health Organization GLOBOCAN data (published in 2008), in Europe it is estimated that approximately 288,000 patients are diagnosed with lung cancer and that nearly 253,000 die from the disease each year. Chemotherapy has shown modest activity in non-small cell lung cancer, or NSCLC, and advanced lung cancer remains an incurable disease. Avastin, approved by the FDA and EMA for use in NSCLC in combination with chemotherapy, and various small molecular VEGF receptor inhibitors have demonstrated modest single-agent activity in lung cancer, but none have been approved.

We have completed a phase 1 clinical trial of tivozanib monotherapy in patients with advanced NSCLC. This clinical trial was designed to test a continuous dosing regimen of tivozanib. We expect that the results will provide further information for our development strategy for tivozanib.

*Orphan Drug Designation*

In June of 2010, the EMA granted orphan medicinal product designation for tivozanib for RCC. According to the EMA, tivozanib was awarded the designation based on the prevalence of RCC among people in the European Union; the life-threatening nature of the disease, particularly for those with advanced or metastatic



---

**Table of Contents**

RCC; and the assumption that tivozanib may provide significant benefit for patients with RCC, and may be more potent and specific than existing treatments with similar mechanism of action as supported by preliminary clinical results. Companies granted orphan medicinal product designation by the EMA receive, among several other benefits, market exclusivity in the European Union for ten years following market authorization. Demonstration of quality, safety and efficacy is necessary before a designated orphan medicinal product can be granted a marketing authorization.

***Ficlatuzumab: Hepatocyte Growth Factor (HGF) Inhibitory Antibody***

Through the use of our Human Response Platform, our scientists have identified the HGF/c-Met pathway as a significant driver of tumor growth. HGF is a protein that circulates in the blood and binds to and activates a receptor called c-Met. HGF is the sole known ligand of c-Met receptor. Activation of c-Met is believed to be important in normal processes in embryonic development and wound healing. Activation of c-Met, however, is also believed to trigger many activities that are involved in cancer development and metastasis. Altered HGF/c-Met signaling is observed in many tumors including lung, head and neck, gastric, bladder, breast, ovarian, prostate, colorectal, certain sarcomas and in multiple myeloma and leukemias. There are no approved therapies that specifically target the HGF/c-Met pathway.

Less than two years after scientists characterized the importance of the HGF/c-Met pathway, we identified our ficlatuzumab antibody, an HGF inhibitory antibody. In preclinical models, ficlatuzumab has demonstrated an ability to inhibit the growth of many different tumors, including lung and colon tumors, glioblastomas and multiple myeloma. In preclinical studies of ficlatuzumab, we have also shown that ficlatuzumab has additive efficacy when given in combination with other approved anti-cancer agents such as Tarceva® (erlotinib), Erbitux® (cetuximab) and Temodar® (temozolomide). In preclinical studies conducted by us, ficlatuzumab was more effective at inhibiting tumor growth (at the dose tested) than a third-party small molecule c-Met inhibitor. Future clinical trials will determine whether the differences observed in these preclinical studies will contribute to greater efficacy in patients.

Preclinical and clinical observations suggest that increased HGF and/or c-Met receptor amplification may confer resistance to EGFR inhibitors. Encouraging phase 2 clinical data were reported at the ASCO Annual Meeting in 2010 with a third party small molecule c-Met inhibitor in combination with an EGFR tyrosine kinase inhibitor, or TKI, in patients with advanced, refractory NSCLC. Additionally, phase 2 clinical data were reported at the 35th Congress of the European Society for Medical Oncology (ESMO) in 2010 with a third party antibody to the c-Met receptor in combination with an EGFR TKI in patients with advanced, refractory NSCLC. These phase 2 clinical data demonstrated encouraging trends in progression-free survival and overall survival for a subset of patients treated with this antibody. Collectively, we believe that these data signal the potential patient benefit from combination therapy of an EGFR TKI and an inhibitor of the HGF/c-Met pathway, particularly in NSCLC.

In a phase 1 clinical trial of ficlatuzumab we conducted, a total of 24 patients received ficlatuzumab as a monotherapy, and 13 patients were dosed with ficlatuzumab in combination with Tarceva. The phase 1 clinical trial showed good tolerability with no dose limiting toxicities (DLT) up to the highest dose tested, 20mg/kg, for the monotherapy cohorts. One patient dosed with ficlatuzumab, 20mg/kg, in combination with Tarceva, experienced a DLT of inflammation of the mucous lining of the mouth. The most frequently observed adverse events for the monotherapy cohorts were tissue swelling, also referred to as edema, mild fatigue, nausea, and headache. Rash and diarrhea were the most frequently observed adverse events in the Tarceva combination cohort. Response data for the monotherapy cohorts showed that 11 out of 24 patients enrolled in the phase 1 clinical trial experienced stable disease lasting for 12 weeks or more and 2 out of 8 patients in the ficlatuzumab/Tarceva cohort experienced stable disease lasting for 12 weeks or more.

We also completed a phase 1 clinical trial in cancer patients with liver metastasis, where we collected pre-treatment and post-treatment tumor biopsies to evaluate changes in HGF/c-Met pathway signaling after treatment with ficlatuzumab. We are currently analyzing the results of this trial, which we plan to present later this year.

---

**Table of Contents**

In May 2010, we commenced the phase 2 portion of a phase 1b/2 clinical trial testing a combination of ficlatuzumab with Iressa<sup>®</sup> (gefitinib), an EGFR TKI, randomized 1:1 versus Iressa alone in patients with newly diagnosed, treatment naïve NSCLC. Patients who demonstrated disease progression during treatment with Iressa alone had the opportunity to be treated with ficlatuzumab in combination with Iressa provided that safety was maintained and the patient continued to meet trial eligibility criteria. This 188-patient, randomized clinical trial, which is being conducted in Asia, is studying response rate and progression-free survival in distinct patient subsets: those with activating EGFR mutations and those with wild-type EGFR. In addition, we are evaluating patient outcome based on c-Met levels expressed in their tumors. We believe this is a well-designed trial to identify the subpopulations of those patients who will benefit most from ficlatuzumab, and we expect data from this trial to help inform our development of ficlatuzumab in and beyond lung cancer. We anticipate reporting top-line data from the phase 2 trial in the second half of 2012.

During the Phase 1b portion, there was a dose escalation of ficlatuzumab (first cohort of three patients received 10 mg/kg and second cohort of twelve patients received 20 mg/kg intravenously every two weeks) in combination with Iressa (250 mg once-daily, oral for full four week cycle) in 15 Asian patients with NSCLC. The objective was to determine the safety, tolerability, DLT, and recommended dose of ficlatuzumab in combination with Iressa for the phase 2 portion. All patients were pre-treated with chemotherapy and ten patients had prior treatment with EGFR TKI. With a median duration of treatment of 14 weeks among patients in the 20 mg/kg cohort, key findings include that no dose limiting toxicities were observed in the dose-escalation cohorts and the recommended phase 2 dose for ficlatuzumab was determined to be 20 mg/kg intravenously every two weeks combined with 250 mg of Iressa once-daily, orally. The combination of ficlatuzumab and Iressa was well tolerated and demonstrated clinical activity in patients with NSCLC. Out of the 12 patients in the recommended 20 mg/kg cohort, five patients (the only five patients with no prior EGFR TKI therapy) experienced a partial response and four patients experienced stable disease.

We are also using our Human Response Platform to identify additional tumor types and patient populations most likely to be responsive to ficlatuzumab therapy. There are very few traditional preclinical models that are driven by HGF/c-Met. Consequently, we have utilized our proprietary technology to develop novel model systems that can be used preclinically to give insights into the best clinical settings in which to test ficlatuzumab anti-tumor activity. We believe that these preclinical models will provide us with an advantage over other competitive programs.

In November 2011, we entered into an agreement with Boehringer Ingelheim for large-scale process development and clinical manufacturing of ficlatuzumab. Boehringer Ingelheim will produce ficlatuzumab for clinical trials at its biopharmaceutical site in Fremont, California. We retained all rights to the development and commercialization of ficlatuzumab.

***AV-203: Anti ErbB3 Antibody Program***

Through the use of our Human Response Platform, our scientists have highlighted the importance of the ErbB3 receptor in tumor growth. ErbB3 belongs to a family of four proteins that also includes EGFR and HER2.

Both EGFR and HER2 have been implicated in promoting the growth of significant numbers of tumors, particularly in breast and lung cancers. Drugs blocking the activity of EGFR have demonstrated clinical benefit in lung, colon and head and neck cancers while drugs targeting HER2 show clinical benefit in the treatment of HER2 overexpressing breast and gastric cancers.

ErbB3 is significantly over-expressed in many human breast, ovarian, prostate, colorectal, pancreatic, gastric, and head and neck cancers and its overexpression generally correlates with poor prognosis. It has also been implicated in resistance to certain drugs which target EGFR in lung cancer and with resistance to radiotherapy. In addition, while the anti-HER2 antibody Herceptin has been very successful in treating many breast tumors that express HER2, HER2 is only overexpressed (HER2 positive) in roughly 25% of breast cancer

## **Table of Contents**

and as many as 60% of HER2 positive patients do not respond, as reported in a 2007 Herceptin review by C.A. Hudis published in *The New England Journal of Medicine*. Because ErbB3 preferentially binds with HER2, we believe that breast cancer patients who do not respond well to anti-HER2 therapy might benefit from drug combinations with an anti-ErbB3 antibody.

Through our discovery efforts, we have identified antibodies that have been shown to be potent and selective inhibitors of ErbB3 in preclinical studies. In preclinical testing, these antibodies have significantly inhibited the growth of a number of different tumors, including breast, prostate and pancreatic cancers. We have completed manufacturing of our lead development candidate in preparation for human clinical trials. We anticipate initiating phase 1 development with AV-203 in 2012.

In March 2009, we entered into an exclusive option and license agreement with Biogen Idec International GmbH, a subsidiary of Biogen Idec, Inc., which we collectively refer to herein as Biogen Idec, under which we granted Biogen Idec an exclusive option to obtain rights to co-develop (with us) and commercialize our ErbB3-targeted antibodies for the potential treatment and diagnosis of cancer and other diseases outside of the United States, Canada and Mexico. Under the agreement, we are responsible for developing ErbB3 antibodies through completion of the first phase 2 clinical trial designed in a manner that, if successful, will generate data sufficient to support advancement to a phase 3 clinical trial.

Within a specified time period after we complete the phase 2 clinical trial and deliver to Biogen Idec a detailed data package containing the results thereof, Biogen Idec may elect to obtain (1) a co-exclusive (with us) worldwide license under our relevant intellectual property to develop and manufacture ErbB3 antibody products, and (2) an exclusive license under our relevant intellectual property to commercialize ErbB3 antibody products in all countries in the world other than in the United States, Canada and Mexico. We retain the exclusive right to commercialize ErbB3 antibody products in the United States, Canada and Mexico. Until completion of the first phase 2 clinical trial, we are solely responsible for the research, development, and manufacturing of ErbB3 antibody(ies) pursuant to a written work plan meeting specific pre-agreed guidelines. We are solely responsible for all expenses incurred through completion of the first phase 2 clinical trial. If Biogen Idec exercises its option to obtain exclusive commercialization rights to ErbB3 products in its territory, then we will be solely responsible, subject to a mutually agreed development plan, budget and the oversight of a joint development committee, for the global development of ErbB3 antibody products, except that Biogen Idec will be solely responsible for ErbB3 antibody product development activities that relate solely to the Biogen Idec territory. We and Biogen Idec will share global development costs (including manufacturing costs to support development) for ErbB3 antibody products equally, except that Biogen Idec will be solely responsible for all development costs associated solely with the development of ErbB3 antibody products for its territory, and we will be solely responsible for all development costs associated solely with the development of ErbB3 antibody products for the United States, Canada and Mexico.

### ***Other Antibody Pipeline Programs***

In addition to the HGF/c-Met pathway and ErbB3, we have utilized our Human Response Platform to identify a number of other targets that appear to be potent drivers of tumor growth. We have further evaluated the involvement of these targets in the development of human cancers using available human cancer databases. Targets with the ability to drive tumor growth in our tumor models and with frequent genetic alterations in human cancers were selected as targets for our next generation of antibody drug discovery programs.

**RON Program.** RON is a receptor closely related to c-Met which is the receptor for HGF, the target of ficlatuzumab. Similarly, the Macrophage Stimulating Protein, which activates RON, is most closely related to HGF. The activation of RON signaling is believed to trigger many of the same cellular activities as activation of the HGF/c-Met pathway. Like c-Met, RON has been implicated in promoting tumor cell metastasis and invasiveness and, in one preclinical breast cancer model, RON expression in tumor cells dramatically increased their ability and propensity to metastasize to bone.

## **Table of Contents**

RON and c-Met are frequently co-expressed in certain tumors. Breast, bladder and colon cancer patients whose tumors have high levels of RON or c-Met have a poor prognosis, and the worst prognosis has been observed in patients in which both receptors were over-expressed.

In May 2011, we entered into an exclusive license agreement with Centocor to develop and commercialize our antibodies targeting the RON receptor. We also granted Centocor an exclusive license to our proprietary RON-driven tumor models and a nonexclusive license to our proprietary list of human genes intended to predict correlation of response to RON-targeted antibodies, or our RON index. Centocor is responsible for all clinical development, manufacturing and commercialization activities and costs. Centocor will also fund certain research for a three-year term to be conducted by us, including translational research studies using our proprietary Human Response Platform to identify biomarkers for patients most likely to benefit from treatment with RON targeted antibodies.

*Fibroblast Growth Factor Program.* Fibroblast growth factors, or FGFs, and their receptors, FGFR1-4, represent a signaling network that plays an important role in the regulation of cell growth, survival, differentiation and angiogenesis. Work in our Human Response Platform identified FGF ligands and receptors as powerful drivers of tumor growth in a variety of tumor models and implicated the activation of the pathway in tumor development. Increasing amounts of human genetic and genomic data also point to the alteration of this pathway in the development of a number of different types of human cancers.

The human Cancer Genome Sequencing project has identified the FGF/FGFR pathway as the most frequently altered signaling pathway in human cancers. Similar studies demonstrated that FGF pathway activation may not only play a role in tumor development but also may be implicated in the development of drug resistance. Different tumors and tumor types exhibit varying profiles of FGF pathway alterations; therefore, targeting individual FGF receptors may have different therapeutic applications.

Certain FGF ligands have been shown to have pro-angiogenic activity and may act synergistically with VEGF to amplify tumor angiogenesis. The upregulation of FGF pathway activity in response to anti-VEGF therapy is thought to play an important role in the development of resistance to VEGF inhibition, suggesting that the combination of FGF and VEGF pathway inhibitors may add to the benefits achievable by targeting VEGF alone.

The goal of our ongoing drug discovery efforts is to identify specific FGFR2 and FGFR3 inhibitory antibodies that prevent activation of these receptors. We will evaluate the activity of candidate antibodies in specific target-driven tumor models created using our Human Response Platform.

*Notch Program.* Genetic screens conducted using our Human Response Platform have demonstrated that activation of the Notch signaling pathway is a potent driver of tumor growth and confirmed its important role in tumor formation, or tumorigenesis. The Notch receptors are a family of four receptors on the surface of cells, Notch1-4, whose activity has been shown to play important roles in normal stem cell function and in multiple aspects of tumor biology.

Notch signaling is also thought to be important for the maintenance of cancer stem cell populations in tumors. Cancer stem cells are thought to represent a distinct cell population within the tumor contributing to tumorigenesis. Cancer stem cells may cause tumor metastasis and relapse following anti-tumor treatments by regenerating the tumor tissue. Eradication of cancer stem cells may lead to increased survival in cancer patients. We intend to use our Notch specific antibodies to investigate the role of Notch signaling in the maintenance of cancer stem cells. We believe that this effort may lead to the development of a novel therapeutic regimen that specifically targets cancer stem cell populations.

The goal of our Notch drug discovery efforts is to identify specific inhibitory antibodies to Notch1 and Notch3 that prevent ligand binding and activation of the receptors. The program has generated functional inhibitory antibodies against both receptors. Our team has demonstrated proof of concept with our lead Notch1

## Table of Contents

antibody candidate in preclinical tumor models. In these preclinical models, our Notch1 antibody shows no evidence of the gastro-intestinal toxicity that has limited the clinical development of other Notch inhibitors. As part of our ongoing Notch1 research, we are also currently evaluating the impact of prolonged, genetic inhibition of Notch1 which recent publications have suggested may result in vascular tumors and hemorrhage in the liver in research conducted in mice.

We are utilizing our Human Response Platform to investigate the context in which Notch inhibition, either alone or in combination with tivozanib, would have the greatest efficacy. Recently, mutational activation of Notch1 in B-cell chronic lymphocytic leukemia has been implicated in the development and recurrence of the disease prompting us to investigate the role of Notch1 activation in that disease. We are also exploring preclinical models to determine which tumors might be uniquely dependent on Notch1 or Notch3 function for survival as another mechanism of action for the drug. Our scientists have identified the HeyL protein as a potential biomarker that predicts that a significant subset of tumors driven by the mutant Ras oncogene may depend on Notch function. Oncogenes are genes that, when mutated, help turn normal cells into cancer cells. Specifically, high levels of HeyL in colon and pancreatic cell lines that carry a mutated form of Ras correlate with the sensitivity of these tumors to Notch pathway inhibitors. In June 2009, we were granted a U.S. patent on a method of identifying cancer tissue likely to be sensitive or resistant to treatment with an inhibitor of Notch receptor activation.

### **Our Human Response Platform**

Our scientific founders, Ronald A. DePinho, M.D. and Lynda Chin, M.D., then of the Harvard Medical School and the Dana Farber Cancer Institute, Tyler Jacks, Ph.D., of the Massachusetts Institute of Technology, and Raju Kucherlapati, Ph.D., of the Harvard Medical School, leaders in the field of cancer modeling and cancer genetics, believed that traditional preclinical cancer models were poorly predictive of drug responses in patients and that work from their various laboratories indicated that substantially better models of cancer could be developed. Accessing key intellectual property and insights from our founders, we have created a series of unique genetically engineered models of cancer, as well as proprietary ways of analyzing complex gene expression data to better translate such data from our models to human patient populations. These innovations help to address three key issues in cancer drug discovery and clinical development:

**Target Identification and Validation:** Identifying and validating which of the many candidate cancer causing genes are most important to tumor growth.

**Drug Discovery:** Enabling the development of tumor models driven by the target gene of interest to facilitate the evaluation of drug candidates directed against the target, and the selection of the most promising candidate.

**Biomarker Identification:** Enabling the identification of genetic markers, or biomarkers, which may help identify patients who are more likely to be responsive or resistant to such drugs by leveraging the naturally occurring genetic variation in our cancer models and their divergent sensitivity to anti-cancer drugs.

We believe that our platform provides unique insights into cancer biology that may provide us and our strategic partners with a competitive advantage in all phases of cancer drug discovery and development. To date, Merck and OSI have entered into agreements with us to utilize our Human Response Platform.

### ***Scientific Background***

Cancer is a disease caused by genetic mutations that accumulate in cells over the lifetime of an individual that can ultimately result in the unrestrained growth of the altered cells and their invasion into surrounding normal tissues. Cancer causing mutations arise at random within a cell, which then undergoes a selective process where any mutation that provides the cell with an increased ability to grow and survive is retained. It is estimated

## **Table of Contents**

that at least a dozen different mutations are required to transform a normal cell into a cancerous one. Even within specific types of cancer that all carry certain powerful cancer causing mutations, there are multiple combinations of additional mutations present such that each individual tumor is slightly different.

During the last 20 years, many of the mutations which promote cancer in people have been identified from human tumors. These have generally fallen into two classes: oncogene activating mutations and tumor suppressor gene mutations. Oncogene activating mutations function to promote cell growth. By analogy to driving a car, oncogene activating mutations act much like pushing the accelerator to the floor, giving a permanent signal to promote cell growth. Examples of these mutations include mutations in EGFR, HER2 and K-Ras. Tumor suppressor gene mutations inactivate mechanisms which turn off cell growth. Elimination of tumor suppressor gene function is analogous to cutting the brake lines in the car: mechanisms to stop the growth of the cell are gone. When a single cell collects an oncogene activating mutation and a tumor suppressor gene mutation, it is not yet transformed into a cancer cell but it is well on its way. Research has shown that introduction of these two types of mutations in many different cell types is sufficient to induce tumor formation over time. During this time, additional spontaneous mutations arise to complete the transformation of the normal cell into a full blown cancer cell capable of unlimited growth.

### ***Limitations of Existing Cancer Models***

Researchers use cancer models to help identify targets for new cancer drugs, to help screen the best drugs directed against such targets and to help identify which cancer patients are most likely to benefit from treatment with such drugs. For these reasons, cancer models which most accurately recreate the attributes of cancer in patients are important to increase the likelihood of successfully developing new safe and effective cancer drugs.

For the past several decades the standard models used by cancer researchers have been xenograft models. A xenograft model is created by adapting cells from a human tumor to grow in a petri dish. These cells are then injected under the skin of a mouse, where they grow into a tumor. Researchers can then test drugs to see if they can inhibit growth of the resulting tumors without causing unacceptable side effects.

This approach has several limitations. First, the process of adapting the human tumor cells to grow in a petri dish results in further unintended changes to the tumor cells that cause them to change in ways that do not reflect the original tumor from which they came. Second, because of the differences between human cells and mouse cells, the human cells are not able to interact in a natural way with the cells in the surrounding tissues. Finally, because there are relatively few of these xenograft models for each human tumor type, it is difficult to understand the reasons why some of these models respond to certain drugs and others do not.

Xenograft models are often poor predictors of the success of cancer drugs in human clinical trials and there is a substantial need in oncology for preclinical models that better replicate human cancer. For example, as reported in a 2006 article by K. Garber in *Journal of National Cancer Institute*, only 3.8% of patients in phase 1 clinical cancer drug trials show a significant clinical response, whereas most of these drugs have been shown to work in xenograft models in mice.

### ***Our Human Response Platform***

We were founded with the goal of developing a fundamentally new kind of cancer model designed to overcome many of the limitations of traditional xenograft models, and thereby improve the probability of success in developing new cancer drugs. We utilize these novel models to identify and validate target genes which drive tumor growth, to identify drugs which can block the function of these targets, and to identify patients who are most likely to respond favorably to treatment with such drugs. We have used these models to advance drugs in our pipeline and in collaboration with our strategic partners such as Merck, OSI, Biogen Idec and Centocor. Our cancer models, together with the various techniques we have developed to use these models to aid in the discovery and development of new cancer drugs, are collectively referred to as our Human Response Platform. Key components of our Human Response Platform are covered by issued patents or pending patent applications.

## **Table of Contents**

### ***Our Novel Approach to Modeling Human Cancer***

We begin the development of our genetically-engineered tumor models by introducing a human oncogene into mouse stem cells in which we have inactivated the function of a tumor suppressor gene. As in human cancer, these are the two key elements which are necessary to begin the process of a cell becoming cancerous. The oncogene is introduced in a manner which allows us to control its expression we can direct in which tissue it will be expressed (e.g., breast or lung or colon), and we can turn it on by adding a simple non-toxic chemical to the animal's drinking water. We refer to this genetic engineering process as the inducible oncogene approach, as it allows the researcher to control whether or when to induce, or turn on, the oncogene.

Originally, we used this inducible oncogene approach in germ line transgenic mice, which we licensed from the Dana Farber Cancer Institute when we were founded, in which the oncogene is expressed in all of the cells of the animal. However, recognizing that in naturally occurring human tumors oncogenes are only activated in a subset of the cells of the body, we subsequently developed an alternate method which are called chimeric mice, in which the oncogene is only activated in a subset of the cells of the animal. This makes it a more realistic model than a germ line transgenic model in which the entire animal is made up of genetically modified cells.

In our patented method of making chimeric mouse models, the key starting mutations that will allow them to develop into cancerous cells are introduced directly into the stem cells. Then, we inject the stem cells into 3-day old mouse embryos, alongside normal cells, and implant the embryos into mice. When the mice are born, we turn on the expression of the oncogene. Animals do not develop tumors right away, but expression of the oncogene begins a process whereby the engineered cells begin to accumulate additional genetic alterations randomly over a period of months. Eventually, most animals develop tumors in the tissue where we have directed the oncogene to be expressed. Importantly, although the initial driving oncogene is the same in every tumor, the additional mutations which accumulate are different from animal to animal, just as would be the case in a human population.

The power and versatility of our mouse model platform is greatly enhanced by our patented method of making chimeric mouse models. Prior to our invention of this patented method, every time a different chimeric model was desired, a germ line transgenic mouse containing all the desired genetic modifications had to be produced by a lengthy process that included at least one, and often several, rounds of breeding, in order to obtain the embryonic stem cells necessary to make the desired chimeric model. For a biopharmaceutical company frequently needing to produce new chimeric models containing different mutations, producing each new chimeric model through the conventional breeding process would be prohibitively time-consuming. We addressed this problem by greatly improving the speed of chimeric model production. In our patented method, it is no longer necessary to do mouse breeding every time a new chimeric model is produced. Instead, all the desired genetic modifications are assembled directly in an individual mouse embryonic stem cell, which is then injected into a mouse embryo. This reduces the time required to produce each new chimeric mouse model by as much as one year. We believe that this ability to produce new chimeric models in a commercially meaningful time frame is an important advance in the state of the art.

In addition to this patented method of making new tumor models, we have also developed a model of human breast cancer in which we have applied many of these same features to genetically modified human breast tissue. This Human-in-Mouse model is created by first isolating normal human breast tissue from surgical specimens, genetically modifying it to express oncogenes and then introducing the modified tissue into specially-engineered mice. The modified breast tissue first grows into normal breast tissue, but then rapidly develops into human breast tumors while growing in the mouse breast tissue. To our knowledge, this is the first and only preclinical model in which normal human breast tissue has been engineered to develop into spontaneous breast tumors in a mouse.

## **Table of Contents**

### ***Advantages of Our Cancer Models***

We believe that our novel cancer models have a number of unique advantages over traditional xenografts and other methods of developing cancer models used in many academic settings. First, because the tumors grow naturally in the animals, the normal interactions between tumors and the tissues around them, including blood vessels, are preserved. This is not the case in traditional xenografts, where human tumor cells are implanted into mice, and certain of the important cellular signals sent by the growing human tumor may not be recognized by the surrounding mouse cells. Second, as is the case in human cancer, the cancer cells grow alongside normal cells, whereas in many other cancer models, all of the cells of the animal contain the cancer-causing mutations. Third, because of the switch that we introduce into our models, we can turn on the cancer-causing mutations after the animals are born, replicating what is seen in many human cancers. In many other models, these mutations are on before the animals are born, and interfere with their normal embryonic development. Finally, because tumors in our model develop spontaneously after introduction of the initial cancer causing mutations, we can develop populations of tumors that exhibit differences in genetic backgrounds, again much more akin to what is seen in a population of human tumors.

### ***Use of Our Models in Target Discovery and Validation***

In a proprietary method called the MaSS screen, we turn off the inducible oncogene driving the growth of the tumors in our models. We then activate other genes in the tumor cells to see if the tumor cells grow with the driving oncogene turned off. This allows us to screen for genes capable of replacing the function of a known oncogene. Such genes are potential new targets for anti-cancer drugs. The MaSS screen technique is protected by issued patents exclusively licensed to us by the Dana-Farber Cancer Institute.

We have conducted MaSS screens in multiple tumor models we developed in different tumor types with different genetic backgrounds. These screens identified many genes important in tumor formation. The most common pathway identified in our screens has been the HGF/c-Met pathway, and this observation triggered the initiation of our program to develop antibodies against HGF (our ficlatuzumab program). Numerous other pathways have also been identified in our screens, including ErbB3, Notch and FGF, all of which are now the basis of certain of our ongoing antibody discovery programs.

The data from all of the screens performed to date are routinely re-evaluated and compared with data coming from other sources, such as mutations identified in the human Cancer Genome Sequencing project. Many target genes originally identified in the screen are poorly understood these targets become more interesting as targets as new data about their function becomes available. This now very large data set provided the basis of our target discovery strategic partnerships with both Merck and OSI. In the case of OSI, scientists from our company and OSI have reevaluated our target data base with a goal of finding novel targets possibly involved in the transition of a tumor cell to a more aggressive phase, where the original epithelial tumor cell becomes more mesenchymal like more invasive and able to survive passage through the blood stream the so-called epithelial-mesenchymal transition.

### ***Use of Our Models in Drug Discovery***

One of the significant challenges in drug discovery can often be identifying preclinical models that are driven by a particular target of interest. Human xenografts, for example, may be driven by multiple targets, and have many other limitations. For this reason, developing tumor models that are known to be driven by a particular target can be an important drug discovery tool for identifying the most potent drug candidates against that target.

Because the driving oncogene in our models can be turned on and off, we can turn off the oncogene and replace it with other genes of interest. For example, in the cells of a breast tumor that was originally driven by HER2, we can turn off the HER2 gene, and replace it with EGFR, another important oncogene. When we do so,



## **Table of Contents**

the tumors that arise from those cells are no longer sensitive to drugs that inhibit HER2, but are sensitive to drugs that inhibit EGFR. These tumors provide an excellent system for studying the relative ability of different EGFR inhibitors, either antibodies or small molecules, to affect tumor growth driven by EGFR. This is a powerful preclinical model for ranking the efficacy of different compounds and an example of our patented directed complementation technique. Frequently, similar systems are not available for new targets or newly discovered mutated forms of existing targets, and, accordingly, this technology provides a convenient way of rapidly generating new drug testing systems. We have used this approach to support our antibody drug discovery and development programs.

### ***Use of Our Models in Biomarker Identification***

Because each of the tumors that develops in our models accumulates random genetic mutations independently, populations of tumors in our models exhibit a significant degree of genetic heterogeneity. Consequently, the tumors that develop in our models, like human tumor populations, typically exhibit variation in response to anti-cancer drugs. The tumors in our models have been studied extensively for genetic characteristics, providing an opportunity to correlate the genetic makeup, or genetic context, of each tumor with its relative sensitivity or resistance to a given anti-cancer drug. By understanding the genetic context of tumors that respond to particular drugs, we hope to identify genetic markers, or biomarkers, that can be measured in patients prior to treatment to select or predict which tumors, tumor subtype, or patient subsets are most likely to respond to a given anti-cancer drug. We are using this approach to identify potential biomarkers for our pipeline drugs and it will be important to demonstrate that the biomarkers we identify translate into clinical benefit in humans.

In our tivozanib program, we have used our Human Response Platform to identify candidate biomarkers that are expected to help to predict responsiveness to tivozanib therapy. Because most traditional xenograft models are highly sensitive to VEGF pathway inhibitors (in fact, more sensitive than human tumors in patients), such models are not useful for identifying biomarkers. In contrast, because we are able to identify both responsive and resistant tumors in our models and compare the genetic makeup of the tumors, our Human Response Platform is useful for identifying candidate biomarkers. We have two issued United States patents on different biomarker tests, or similar tests, for identifying patients likely to be sensitive or resistant to treatment with tivozanib. We intend to use these candidate biomarker tests in clinical trials of tivozanib.

In February 2011, we initiated patient enrollment in a multi-center phase 2 exploratory biomarker study of tivozanib in patients with RCC. A key primary objective of the study is to evaluate biomarkers in blood and archived tissue samples and their correlation with tivozanib clinical activity to further inform the potential future design of rational combinations in RCC, as well as in other cancers.

Efforts to identify predictive biomarkers for our other development programs are ongoing.

### **Competition**

The biotechnology and pharmaceutical industries are highly competitive. There are many pharmaceutical companies, biotechnology companies, public and private universities, and research organizations actively engaged in the research and development of products that may be similar to our products. A number of multinational pharmaceutical companies, as well as large biotechnology companies, including Roche Laboratories, Inc., or Roche, Pfizer Inc., or Pfizer, Bayer HealthCare AG, or Bayer, Sanofi-Aventis, US, LLC, Amgen, Inc. and GlaxoSmithKline plc, or GSK, are pursuing the development or are currently marketing pharmaceuticals that target VEGF, HGF and ErbB3, or other oncology pathways on which we are focusing. It is probable that the number of companies seeking to develop products and therapies for the treatment of unmet needs in oncology will increase.

Many of our competitors, either alone or with their strategic partners, have greater financial, technical and human resources than we do and greater experience in the discovery and development of product candidates,

**Table of Contents**

obtaining FDA and other regulatory approvals of products and the commercialization of those products. Accordingly, our competitors may be more successful than we may be in obtaining approval for drugs and achieving widespread market acceptance. Our competitors' drugs may be safer and more effective, or more effectively marketed and sold, than any drug we may commercialize and may render our product candidates obsolete or non-competitive before we can recover the expenses of developing and commercializing any of our product candidates. We anticipate that we will face intense and increasing competition as new drugs enter the market and advanced technologies become available.

***Tivozanib Competition***

Angiogenesis inhibitors represent a rapidly growing drug category in oncology with 2011 sales estimated to be in excess of \$8.0 billion worldwide, based on 2011 quarterly and annual reports made publicly available by companies marketing such drugs. There are currently five FDA-approved drugs in oncology which target the angiogenesis pathway. Avastin, marketed by Roche, is an infused monoclonal antibody approved in combination with other anti-cancer agents for the treatment of metastatic colorectal cancer, metastatic non-small cell lung cancer, and advanced RCC. It is also approved as a monotherapy for the treatment of glioblastoma in patients with progressive disease following prior therapy. There are four FDA-approved oral small molecule VEGF receptor TKIs. Nexavar, marketed by Bayer and Onyx Pharmaceuticals, Inc., Sutent and Inlyta, marketed by Pfizer, and Votrient, marketed by GSK. Most of these approved VEGF TKIs are not specific to the VEGF receptors. Nexavar is approved as a monotherapy for advanced RCC and unresectable hepatocellular cancer. Sutent is approved as a monotherapy for advanced RCC, gastrointestinal stromal tumors, and progressive, well-differentiated pancreatic neuroendocrine tumors. Inlyta is approved for advanced RCC after failure of one prior systemic therapy. Votrient is approved as a monotherapy for advanced RCC. Other approved agents for the treatment of RCC are Torisel, marketed by Pfizer and Afinitor, marketed by Novartis Pharmaceuticals Corporation, both of which inhibit mTOR.

We are aware of a number of companies that have ongoing programs to develop both small molecules and biologics that target the VEGF pathway. Other VEGF pathway inhibitors that have launched or are in late-stage development in other cancer types include Amgen Inc.'s and Takeda Pharmaceutical Company Limited's AMG706 (motesanib), Abbott's ABT-869 (linifanib), AstraZeneca plc's AZD2171 (Recentin, cediranib) and AZD6474 (Zactima, vandetanib), Bayer's BAY-73-4506 (regorafenib), Boehringer Ingelheim International GmbH's BIBF-1120 (nintedanib), Bristol-Myers Squibb Company's BMS-582664 (brivanib alaninate), Eisai Co. Ltd.'s E-7080 (lenvatinib mesylate), Exelixis Inc.'s XL-184 (cabozantinib), ImClone LLC's IMC-1121b (ramucirumab), Kadmon Corporation, LLC's KD-019, Novartis Pharmaceuticals Corp.'s dovitinib, Onco Therapy Science Inc.'s OTS-102 (elpamotide), Progen Pharmaceuticals Ltd.'s PI-88 (muparfostat), and Regeneron Pharmaceuticals, Inc.'s and Sanofi-Aventis US LLC's aflibercept.

***Ficlatuzumab Competition***

We believe the products in development targeting HGF consist of Amgen's AMG-102 (rilotumumab), currently in phase 2 clinical trials, and Takeda's TAK-701 (HuL2G7, under license from Galaxy Biotech, LLC), currently in phase 1 clinical trials.

Other clinical-stage drugs which target the HGF/c-Met pathway include Roche's onartuzumab (MetMab / 5D5 Fab), ArQule, Inc.'s / Daiichi Sankyo, Inc.'s ARQ-197 (tivantinib), MethylGene, Inc.'s MGCD-265, Eisai Co. Ltd.'s E-7050 (golvatinib), Exelixis Inc.'s XL-184 (cabozantinib), Exelixis Inc.'s and GSK's XL-880 (foretinib), Incyte Corp.'s and Novartis Pharmaceuticals Corp.'s INCB-028060, and Pfizer's PF-2341066 (crizotinib).

**Table of Contents****AV-203 Program Competition**

We believe the most direct competitors to our AV-203 program are monoclonal antibodies that specifically target the ErbB3 receptor, including Merrimack Pharmaceuticals, Inc. s and Sanofi-Aventis US LLC s MM-121, which is currently in phase 2 clinical development, and Daiichi Sankyo, Inc. s and Amgen, Inc. s U3-1287 / AMG-888, which is also in phase 2 clinical development. Other clinical-stage competitors include Ambit Biosciences, Inc. s AC-480, Merrimack Pharmaceuticals, Inc. s MM-111, PharmaMar SA s elisidepsin, and AstraZeneca plc s AZD-8931.

**Strategic Partnerships**

We have entered into multiple strategic partnerships in which we have granted rights to tivozanib, our antibody candidates and certain aspects of our Human Response Platform. These agreements provide us with a source of cash flow in the form of up-front payments, equity investments, research and development funding, payments upon achievement of specified milestones, and potential royalties from product sales.

Pursuant to the following strategic partnerships entered into as of December 31, 2011, we have acquired rights to products, granted rights to our product candidates, or have utilized, or granted rights to certain elements of, our Human Response Platform:

Strategic Partner	Initial Date of		Payments Received as of December 31, 2011 <sup>(1)</sup>
	Agreement	Subject Matter	
Kyowa Hakko Kirin	December 2006	Tivozanib <sup>(2)</sup>	N/A
Centocor	May 2011	RON receptor	\$ 16.3 million
Astellas	February 2011	Tivozanib	\$ 146.4 million <sup>(3)</sup>
Biogen Idec	March 2009	AV-203	\$ 60.0 million <sup>(4)</sup>
OSI	September 2007	Target and Biomarker Identification	\$ 78.5 million

(1) Includes up-front payments, equity investments, research and development funding and milestone payments.

(2) In December 2006, we in-licensed the rights to our lead product candidate, tivozanib, in all territories of the world, except for Asia.

(3) Includes payments received, offset by payments made.

(4) Includes an equity investment made prior to the initial date of the agreement.

**Kyowa Hakko Kirin**

In December 2006, we entered into a license agreement with Kirin Brewery Co. Ltd. (now Kyowa Hakko Kirin), which we sometimes refer to as KHK, under which we obtained an exclusive license to research, develop, manufacture and commercialize tivozanib (f/k/a KRN951), pharmaceutical compositions thereof and associated biomarkers. In this description, our references to tivozanib include pharmaceutical compositions thereof and associated biomarkers. Our exclusive license covers all territories in the world, except for Asia. The territory in which we are licensed is referred to as our territory. Kyowa Hakko Kirin has retained rights to tivozanib in Asia, including the People s Republic of China, India and Japan. Under the license agreement, we obtained exclusive rights in our territory under certain Kyowa Hakko Kirin patents, patent applications and know-how related to tivozanib, to research, develop, make, have made, use, import, offer for sale, and sell tivozanib for the diagnosis, prevention and treatment of any and all human diseases and conditions. We have the right to grant sublicenses under the foregoing licensed rights, subject to certain restrictions. In addition, we may, but are not obligated to, apply our Human Response Platform to identify optimal chemotherapy combinations, as well as additional patient populations likely to respond to tivozanib monotherapy and combination therapy. We and Kyowa Hakko Kirin each have access to and can benefit from the other party s clinical data and regulatory filings with respect to tivozanib and biomarkers identified in the conduct of activities under the license agreement.

## **Table of Contents**

Under the license agreement, we are obligated to use commercially reasonable efforts to develop and commercialize tivozanib in our territory, including meeting certain specified diligence goals. We also must obtain Kyowa Hakko Kirin's consent if we intend to change the initial indication for which we seek marketing approval for tivozanib to an indication other than RCC. Prior to the first anniversary of the first post-marketing approval sale of tivozanib in our territory, neither we nor any of our subsidiaries has the right to clinically develop, seek marketing approval for or commercialize any other product that also works by inhibiting the activity of the VEGF receptor.

Upon entering into the license agreement, we made a cash payment in the amount of \$5.0 million. In March 2010, we made a cash payment in the amount of \$10.0 million in connection with the initial dosing of patients in the TIVO-1 study. In addition, we are required to make certain milestone payments which could total, in the aggregate, \$50.0 million, upon the achievement of specified regulatory milestones. In connection with the execution of our collaboration agreement with Astellas Pharma Inc., or Astellas, discussed below, we are required to pay Kyowa Hakko Kirin a specified percentage of the license fee received from Astellas as well as certain amounts we may receive from Astellas in connection with Astellas' development and commercialization activities outside of North America and Asia related to tivozanib, other than amounts we receive in respect of research and development funding or equity investments, subject to certain limitations. We are also required to pay Kyowa Hakko Kirin tiered royalty payments on net sales we make of tivozanib in North America, which range from the low to mid-teens as a percentage of net sales. The royalty rate escalates within this range based on increasing tivozanib sales. Our royalty payment obligations in a particular country in our territory begin on the date of the first commercial sale of tivozanib in that country, and end on the later of 12 years after the date of first commercial sale of tivozanib in that country or the date of the last to expire of the patents covering tivozanib that have been issued in that country.

The license agreement will remain in effect until the expiration of all of our royalty and sublicense revenue obligations to Kyowa Hakko Kirin, determined on a product-by-product and country-by-country basis, unless we elect to terminate the license agreement earlier. If we fail to meet our obligations under the agreement and are unable to cure such failure within specified time periods, Kyowa Hakko Kirin can terminate the agreement, resulting in a loss of our rights to tivozanib and an obligation to assign or license to Kyowa Hakko Kirin any intellectual property or other rights we may have in tivozanib, including our regulatory filings, regulatory approvals, patents and trademarks for tivozanib.

### ***Centocor Ortho Biotech***

In May 2011, we entered into an exclusive license agreement with Centocor for the worldwide development and commercialization of our internally-discovered antibodies targeting the RON receptor. We also granted Centocor an exclusive, worldwide license to our proprietary RON-driven tumor models and a nonexclusive, non-sublicensable, worldwide license to our proprietary list of human genes intended to predict correlation of response to RON-targeted antibodies, or our RON index. Centocor is responsible for all clinical development, manufacturing and commercialization activities and costs. Subject to an agreed-upon research plan and budget, Centocor will also fund certain research for a three-year term to be conducted by us, including translational research studies using our proprietary Human Response Platform to identify biomarkers for patients most likely to benefit from treatment with RON targeted antibodies.

In connection with the Centocor license agreement, we received a one-time cash payment in the amount of \$7.5 million and a separate equity investment in the amount of approximately \$7.5 million through the purchase by Johnson & Johnson Development Corporation, an affiliate of Centocor, of 438,340 newly issued shares of our common stock at a purchase price of \$17.11 per share. Centocor also agreed to fund certain research and development activities. Milestone payments for the successful development and commercialization of a RON-targeted antibody, if all approvals in multiple indications and all sales milestones are achieved, could total, in the aggregate, \$540 million. Upon commercialization, we are eligible to receive tiered double-digit royalty payments on Centocor's net sales of any RON-targeted antibody, as a percentage of net sales. Centocor's royalty

---

**Table of Contents**

obligations in a particular country begin on the date of first commercial sale of a product in that country, and end on the later of 10 years after the date of first commercial sale of the product in that country or the date of the last to expire of the issued patents covering the product in that country. All milestone payments and royalties will be reduced by a specified percentage if Centocor develops or commercializes a RON-targeted antibody which has incorporated significant, meaningful improvements made after a specified period by Centocor to the antibodies delivered by us. The royalties will also be reduced by a specified percentage on a country-by-country basis upon the entry of a generic competitor.

The Centocor license agreement will remain in effect until the expiration of all of Centocor's royalty obligations to us, determined on a product-by-product and country-by-country basis. Prior to the filing of an investigational new drug application with the FDA or a similar application filed with another regulatory authority outside of the United States (which we refer to as IND submission), Centocor has the right to terminate the Centocor license agreement at will upon 90 days written notice to us. After IND submission, Centocor may terminate the Centocor license agreement at will upon 180 days written notice to us. Either party has the right to terminate the Centocor license agreement in connection with an insolvency event involving the other party or a material breach of the Centocor license agreement by the other party that remains uncured for a specified cure period. In the event that Centocor terminates the Centocor license agreement at will, or if we terminate the Centocor license agreement due to Centocor's material breach or insolvency, worldwide rights to the development, manufacture, and commercialization of RON-targeted antibodies revert back to us.

***Astellas Pharma***

In February 2011, we entered into a collaboration and license agreement with Astellas and certain of its indirect wholly-owned subsidiaries in connection with which we and Astellas will develop and commercialize tivozanib for the treatment of a broad range of cancers, including RCC, and breast and colorectal cancers. Under the terms of the collaboration agreement, we and Astellas share responsibility for continued development and commercialization of tivozanib in the United States, Mexico and Canada, or North America, and in Europe under the joint development plan and joint commercialization plan, respectively. Throughout the rest of the world, which we refer to as the royalty territory (which excludes North America, Europe and Asia), Astellas has an exclusive, royalty-bearing license to develop and commercialize tivozanib. Our plan to commercialize tivozanib in collaboration with Astellas, as described herein, is subject to our and Astellas's receipt of necessary regulatory approvals from the FDA and foreign regulatory authorities based upon favorable results in clinical trials. There can be no assurance that such approvals will be obtained.

Assuming successful approvals of tivozanib by applicable regulatory agencies, we will hold all marketing authorizations in North America, including any new drug application in the United States, and Astellas will hold all marketing authorizations in the rest of the world, other than Asia.

Assuming successful approvals of tivozanib by applicable regulatory agencies, we, as the lead commercialization party in North America, have lead responsibility for formulating the commercialization strategy for North America under the joint commercialization plan, with each of us and Astellas responsible for conducting fifty percent (50%) of the sales efforts and medical affairs activities in North America. Astellas will have lead responsibility for commercialization activities in Europe under the joint commercialization plan, and we are responsible for conducting fifty percent (50%) of the medical affairs activities in the major European countries. We have not yet completed our assessment of our accounting for the Astellas arrangement at commercialization, however, we expect to record all sales of tivozanib in North America, if any, and Astellas will record all sales of tivozanib in Europe, if any. All costs associated with each party's conduct of development and commercialization activities in North America (including any regulatory milestones and royalties associated with tivozanib in North America which may become payable by us to KHK under our license agreement with KHK), and any resulting profits or losses, will be shared equally between the parties. All costs associated with each party's conduct of development and commercialization activities in Europe, and any resulting profits or losses, will be shared equally between the parties. As between the parties, we will remain responsible for complying with our sublicense revenue sharing obligations, if any, to KHK under our license agreement with KHK in connection with the development and commercialization of tivozanib outside of North America.

---

**Table of Contents**

The collaboration activities in North America and Europe are governed by a joint steering committee and specified development, medical affairs, manufacturing and commercialization subcommittees, each comprised of an equal number of representatives from each party. The joint steering committee is responsible for approving, by unanimous consent, the joint development plan and various aspects of the joint commercialization plan for North America and Europe, including commercialization strategy.

We are responsible for manufacturing, through our third party manufacturer, all of Astellas's requirements for tivozanib pursuant to a clinical supply agreement with Astellas and a commercial supply agreement to be negotiated with Astellas. However, Astellas will be solely responsible for packaging and labeling with respect to commercial supply of tivozanib for all areas of the world other than North America and Asia. The parties will share equally the manufacturing costs for supply of tivozanib for North America and Europe, and Astellas's manufacturing costs for packaging and labeling with respect to commercial supply of tivozanib for Europe, and Astellas is obligated to pay us a specified fee for supply of tivozanib for the royalty territory.

Each party is obligated to use commercially reasonable efforts to develop and commercialize tivozanib in each of the United States, Mexico and Canada, and to develop and commercialize tivozanib in each European country specified in the agreement. Astellas is also obligated to use commercially reasonable efforts to develop and commercialize tivozanib in each country in the royalty territory.

During the term of the agreement, neither party nor its controlled affiliates may commercialize anywhere in North America, Europe or the royalty territory any product that has a specified mechanism of action (as further defined in the collaboration agreement) for any oncology indication, except that Astellas may commercialize specified compounds for hematological cancer. Astellas may also commercialize products (other than tivozanib) in the royalty territory, on a country-by-country basis, upon expiration of the applicable royalty term, and in North America and Europe upon expiration of all valid claims under the licensed patents.

In connection with the agreement, we received an initial cash payment of \$125 million, comprised of a \$75 million license fee and \$50 million in research and development funding, both of which are non-creditable and non-refundable against any amounts due under the collaboration agreement. We retained net proceeds of approximately \$97.6 million of the initial cash payment from Astellas, after payments to KHK and strategic, legal and financial advisors. We are also eligible to receive an aggregate of approximately \$1.3 billion in potential milestone payments, comprised of (i) up to \$85 million in milestone payments upon achievement of specified clinical and development milestone events, (ii) up to \$490 million in milestone payments upon achievement of specified regulatory milestone events, including up to \$90 million in milestone payments in connection with specified regulatory filings, and receipt of marketing approvals, for tivozanib to treat RCC in the United States and Europe, and (iii) up to \$780 million in milestone payments upon the achievement of specified sales events. In addition, if tivozanib is successfully developed and launched in the royalty territory, Astellas will be required to pay to us tiered, double digit royalties on net sales of tivozanib in the royalty territory, if any, subject to offsets under certain circumstances. We are required to pay to KHK a specified percentage of milestones and royalties we may receive from Astellas in connection with Astellas's development and commercialization activities in Europe and the royalty territory.

Unless terminated earlier in accordance with its terms, the collaboration agreement with Astellas expires (a) with respect to the royalty territory, on a country-by-country basis, upon the latest to occur of: (i) the expiration of the last-to-expire valid claim of an AVEO patent or joint patent covering the composition of tivozanib, (ii) the expiration of the last-to-expire valid claim of an AVEO patent or joint patent covering the use of tivozanib, but only for so long as no generic competition exists in such country, and (iii) twelve years from first commercial sale of tivozanib in such country, and (b) with respect to North America and Europe as a whole, upon the expiration of all payment obligations between the parties related to development and commercialization of tivozanib in North America and Europe. After the second anniversary of the effective date of the collaboration agreement, Astellas has the right to terminate the collaboration agreement, in its entirety or solely with respect to the royalty territory, at any time upon 180 days prior written notice to us. Either party may terminate the

---

**Table of Contents**

collaboration agreement with respect to a specified territory or country as set forth in the collaboration agreement, if the other party fails to cure a material breach related to such territory or country, as applicable. We may also terminate the collaboration agreement in its entirety upon a patent-related challenge by Astellas, its affiliates or sublicensees, if such patent-related challenge is not withdrawn within 30 days following our notice to Astellas of such termination.

***Biogen Idec***

In March 2009, we entered into an exclusive option and license agreement with Biogen Idec regarding the development and commercialization of our discovery-stage ErbB3-targeted antibodies for the potential treatment and diagnosis of cancer and other diseases outside of the United States, Canada and Mexico. Under the agreement, we are responsible for developing ErbB3 antibodies through completion of the first phase 2 clinical trial designed in a manner that, if successful, will generate data sufficient to support advancement to a phase 3 clinical trial. Within a specified time period after we complete the phase 2 clinical trial and deliver to Biogen Idec a detailed data package containing the results of the trial, Biogen Idec may elect to obtain (1) a co-exclusive (with us), worldwide license, including the right to grant sublicenses, under our relevant intellectual property to develop and manufacture ErbB3 antibody products, and (2) an exclusive license, including the right to grant sublicenses, under our relevant intellectual property, to commercialize ErbB3 antibody products in all countries in the world other than the United States, Canada and Mexico. We retain the exclusive right to commercialize ErbB3 antibody products in the United States, Canada and Mexico. In this description, the countries in the world other than the United States, Canada and Mexico are referred to as Biogen Idec's territory, and the United States, Canada and Mexico are referred to as our territory. If Biogen Idec exercises its exclusive option to ErbB3 antibody products, Biogen Idec will grant us (a) co-exclusive (with Biogen Idec), worldwide license under Biogen Idec's relevant intellectual property, to develop and manufacture ErbB3 antibody products anywhere in the world, and (b) an exclusive license under Biogen Idec's relevant intellectual property, to commercialize ErbB3 antibody products in the United States, Canada and Mexico.

Until completion of the first phase 2 clinical trial, we are solely responsible for the research, development and manufacture of ErbB3 antibody(ies) pursuant to a written work plan meeting specific pre-agreed guidelines. We will share the written work plan with Biogen Idec for its review and comment, and we are required to use commercially reasonable efforts to perform the activities set forth in the work plan. We are solely responsible for all expenses incurred through completion of the first phase 2 clinical trial. If Biogen Idec exercises its option to obtain exclusive commercialization rights to ErbB3 products in its territory, we will then be solely responsible, subject to a mutually agreed development plan, budget and the oversight of a joint development committee, for the global development of ErbB3 antibody products, except that Biogen Idec will be solely responsible for ErbB3 antibody product development activities that relate solely to the Biogen Idec territory. Further, neither party has the right to conduct development activities in its respective territory if those development activities would materially and adversely affect the development of ErbB3 antibody products in the other party's territory. We and Biogen Idec will share global development costs (including manufacturing costs to support development) for ErbB3 antibody products equally, except that Biogen Idec will be solely responsible for all development costs associated solely with the development of ErbB3 antibody products for its territory, and we will be solely responsible for all development costs associated solely with the development of ErbB3 antibody products for the United States, Canada and Mexico. If either party wishes to develop a new ErbB3 antibody product under the agreement, and the other party does not also wish to develop that product, the party that desires to conduct development activities regarding the new ErbB3 antibody product has the right to independently, and at its sole cost, develop and manufacture the new ErbB3 antibody product for commercialization solely in its territory.

We are solely responsible for, and obligated to use commercially reasonable efforts to, manufacture and supply clinical and commercial quantities of ErbB3 antibody products for the Biogen Idec territory and for the United States, Canada and Mexico. If we determine to retain a third party to manufacture and supply ErbB3 antibody products for phase 3 clinical trials and/or for commercialization in the United States, Canada and Mexico or the Biogen Idec territory, then we must first notify Biogen Idec thereof, and, subject to certain limitations, Biogen Idec may elect to become the sole supplier of ErbB3 antibody product for phase 3 clinical trials and for worldwide commercialization.

---

**Table of Contents**

Pursuant to the agreement, commercialization efforts will be discussed and coordinated at meetings of the joint commercialization committee, comprised of our and Biogen Idec's representatives. We have the sole right, at our sole expense (including manufacturing costs), to commercialize ErbB3 antibody products in the United States, Canada and Mexico, and we are required to use commercially reasonable efforts to do so in countries in our territory where marketing approval has been obtained. Biogen Idec has the sole right, at its sole expense (including manufacturing costs) to commercialize ErbB3 antibody products in its territory, and is required to use commercially reasonable efforts to do so in countries in its territory where marketing approval has been obtained.

We have agreed that, prior to Biogen Idec's exercise of its exclusive option, or until the expiration of Biogen Idec's option right, we and our affiliates will not grant any third party rights to develop ErbB3 antibodies in our territory or in the Biogen Idec territory. We have also agreed that, during the term of the agreement, we will not grant any third party rights to develop or commercialize ErbB3 antibody products if such third party is independently developing or commercializing its own product containing an ErbB3 antibody. Prior to entering into discussions with, or granting a license or sublicense to, any third party with respect to the commercialization of ErbB3 antibody products, we are required to negotiate in good faith with Biogen Idec for a limited time period with respect to granting such rights to Biogen Idec. We have also agreed that, except pursuant to our agreement with Biogen Idec, during the term of the agreement, neither we nor our affiliates, alone or with or on behalf of any third party, will develop, manufacture or commercialize any ErbB3 antibody for therapeutic or diagnostic use in humans, or grant rights to any third party to do any of the foregoing.

Upon entering into the exclusive option and license agreement with Biogen Idec, we received a one-time cash payment in the amount of \$5.0 million and an equity investment in the amount of \$30.0 million. In each of June 2009, April 2010 and June 2011, we received a \$5.0 million milestone payment for achievement of three pre-clinical discovery milestones under the agreement. We could also receive an option exercise fee and regulatory milestone payments of \$50.0 million in the aggregate if Biogen Idec exercises its option to obtain exclusive rights to commercialize ErbB3 antibody products in its territory and we achieve such regulatory milestone events. If Biogen Idec exercises its exclusive option, Biogen Idec will pay us royalties on its sales of ErbB3 antibody products in the Biogen Idec territory, and we will pay Biogen Idec royalties on our sales of ErbB3 antibody products in the United States, Canada and Mexico. Biogen Idec's royalty obligations to us, and our royalty obligations to Biogen Idec, determined on a product-by-product and country-by-country basis, commence on the first commercial sale of the ErbB3 antibody product in the applicable country, and expire on the later of the date of expiration of (1) the last applicable patent covering the ErbB3 antibody product in the applicable country, and (2) any regulatory exclusivity applicable to the ErbB3 antibody product in that country.

If Biogen Idec fails to exercise its exclusive option to co-develop and commercialize ErbB3 antibody products, then the agreement will terminate on the date Biogen Idec's option right expires, and we will retain all of our rights to develop, manufacture and commercialize our ErbB3 antibody products. If Biogen Idec exercises its exclusive option to co-develop and commercialize ErbB3 antibody products, then, unless earlier terminated, the agreement will remain in effect until the last to expire of all royalty obligations under the agreement, or, if later, upon completion of any development activities that were pending before the expiration of all royalty obligations under the agreement.

Biogen Idec may terminate the agreement for convenience with respect to any product(s), by providing us with three months' prior written notice. Either party may terminate the agreement due to a material breach of the agreement by the other party that is not cured within a short period.

If Biogen Idec terminates the agreement for convenience, or if we terminate the agreement due to a material breach of the agreement by Biogen Idec, in each case prior to Biogen Idec's exercise of its exclusive option (and prior to the expiration of the option exercise period), then Biogen Idec's exclusive option will terminate.

If Biogen Idec terminates the agreement for convenience, or if we terminate the agreement due to a material breach of the agreement by Biogen Idec, in each case with respect to one or more ErbB3 antibody products after Biogen Idec's exercise of its exclusive option, then at our election, (1) Biogen Idec will lose all rights to the



**Table of Contents**

terminated product(s), (2) we will have the worldwide right to develop, manufacture and commercialize the terminated product(s), subject to milestone and royalty obligations to Biogen Idec in our territory and in the Biogen Idec territory, and (3) Biogen Idec will be required to transfer to us all regulatory approvals, data, promotional materials and other documents, materials and information reasonably necessary to enable us to develop, manufacture and commercialize the terminated products in the Biogen Idec territory. Further, in the case of termination by Biogen Idec for convenience, Biogen Idec will be required to continue to pay its share of all development costs with respect to the terminated product for a specified period after the effective date of termination.

If Biogen Idec terminates the agreement due to our material breach of the agreement, at Biogen Idec's election (1) if not yet exercised, Biogen Idec will be deemed to have exercised its exclusive option and will not be required to pay us the option exercise fee, (2) Biogen Idec will have no further milestone payment obligations to us, (3) we will lose all rights to the terminated product(s), (4) Biogen Idec will have the worldwide right to develop, manufacture and commercialize the terminated product(s), subject to royalty obligations to us based on worldwide net sales, and (5) we will be required to transfer to Biogen Idec all regulatory approvals, data, promotional materials and other documents, materials and information reasonably necessary to enable Biogen Idec to develop, manufacture and commercialize the terminated products in the Biogen Idec's territory.

If all of our assets are acquired by, or we merge with, another entity, and the other entity is independently developing or commercializing a product containing an ErbB3 antibody and fails to divest the ErbB3 product within a specified time period, Biogen Idec will have the option to either terminate the agreement or maintain the agreement. If Biogen Idec elects to terminate the agreement, then each party will have the right to develop, manufacture and commercialize ErbB3 antibody products for its respective territory, subject to reduced royalty obligations to the other party, and Biogen Idec's activities will not be subject to the oversight of the joint committee. If Biogen Idec elects to maintain the agreement, Biogen Idec will have the right to assume the key development, manufacturing, budgeting and governance rights, responsibilities, and obligations under the agreement that had previously been our rights and obligations.

***OSI Pharmaceuticals***

In September 2007, we entered into a collaboration and license agreement with OSI Pharmaceuticals, Inc., or OSI (a wholly-owned subsidiary of Astellas US Holding, Inc., a holding company owned by Astellas), which provided for the use of our proprietary *in vivo* models by our scientists at our facilities, use of our bioinformatics tools and other target validation and biomarker research to further develop and advance OSI's small molecule drug discovery and translational research related to cancer and other diseases. The collaborative research under this strategic partnership, which concluded in July 2011, was focused primarily on the identification and validation of genes and targets involved in the processes of epithelial-mesenchymal transition, or EMT, or mesenchymal-epithelial transition, or MET, in cancer. EMT/MET processes are of emerging significance in tumor development and disease progression. Key elements of our strategic partnership with OSI included:

identification and validation of a pre-agreed number of oncology targets for small molecule drug discovery, development and commercialization by OSI;

generation of target-driven *in vivo* mouse tumor models for use in drug screening and biomarker validation to support OSI's drug discovery and translational research activities; and

application of our Human Response Platform to identify genetic profiles that correlate with drug response to compounds in certain of OSI's small molecule drug discovery programs.

Under the terms of our agreement, OSI elected to obtain exclusive rights, with the right to grant sublicenses, under certain aspects of our intellectual property, to research, develop, make, sell and import drug products and associated diagnostics directed to a specified number of targets identified and/or validated under the agreement. OSI has sole responsibility and is required to use commercially reasonable efforts to develop and commercialize drugs and associated diagnostics directed to the targets to which it has obtained rights.

---

**Table of Contents**

In November 2010, OSI exercised its option, granted in connection with the July 2009 expansion of our strategic partnership, to obtain:

a non-exclusive license to access our proprietary bioinformatics platform;

non-exclusive perpetual licenses to use bioinformatics data and to use a proprietary gene index related to a specific target pathway;  
and

non-exclusive perpetual rights to certain elements of our Human Response Platform and our bioinformatics platform, including the right to obtain certain of our tumor models and tumor archives.

The technology transfer related to the granting of these rights to OSI was completed in July 2011.

Upon entering into the initial collaboration and license agreement with OSI in September 2007, we received a one-time cash payment of \$7.5 million and an equity investment in the amount of \$5.5 million. In July 2009, in connection with the expanded rights we granted to OSI, we received a one-time cash payment of \$5.0 million and an equity investment in the amount of \$15.0 million. In connection with OSI's exercise of its option under the parties' July 2009 expansion of the agreement to obtain a non-exclusive, perpetual license to certain elements of our proprietary technology platform, OSI paid us \$25.0 million in license expansion fees. In March 2011, we earned \$1.5 million related to deliverables and research milestones under the agreement. As of December 31, 2011, we have received approximately \$16.2 million in research and development funding under the agreement. To date, we have received milestone payments under the agreement in the amount of \$29.3 million. If all applicable milestones are achieved, payments for the successful achievement of discovery, development and commercialization milestones under the agreement could total, in the aggregate, over \$94.0 million for each target and its associated products. Upon commercialization of products under the agreement, we are eligible to receive tiered royalty payments on sales of products by OSI, its affiliates and sublicensees. OSI's royalty obligations to us in a particular country begin on the date of first commercial sale of the product in that country, and end on the latest to occur of: (i) 10 years after the first commercial sale of the product, (ii) expiration of regulatory exclusivity applicable to the product (if any) and (iii) the date of expiration of the last to expire issued patent covering the product in the applicable country.

At the conclusion of the research program in June 2011, we retained rights to any targets that were included in the strategic partnership but were not selected by OSI. We have also obtained exclusive rights to certain intellectual property developed by OSI under our strategic partnership to develop and commercialize small molecule products and associated diagnostics with respect to the targets that were returned to us, and to develop and commercialize antibody products against any target, other than the targets OSI selected for the development of antibody products. In connection with the licenses granted to us from OSI, we are required to make a one-time milestone payment upon regulatory approval and to pay a royalty on sales of each product where the regulatory approval of the product includes a claim in the product label for a targeted patient population and such claim in the product label is covered by patent rights developed under our strategic partnership.

The collaboration and license agreement will remain in effect until the expiration of both OSI's royalty obligations to us, and our royalty obligations to OSI, in each case determined on a product-by-product and country-by-country basis. OSI has the right to terminate the agreement with respect to any or all collaboration targets and all associated products. Either party has the right to terminate the agreement in connection with a material breach of the agreement by the other party that remains uncured for a specified cure period. If OSI elects to terminate the agreement due to our material breach, we will lose our rights to certain intellectual property developed under the strategic partnership, and OSI will have the right to reduce its milestone and royalty obligations to us by the amount of monetary damages suffered by OSI as a direct result of our material breach. If OSI elects to terminate the agreement with respect to one or more collaboration targets and all associated products, OSI's licenses to such targets and products will terminate and revert to us, or if we elect to terminate the agreement due to OSI's material breach of the agreement, OSI's licenses to all targets and products will terminate and revert to us, in either case subject to our continued milestone and royalty payment obligations to

**Table of Contents**

OSI, which we will have the right to reduce by the amount of monetary damages we suffer as a direct result of OSI's breach. In addition, if OSI elects to terminate the agreement with respect to one or more collaboration targets and associated products, for a specified time period after such termination OSI and its affiliates may not, nor may they grant third parties the right to, conduct research or development activities with respect to the terminated collaboration target(s).

**Patents and Proprietary Rights**

*General Intellectual Property Considerations*

We have been building and will seek to continue to build a strong intellectual property portfolio. In this regard, we have focused on patents, patent applications and other intellectual property covering:

tivozanib and related technologies

U.S. patents: 6 issued; 3 pending; expirations ranging from 2018 to 2032

European patents: 3 granted; 1 pending; expirations ranging from 2018 to 2029

Canadian patents: 1 granted; 1 pending; expiration 2022-2029

Australian patents: 1 granted; 1 pending; expiration 2022-2029

International applications: 2 pending

our antibody product pipeline and related technologies

U.S. patents: 5 issued; 8 pending; expirations ranging from 2027 to 2032

European patents: 2 granted; 4 pending; expirations 2027 to 2029

Canadian patents: none granted; 3 pending; expirations 2027 to 2029

Australian patents: none granted; 3 pending; expirations 2027 to 2029

International applications: 5 pending

various facets of our technology platform

## Edgar Filing: AVEO PHARMACEUTICALS INC - Form 10-K

U.S. patents: 4 issued; 3 pending; expirations ranging from 2020 to 2035

European patents: 1 granted; 4 pending; expirations ranging from 2022 to 2026

Australian patents: 4 granted; none pending; expirations ranging from 2022 to 2026

We strive for multi-tiered patent protection, where possible. For example, with respect to tivozanib, we have exclusively licensed patents that cover the molecule and its therapeutic use (patent expiration 2022, with the possibility of patent term extension to 2025 in the United States), a key step in manufacturing the molecule, and a crystal form of the molecule, i.e., a polymorph with low hygroscopicity used in the clinical formulation. Complementing these in-licensed patents relating to tivozanib are two of our own issued U.S. patents that cover different biomarker tests for identifying human patients likely to respond to treatment with tivozanib, and an issued U.S. patent on a method of using tivozanib in combination with temsirolimus.

We own issued U.S. patents containing composition-of-matter claims that cover our HGF antibodies, including ficlatuzumab. In addition, we own pending patent applications covering our HGF antibodies, our FGFR3 antibodies, ErbB3 antibodies, FGFR2 antibodies, EGFR antibodies, RON antibodies, Notch1 antibodies, Notch3 antibodies, and methods of making and using those antibodies. We are prepared to file patent applications on other antibodies in our antibody product pipeline soon after the experimental data necessary for an application becomes available.

## **Table of Contents**

In addition to filing and prosecuting patent applications in the United States, we file counterpart patent applications in Europe, Canada, Japan, Australia (and sometimes additional countries), in cases where we think such foreign filing is likely to be cost-effective.

The term of individual patents depends upon the legal term of the patents in the countries in which they are obtained. In most countries in which we file, the patent term is 20 years from the earliest date of filing a non-provisional patent application. In the United States, a patent's term may be lengthened by patent term adjustment, which compensates a patentee for administrative delays by the U.S. Patent and Trademark Office in granting a patent. A U.S. patent term may be shortened, if a patent is terminally disclaimed by its owner, over another patent.

The patent term of a patent that covers an FDA-approved drug may also be eligible for patent term extension, which permits patent term restoration as compensation for the patent term lost during the FDA regulatory review process. The Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Act, permits a patent term extension of up to five years beyond the expiration of the patent. The length of the patent term extension is related to the length of time the drug is under regulatory review. Patent extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, and only one patent applicable to an approved drug may be extended. Similar provisions are available in Europe and other foreign jurisdictions to extend the term of a patent that covers an approved drug. In the future, if and when our pharmaceutical products receive FDA approval, we expect to apply for patent term extensions on patents covering those products.

In addition to patents relating to tivozanib, ficlatuzumab and other therapeutic antibodies in our product pipeline, our patent portfolio contains a number of other patents and patent applications relevant to our business. For example, we own a granted U.S. patent and pending foreign counterpart applications covering a method of making a chimeric mouse cancer model. We also own a granted U.S. patent and pending foreign counterpart patent applications covering a method of producing primary tumor material via directed complementation. We also own pending U.S. and foreign patent applications covering a mouse model that contains a human breast tumor. We own a granted U.S. patent and a pending foreign counterpart patent application covering a method of identifying cancer tissue likely to be sensitive or resistant to treatment with an inhibitor of Notch receptor activation. We own a pending patent application on a predictive biomarker for identifying patients likely to respond to one of our antibodies. We own a pending patent application that covers a general method for identifying new, multi-gene biomarkers for predicting response to an anti-cancer drug of interest, as well as specific multi-gene biomarkers identified by using the method. Besides having a portfolio of patents and pending patent applications owned by us covering our platform technology, we are exclusively licensed under Dana-Farber patents that cover germ line transgenic mouse models of cancer, and a method of using spontaneous inducible mouse tumor models to screen for, and identify, novel targets for new cancer drugs, which we refer to as our MaSS screen technology.

For some aspects of our proprietary technology, trade secret protection is more appropriate than patent protection. For example, our proprietary bioinformatics software tools and databases are protected as trade secrets. Our bioinformatics tools and databases give us the means to store, analyze, interpret and integrate the large volume of data generated from our various tumor models and from analysis of human clinical samples from clinical trials. We continually make incremental improvements in our proprietary software tools, as we tailor them to the changing needs of our research and development programs. In general, trade secret protection can accommodate this continuing evolution of our bioinformatics system better than other forms of intellectual property protection.

Many pharmaceutical companies, biotechnology companies and academic institutions are competing with us in the field of oncology and filing patent applications potentially relevant to our business. In order to contend with the inevitable possibility of third party intellectual property conflicts, we make freedom-to-operate studies an ongoing part of our business operations. With regard to tivozanib, we are aware of a third party United States

## **Table of Contents**

patent, and corresponding foreign counterparts, that contain broad claims related to the use of an organic compound that, among other things, inhibits tyrosine phosphorylation of a VEGF receptor caused by VEGF binding to such VEGF receptor. We are also aware of third party United States patents that contain broad claims related to the use of a tyrosine kinase inhibitor in combination with a DNA damaging agent such as chemotherapy or radiation and we have received written notice from the owners of such patents indicating that they believe we may need a license from them in order to avoid infringing their patents. With regard to ficlatuzumab, we are aware of two separate families of United States patents, United States patent applications and foreign counterparts, with each of the two families being owned by a different third party, that contain broad claims related to anti-HGF antibodies having certain binding properties and their use. We are aware of a United States patent that contains claims related to a method of treating a tumor by administering an agent that blocks the ability of HGF to promote angiogenesis in the tumor. With regard to AV-203, we are aware of a third party United States patent that contains broad claims relating to anti-ErbB3 antibodies. Based on our analyses, if any of the above third party patents were asserted against us, we do not believe our proposed products or activities would be found to infringe any valid claim of these patents. If we were to challenge the validity of any issued United States patent in court, we would need to overcome a statutory presumption of validity that attaches to every United States patent. This means that in order to prevail, we would have to present clear and convincing evidence as to the invalidity of the patent's claims. There is no assurance that a court would find in our favor on questions of infringement or validity.

From time to time, we find it necessary or prudent to obtain licenses from third party intellectual property holders. Where licenses are readily available at reasonable cost, such licenses are considered a normal cost of doing business. In other instances, however, we may use the results of freedom-to-operate studies to guide our early-stage research away from areas where we are likely to encounter obstacles in the form of third party intellectual property. For example, where a third party holds relevant intellectual property and is a direct competitor, a license might not be available on commercially reasonable terms or available at all. We strive to identify potential third party intellectual property issues in the early stages of research of our research programs, in order to minimize the cost and disruption of resolving such issues.

In spite of these efforts to avoid obstacles and disruptions arising from third party intellectual property, it is impossible to establish with certainty that our technology platform or our product programs will be free of claims by third party intellectual property holders. Even with modern databases and on-line search engines, literature searches are imperfect and may fail to identify relevant patents and published applications. Even when a third party patent is identified, we may conclude upon a thorough analysis, that we do not infringe the patent or that the patent is invalid. If the third party patent owner disagrees with our conclusion and we continue with the business activity in question, we might have patent litigation initiated against us. Alternatively, we might decide to initiate litigation in an attempt to have a court declare the third party patent invalid or non-infringed by our activity. In either scenario, patent litigation typically is costly and time-consuming, and the outcome is uncertain. The outcome of patent litigation is subject to uncertainties that cannot be quantified in advance, for example, the credibility of expert witnesses who may disagree on technical interpretation of scientific data. Ultimately, in the case of an adverse outcome in litigation, we could be prevented from commercializing a product or using certain aspects of our technology platform as a result of patent infringement claims asserted against us. This could have a material adverse affect on our business.

To protect our competitive position, it may be necessary to enforce our patent rights through litigation against infringing third parties. Litigation to enforce our own patent rights is subject to the same uncertainties discussed above. In addition, however, litigation involving our patents carries the risk that one or more of our patents will be held invalid (in whole or in part, on a claim-by-claim basis) or held unenforceable. Such an adverse court ruling could allow third parties to commercialize our products or our platform technology, and then compete directly with us, without payment to us.

## **Table of Contents**

### ***In-Licenses***

*Dana-Farber Cancer Institute.* When forming the company in March 2002, we entered into a license agreement with Dana-Farber Cancer Institute, or DFCI. Under the agreement, we have: exclusive, worldwide rights under certain DFCI patents and patent applications relating to spontaneous, inducible mouse tumor models; the right to grant sublicenses; and sole ownership rights to any improvements made solely by our employees to the mouse model technology licensed from DFCI. We have fulfilled certain milestone payment obligations to DFCI. We will have no royalty obligation to DFCI based on sales of products discovered, designed, developed or tested using the licensed mouse tumor models. Our license from DFCI will expire on the expiration date of the last-to-expire of the underlying patents.

*Kyowa Hakko Kirin.* In December 2006, we entered into a license agreement with Kirin Brewery Co. Ltd. (now Kyowa Hakko Kirin) under which we obtained an exclusive license to research, develop, manufacture and commercialize tivozanib (f/k/a KRN951), pharmaceutical compositions thereof and associated biomarkers for the diagnosis, prevention and treatment of any and all human diseases and conditions. Our exclusive license covers all territories in the world, except for Asia. Kyowa Hakko Kirin has retained rights to tivozanib in Asia. For further discussion of this agreement, please see Strategic Partnerships Kyowa Hakko Kirin.

*Other.* We hold several non-exclusive licenses from other third parties that give us access to various technologies involved in building and using our technology platform and discovering and developing our antibody pipeline.

### **Manufacturing**

We currently contract with third parties for the manufacture of our product candidates for preclinical studies and clinical trials and intend to do so in the future. We do not own or operate manufacturing facilities for the production of clinical or commercial quantities of our product candidates. We currently have no plans to build our own clinical or commercial scale manufacturing capabilities. Although we rely on contract manufacturers, we have personnel with extensive manufacturing experience to oversee the relationships with our contract manufacturers.

One of our contract manufacturers has manufactured what we believe to be sufficient quantities of tivozanib's drug substance to support the ongoing phase 1, 2 and 3 clinical trials. We believe the current manufacturing process for the drug substance for tivozanib is adequate to support future development and commercial demand. In addition, we currently engage a separate contract manufacturer to manufacture, package and distribute clinical supplies of tivozanib. While we believe that our existing suppliers of drug substance and drug product would be capable of producing commercial quantities, we will need to fully validate their ability to produce drug substance and drug product on commercial scale. If we are unable to validate our third-party manufacturing sources' ability to supply on a commercial basis, or fail to establish commercially reasonable terms for commercial supply with an alternative vendor, we may not be able to successfully produce and market tivozanib or would be delayed in doing so.

As of December 27, 2010, the effective date of the termination of our collaboration with Merck relating to ficlatuzumab, we became responsible for all process development and all manufacturing of ficlatuzumab for future development and commercialization. Prior to Merck's termination of its collaboration agreement with us, multiple batches of drug product were produced by Merck to support clinical trials of ficlatuzumab through phase 2 clinical trials. We have purchased a supply of ficlatuzumab from Merck which we expect will allow us to complete our ongoing phase 1 and phase 2 clinical trials of ficlatuzumab. In November 2011, we entered into an agreement with Boehringer Ingelheim for large-scale process development and clinical manufacturing of ficlatuzumab. Boehringer Ingelheim will produce ficlatuzumab for clinical trials at its biopharmaceutical site in Fremont, CA.

## **Table of Contents**

To date, our third-party manufacturers have met our manufacturing requirements. We believe that there are alternate sources of supply that can satisfy our clinical and commercial requirements, although we cannot be certain that identifying and establishing relationships with such sources, if necessary, would not result in significant delay or material additional costs.

### **Sales and Marketing**

If tivozanib is approved for sale, it is our goal to maximize its potential value in the U.S. and Europe by demonstrating tivozanib's potential favorable efficacy and safety profile and establishing tivozanib as a first-line treatment of choice for patients with advanced RCC.

In order to achieve this goal, we entered into a strategic partnership with Astellas in connection with which we and Astellas will seek to develop and commercialize tivozanib in North America and Europe. We intend to build a commercial infrastructure in the United States necessary to effectively support the commercialization of tivozanib and future oncology products, if approved. The commercial infrastructure for specialty oncology products typically consists of a targeted, field based specialty sales force that calls on a focused group of physicians. This sales force would be supported by sales management and sales training, as well as internal and outsourced commercial groups including sales and commercial operations, marketing, market research, reimbursement services and distribution. Additional capabilities important to the oncology marketplace include the management of key accounts such as managed care organizations, group-purchasing organizations, specialty pharmacies, oncology group networks, and government accounts, all responsibilities and costs which we would share with our partner, Astellas. To develop the appropriate commercial infrastructure, we would have to invest significant amounts of financial and management resources, some of which would be committed prior to any confirmation that tivozanib will be approved. In Europe, although Astellas would be the lead commercialization party, we are obligated to contribute up to 50% of the medical science liaisons in the major European countries as well as formulate with Astellas the European commercial strategy, including the strategic plan and allocation of resources.

### **Government Regulation**

Government authorities in the United States (including federal, state and local authorities) and in other countries, extensively regulate, among other things, the manufacturing, research and clinical development, marketing, labeling and packaging, distribution, post-approval monitoring and reporting, advertising and promotion, and export and import of pharmaceutical products, such as those we are developing. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources.

#### ***United States Government Regulation***

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and related regulations. Drugs are also subject to other federal, state and local statutes and regulations. Biological products are subject to regulation by the FDA under the FDCA, the Public Health Service Act, and related regulations, and other federal, state and local statutes and regulations. Failure to comply with the applicable U.S. regulatory requirements at any time during the product development process, approval process or after approval, may subject an applicant to administrative or judicial sanctions. These sanctions could include the imposition by the FDA or an Institutional Review Board, or IRB, of a clinical hold on trials, the FDA's refusal to approve pending applications or supplements, withdrawal of an approval, warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, civil penalties or criminal prosecution. Any agency or judicial enforcement action could have a material adverse effect on us.



---

## **Table of Contents**

### ***The Investigational New Drug Process***

An Investigational New Drug application, or an IND, is a request for authorization from the FDA to administer an investigational drug or biological product to humans. Such authorization must be secured prior to interstate shipment (usually to clinical investigators) and administration of any new drug or biological product to humans that is not the subject of an approved New Drug Application or Biologics License Application, except under limited circumstances.

To conduct a clinical investigation with an investigational new drug or biological product, we are required to file an IND with the FDA in compliance with Title 21 of the Code of Federal Regulations (CFR), Part 312. These regulations contain the general principles underlying the IND submission and the general requirements for an IND's content and format.

The central focus of the initial IND submission is on the general investigational plan and the protocol(s) for human studies. The IND also includes results of animal studies or other human studies, as appropriate, as well as manufacturing information, analytical data and any available clinical data or literature to support the use of the investigational new drug or biological product. An IND must become effective before human clinical trials may begin. An IND will automatically become effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions related to the proposed clinical trials as outlined in the IND. In such a case, the IND may be placed on clinical hold and the IND sponsor and the FDA must resolve any outstanding concerns or questions before clinical trials can begin. Accordingly, submission of an IND may or may not result in the FDA allowing clinical trials to commence.

Clinical trials involve the administration of the investigational drug or biological product to patients under the supervision of qualified investigators in accordance with Good Clinical Practices, or GCPs. Clinical trials are conducted under protocols detailing, among other things, the objectives of the study, the parameters to be used in monitoring safety, and the efficacy criteria to be evaluated. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. Additionally, approval must also be obtained from each clinical site's independent IRB before the trials may be initiated. All participants in our clinical trials must provide their informed consent in writing in compliance with GCPs and the ethical principles that have their origin in the Declaration of Helsinki.

The clinical investigation of an investigational drug or biological product is generally divided into three phases. Although the phases are usually conducted sequentially, they may overlap or be combined. The three phases of an investigation are as follows:

**Phase 1.** Phase 1 includes the initial introduction of an investigational new drug or biological product into humans. Phase 1 clinical trials are typically closely monitored and may be conducted in patients with the target disease or condition or healthy volunteers. These studies are designed to evaluate the safety, dosage tolerance, metabolism and pharmacologic actions of the investigational drug or biological product in humans, the side effects associated with increasing doses, and if possible, to gain early evidence on effectiveness. During phase 1 clinical trials, sufficient information about the investigational drug's or biological product's pharmacokinetics and pharmacological effects may be obtained to permit the design of well-controlled and scientifically valid phase 2 clinical trials. The total number of participants included in phase 1 clinical trials varies, but is generally in the range of 20 to 80.

**Phase 2.** Phase 2 includes the controlled clinical trials conducted to preliminarily or further evaluate the effectiveness of the investigational drug or biological product for a particular indication(s) in patients with the disease or condition under study, to determine dosage tolerance and optimal dosage, and to identify possible adverse side effects and safety risks associated with the drug or biological product. Phase 2 clinical trials are typically well-controlled, closely monitored, and conducted in a limited patient population, usually involving no more than several hundred participants.

---

## **Table of Contents**

**Phase 3.** Phase 3 clinical trials are generally controlled clinical trials conducted in an expanded patient population generally at geographically dispersed clinical trial sites. They are performed after preliminary evidence suggesting effectiveness of the drug or biological product has been obtained, and are intended to further evaluate dosage, clinical effectiveness and safety, to establish the overall benefit-risk relationship of the investigational drug or biological product, and to provide an adequate basis for product approval. Phase 3 clinical trials usually involve several hundred to several thousand participants.

The FDA's primary objectives in reviewing an IND are to assure the safety and rights of patients and to help assure that the quality of the investigation will be adequate to permit an evaluation of the drug's effectiveness and safety and of the biological product's safety, purity and potency. The decision to terminate development of an investigational drug or biological product may be made by either a health authority body such as the FDA (or IRB/ethics committees), or by us for various reasons. Additionally, some trials are overseen by an independent group of qualified experts organized by the trial sponsor, known as a data safety monitoring board or committee. This group provides authorization for whether or not a trial may move forward at designated check points based on access that only the group maintains to available data from the study. Suspension or termination of development during any phase of clinical trials can occur if it is determined that the participants or patients are being exposed to an unacceptable health risk. Other reasons for suspension or termination may be made by us based on evolving business objectives and/or competitive climate.

In addition, there are requirements and industry guidelines to require the posting of ongoing clinical trials on public registries, and the disclosure of designated clinical trial results.

Assuming successful completion of all required testing in accordance with all applicable regulatory requirements, detailed investigational drug or biological product information is submitted to the FDA in the form of an NDA or Biologics License Application, or BLA, requesting approval to market the product for one or more indications.

### ***The NDA/BLA Approval Process***

In order to obtain approval to market a drug or biological product in the United States, a marketing application must be submitted to the FDA that provides data establishing the safety and effectiveness of the drug product for the proposed indication, and the safety, purity and potency of the biological product for its intended indication. The application includes all relevant data available from pertinent preclinical and clinical trials, including negative or ambiguous results as well as positive findings, together with detailed information relating to the product's chemistry, manufacturing, controls and proposed labeling, among other things. Data can come from company-sponsored clinical trials intended to test the safety and effectiveness of a use of a product, or from a number of alternative sources, including studies initiated by investigators. To support marketing approval, the data submitted must be sufficient in quality and quantity to establish the safety and effectiveness of the investigational drug product and the safety, purity and potency of the biological product to the satisfaction of the FDA.

The steps required before an investigational drug or biological product may be marketed in the United States generally include:

Completion of preclinical laboratory tests, animal studies and formulation studies in compliance with the FDA's Good Laboratory Practices, or GLP, regulations;

Submission to the FDA of an IND to support human clinical testing;

Approval by an IRB at each clinical site before each trial may be initiated;

Performance of adequate and well-controlled clinical trials in accordance with GCP to establish the safety and efficacy of the investigational drug product for each targeted indication or the safety, purity and potency of the biological product for its intended indication;

**Table of Contents**

Submission of an NDA or BLA to the FDA;

Satisfactory completion of an FDA Advisory Committee review, if applicable;

Satisfactory completion of an FDA inspection of the manufacturing facilities at which the investigational drug or biological product is produced to assess compliance with current good manufacturing practices, or cGMP, and to assure that the facilities, methods and controls are adequate to preserve the product's identity, strength, quality and purity; and

FDA review and approval of the NDA or BLA.

In most cases, the NDA or BLA must be accompanied by a substantial user fee; there may be some instances in which the user fee is waived.

The FDA will initially review the NDA or BLA for completeness before it accepts the NDA or BLA for filing. The FDA has 60 days from its receipt of an NDA to determine whether the application will be accepted for filing based on the agency's threshold determination that it is sufficiently complete to permit substantive review. After the NDA submission is accepted for filing, the FDA reviews the NDA to determine, among other things, whether the proposed product is safe and effective for its intended use, and whether the product is being manufactured in accordance with cGMP to assure and preserve the product's identity, strength, quality and purity. The FDA reviews a BLA to determine, among other things, whether the product is safe, pure and potent and the facility in which it is manufactured, processed, packaged or held meets standards designed to assure the product's continued safety, purity and potency. The FDA may refer applications for novel drug or biological products or drug or biological products which present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

Before approving an NDA or BLA, the FDA will inspect the facilities at which the product is manufactured. The FDA will not approve the product unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA or BLA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP. If the FDA determines the application, manufacturing process or manufacturing facilities are not acceptable, it will outline the deficiencies in the submission and often will request additional testing or information. Notwithstanding the submission of any requested additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

The testing and approval process requires substantial time, effort and financial resources, and each may take several years to complete. Data obtained from clinical activities are not always conclusive and may be susceptible to varying interpretations, which could delay, limit or prevent regulatory approval. The FDA may not grant approval on a timely basis, or at all. We may encounter difficulties or unanticipated costs in our efforts to develop our product candidates and secure necessary governmental approvals, which could delay or preclude us from marketing our products. Even if the FDA approves a product, it may limit the approved indications for use or place other conditions on any approvals that could restrict the commercial application of the products such as a requirement that we implement special risk management measures through a Risk Evaluation and Mitigation Strategy. After approval, some types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further testing requirements and FDA review and approval.

## **Table of Contents**

### ***Post-Approval Regulation***

After regulatory approval of a drug or biological product is obtained, we are required to comply with a number of post-approval requirements. For example, as a condition of approval of an NDA or BLA, the FDA may require post-marketing testing, including phase 4 clinical trials, and surveillance to further assess and monitor the product's safety and effectiveness after commercialization. Regulatory approval of oncology products often requires that patients in clinical trials be followed for long periods to determine the overall survival benefit of the drug or biologic. In addition, as a holder of an approved NDA or BLA, we would be required to report, among other things, certain adverse reactions and production problems to the FDA, to provide updated safety and efficacy information, and to comply with requirements concerning advertising and promotional labeling for any of our products. Also, quality control and manufacturing procedures must continue to conform to cGMP after approval to assure and preserve the long term stability of the drug or biological product. The FDA periodically inspects manufacturing facilities to assess compliance with cGMP, which imposes extensive procedural, substantive and record keeping requirements. In addition, changes to the manufacturing process are strictly regulated, and, depending on the significance of the change, may require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting and documentation requirements upon us and any third party manufacturers that we may decide to use. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain compliance with cGMP and other aspects of regulatory compliance.

We rely, and expect to continue to rely, on third parties for the production of clinical and commercial quantities of our product candidates. Future FDA, foreign regulatory authorities, and state inspections may identify compliance issues at our facilities or at the facilities of our contract manufacturers that may disrupt production or distribution, or require substantial resources to correct. In addition, discovery of previously unknown problems with a product or the failure to comply with applicable requirements may result in restrictions on a product, manufacturer or holder of an approved NDA or BLA, including withdrawal or recall of the product from the market or other voluntary, FDA-initiated or judicial action that could delay or prohibit further marketing. Newly discovered or developed safety or effectiveness data may require changes to a product's approved labeling, including the addition of new warnings and contraindications, and also may require the implementation of other risk management measures.

Also, new government requirements, including those resulting from new legislation, may be established, or the FDA's policies may change, which could delay or prevent regulatory approval of our products under development and/or could significantly impact the requirements imposed on us after approval.

### ***Europe / Rest of World Government Regulation***

In addition to regulations in the United States, we will be subject to a variety of regulations in other jurisdictions governing, among other things, clinical trials and any commercial sales and distribution of our products.

Whether or not we obtain FDA approval for a product, we must obtain the requisite approvals from regulatory authorities in foreign countries prior to the commencement of clinical trials or marketing of the product in those countries. Certain countries outside of the United States have a similar process that requires the submission of a clinical trial application much like the IND prior to the commencement of human clinical trials. In Europe, for example, a clinical trial application, or CTA, must be submitted to each country's national health authority and an independent ethics committee, much like the FDA and IRB, respectively. Once the CTA is approved in accordance with a country's requirements, and relevant ethics committees have issued positive opinions, the clinical trial covered by the CTA may proceed.

## **Table of Contents**

The requirements and process governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country. In all cases, the clinical trials are conducted in accordance with GCP and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki.

To obtain regulatory approval of an investigational drug or biological medicinal product under European Union regulatory systems, we must submit a marketing authorization application. The application used to file the NDA or BLA in the United States is similar to that required in Europe, with the exception of, among other things, country-specific document requirements.

For other countries outside of the European Union, such as countries in Eastern Europe, Latin America or Asia, the requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country. In all cases, again, the clinical trials are conducted in accordance with GCP and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki.

If we fail to comply with applicable foreign regulatory requirements, we may be subject to, among other things, fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

### ***Compliance***

During all phases of development (pre- and post-marketing), failure to comply with the applicable regulatory requirements may result in administrative or judicial sanctions. These sanctions could include the FDA's imposition of a clinical hold on trials or the suspension of clinical trials by other regulatory authorities, refusal to approve pending applications, withdrawal of an approval, warning letters, product recalls, product seizures, total or partial suspension of production or distribution, product detention or refusal to permit the import or export of products, injunctions, fines, civil penalties or criminal prosecution. Any agency or judicial enforcement action could have a material adverse effect on us.

### ***Available Special Regulatory Procedures***

#### ***Formal Meetings***

We are encouraged to engage and seek guidance from health authorities relating to the development and review of investigational drugs and biologics, as well as marketing applications. In the United States, there are different types of official meetings that may occur between us and the FDA. Each meeting type is subject to different procedures. Conclusions and agreements from each of these meetings are captured in the official final meeting minutes issued by the FDA.

The EMA and national medicines regulators within the EU also provide the opportunity for dialogue with us. At the EMA level, this is usually done in the form of Scientific Advice, which is given by the Scientific Advice Working Party of the Committee for Medicinal Products for Human Use, or CHMP. A fee is incurred with each Scientific Advice procedure.

Advice from either the FDA or EMA is typically provided based on questions concerning, for example, quality (chemistry, manufacturing and controls testing), nonclinical testing and clinical studies, and pharmacovigilance plans and risk-management programs. Advice is not legally binding with regard to any future marketing authorization application of the product concerned. To obtain binding commitments from the FDA on the design and size of clinical trials intended to form the primary basis of an effectiveness claim, Special Protocol Assessment procedures are available. Where the FDA agrees to a Special Protocol Assessment, or SPA, the agreement may not be changed by either the sponsor or the FDA except if the sponsor and the FDA agree to a change, or a senior FDA official determines that a substantial scientific issue essential to determining the safety

## **Table of Contents**

or effectiveness of the product was identified after the testing began. A SPA is not binding if new circumstances arise, and there is no guarantee that a study will ultimately be adequate to support an approval even if the study is conducted according to the terms of a SPA.

### *Orphan Drug Designation*

The FDA may grant orphan drug designation to drugs and biological products intended to treat a rare disease or condition that affects fewer than 200,000 individuals in the United States, or if it affects more than 200,000 individuals in the United States and there is no reasonable expectation that the cost of developing and making the drug or biological product for this type of disease or condition will be recovered from sales in the United States. In the European Union, the EMA's Committee for Orphan Medicinal Products, or COMP, may recommend orphan drug designation to promote the development of products that are intended for the diagnosis, prevention or treatment of life-threatening or chronically debilitating conditions affecting not more than 5 in 10,000 persons in the European Union. Additionally, designation is granted for products intended for the diagnosis, prevention or treatment of a life-threatening, seriously debilitating or serious and chronic condition and when, without incentives, it is unlikely that sales of the drug in the European Union would be sufficient to justify the necessary investment in developing the drug or biological product. In addition, the COMP may only recommend orphan drug designation when the product in question offers a significant clinical benefit over existing approved products for the relevant indication. Following a positive opinion by the COMP, the European Commission adopts a decision granting orphan status. The COMP will reassess orphan status in parallel with EMA review of a marketing authorization application and orphan status may be withdrawn at that stage if it no longer fulfills the orphan criteria.

In the United States, orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and user-fee waivers. In addition, if a product receives the first FDA approval for the indication for which it has orphan designation, the product is entitled to orphan drug exclusivity, which means the FDA may not approve any other application to market the same drug or biological product for the same indication for a period of 7 years, except in limited circumstances, such as a showing of clinical superiority over the product with orphan exclusivity or if the product with orphan exclusivity experiences a shortage.

In the European Union, orphan drug designation also entitles a party to financial incentives such as reduction of fees or fee waivers and 10 years of market exclusivity is granted following drug or biological product approval. During this period, regulators may not accept or approve any similar medicinal product, unless it offers a significant clinical benefit. This period may be reduced to 6 years if the orphan drug designation criteria are no longer met, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity.

Orphan drug designation must be requested before submitting an application for marketing approval. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

### *Pediatric Development*

In the United States, Section 505A of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355a, Pediatric Studies of Drugs) provides for an additional 6 months of marketing exclusivity for a drug if reports are filed of investigations studying the use of the drug product in a pediatric population in response to a written request from the FDA. Separate from this potential exclusivity benefit, NDAs and BLAs must contain data (or a proposal for post-marketing activity) to assess the safety and effectiveness of an investigational drug or biological product for the claimed indications in all relevant pediatric populations in order to support dosing and administration for each pediatric subpopulation for which the drug is safe and effective. The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the

## **Table of Contents**

product for use in adults or full or partial waivers if certain criteria are met. Discussions about pediatric development plans can be discussed with the FDA at any time, but usually occur any time between the end-of-phase 2 meeting and submission of the NDA or BLA.

For the EMA, a Pediatric Investigation Plan, and/or a request for waiver or deferral, is required for submission prior to submitting a marketing authorization application.

### *Authorization Procedures in the European Union*

There are two types of authorization procedures for medicinal products in the European Union; the centralized authorization procedure and national authorization procedures.

**Centralized procedure.** The centralized procedure gives rise to marketing authorizations that are valid throughout the European Union and, by extension, in three European Economic Area, or EEA member states, Norway, Iceland and Liechtenstein. Applicants file marketing authorizations with the EMA, where they are reviewed by a relevant scientific committee, which is most likely the Committee for Medicinal Products for Human Use, or CHMP. The EMA forwards CHMP positive opinions to the European Commission, which uses them as the basis for a decision granting a marketing authorization. The centralized procedure is compulsory for human medicines that are: derived from biotechnology processes, such as recombinant DNA technology, controlled expression of genes in prokaryotes and eukaryotes and hybridoma and monoclonal antibody methods. It is also mandatory for products containing a new active substance indicated for the treatment of certain diseases, such as HIV/AIDS, cancer, diabetes, neurodegenerative disorders, viral diseases or autoimmune diseases and other immune dysfunctions, and officially designated orphan medicines. For medicines that do not fall within these categories, an applicant has the option of submitting an application for a centralized marketing authorization to the EMA, as long as the CHMP accepts that the medicine concerned is a significant therapeutic, scientific or technical innovation, or if its authorization would be in the interest of public health.

**National authorization procedures.** There are also two other possible routes to authorize medicinal products in more than one EU or EEA country, which are available for investigational drug products that fall outside the scope of the centralized procedure:

*Decentralized procedure.* Using the decentralized procedure, an applicant may apply for simultaneous authorization in more than one European Union country of medicinal products that have not yet been authorized in any European Union country and that do not fall within the mandatory scope of the centralized procedure. The applicant selects a so-called reference member state, or RMS, to take the lead in the review of the application. Other member states are expected to recognize the RMS decision, unless they identify a serious risk to public health. If the member states cannot resolve any such concerns between themselves, the matter is referred to the CHMP for an opinion and ultimately a binding European Commission decision.

*Mutual recognition procedure.* In the mutual recognition procedure, a medicine is first authorized in one European Union RMS, in accordance with the national procedures of that country. Following this, further marketing authorizations can be sought from other European Union countries in a procedure whereby the countries concerned agree to recognize the validity of the original, national marketing authorization. As in the decentralized procedure, these concerned member states must recognize the RMS approval unless they identify a serious risk to the public health. If the member states cannot reach a consensus between themselves, the matter can be referred to the CHMP.

### *Priority Review / Standard Review (United States) and Accelerated Review (European Union)*

Based on results of the phase 3 clinical trial(s) submitted in an NDA or BLA, upon the request of an applicant a priority review designation may be granted to a product by the FDA. Under the FDA's current policies, this sets the target date for FDA action on the application at 6 months; the FDA has proposed changing

## **Table of Contents**

this so that the 6-month period begins after the FDA accepts an NDA or BLA for review, which typically occurs two months after the NDA or BLA is first filed. Priority review is given where preliminary estimates indicate that a product, if approved, has the potential to provide a safe and effective therapy where no satisfactory alternative therapy exists, or a significant improvement compared to marketed products is possible. If criteria are not met for priority review, the standard FDA review period is 10 months. Under current FDA policies, the 10-month period runs from when the NDA or BLA is first submitted to the FDA; the FDA has proposed that the 10-month period run instead from when the FDA accepts the NDA or BLA for review, which typically occurs two months after the NDA or BLA is first filed. Priority review designation does not change the scientific/medical standard for approval or the quality of evidence necessary to support approval.

Under the Centralized Procedure in the European Union, the maximum timeframe for the evaluation of a marketing authorization application is 210 days (excluding clock stops, when additional written or oral information is to be provided by the applicant in response to questions asked by the CHMP. Accelerated evaluation might be granted by the CHMP in exceptional cases, when a medicinal product is expected to be of a major public health interest, defined by three cumulative criteria: the seriousness of the disease (e.g. heavy disabling or life-threatening diseases) to be treated; the absence or insufficiency of an appropriate alternative therapeutic approach; and anticipation of high therapeutic benefit. In this circumstance, EMA ensures that the opinion of the CHMP is given within 150 days.

### ***Pharmaceutical Coverage, Pricing and Reimbursement***

Significant uncertainty exists as to the coverage and reimbursement status of any drug products for which we obtain regulatory approval. In the United States and markets in other countries, sales of any products for which we receive regulatory approval for commercial sale will depend in part on the availability of reimbursement from third party payors. Third party payors include government health administrative authorities, managed care providers, private health insurers and other organizations. The process for determining whether a payor will provide coverage for a drug product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the drug product. Third party payors may limit coverage to specific drug products on an approved list, or formulary, which might not include all of the FDA-approved drugs for a particular indication. Third party payors are increasingly challenging the price and examining the medical necessity and cost-effectiveness of medical products and services, in addition to their safety and efficacy. We may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of our products, in addition to the costs required to obtain FDA approvals. Our product candidates may not be considered medically necessary, cost-effective, or effective in comparison to other treatment options. A payor's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. Adequate third party reimbursement may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development.

In recent years, Congress and some state legislatures have considered a number of proposals and have enacted laws that could effect major changes in the healthcare system, either nationally or at the state level.

In 2010, Congress enacted sweeping healthcare reform legislation. This legislation is changing the way that healthcare is financed by both governmental and private insurers and significantly affects the pharmaceutical industry. Among the provisions of the legislation are provisions governing enrollment in federal healthcare programs, increases in the rebates pharmaceutical manufacturers must pay to state Medicaid programs, expansion of the entities eligible for discounted 340B pricing, a manufacturer-funded 50% discount on prescriptions for branded products filled while the beneficiary is in the Medicare Part D coverage gap, and a significant annual fee on companies that manufacture or import branded prescription drug products. The legislation also includes substantial new provisions affecting compliance, including reporting provisions that relate to transfers of value to healthcare providers and to the distribution of product samples to healthcare providers. In addition, the federal government has been given additional enforcement authority.



## **Table of Contents**

Federal, state and local governments in the United States continue to consider legislation to limit the growth of healthcare costs, including the cost of prescription drugs. We are unable to predict the future course of federal or state healthcare legislation and regulations, including regulations that will be issued to implement provisions of the healthcare reform legislation. The enacted legislation and related and future developments could limit payments or sales volume for pharmaceuticals such as the drug candidates that we are developing or could impose taxes or other costs of doing business on pharmaceutical manufacturers.

Different pricing and reimbursement schemes exist in other countries. In the European Union, governments influence the price of pharmaceutical products through their pricing and reimbursement rules and control of national healthcare systems that fund a large part of the cost of those products to consumers. Some jurisdictions operate positive and negative list systems under which products may only be marketed once a reimbursement price has been agreed. To obtain reimbursement or pricing approval, some of these countries may require the completion of clinical trials that compare the cost-effectiveness of a particular product candidate to currently available therapies. Other member states allow companies to fix their own prices for medicines, but monitor and control company profits. The downward pressure on healthcare costs in general, particularly prescription drugs, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products. In addition, in some countries, cross-border imports from low-priced markets exert a commercial pressure on pricing within a country. The healthcare reform legislation, and the 2009 economic stimulus legislation, contained significant amounts of funding for comparative effectiveness research, which may lead to an increase in the dissemination of information comparing the effectiveness of drugs or other healthcare treatment options, which may negatively impact coverage and pricing decisions for our products.

The marketability of any products for which we receive regulatory approval for commercial sale may suffer if the government and third party payors fail to provide adequate coverage and reimbursement. In addition, an increasing emphasis on managed care in the United States has increased and we expect will continue to increase the pressure on pharmaceutical pricing. Coverage policies and third party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

### ***Biosimilars***

The 2010 healthcare reform legislation created an approval pathway for biosimilars (i.e., follow-on version of innovative biologics). The European regulatory bodies also have authority to approve biosimilars. Because many issues under the U.S. biosimilar legislation remain unresolved (including the scope of exclusivity for new biologics), it is difficult to predict how this legislation will affect us. Our products may face significant competition from biosimilars (as well as traditional generic drugs) in the United States and abroad.

### ***Other Healthcare Laws and Compliance Requirements***

In the United States, our activities are potentially subject to regulation by various federal, state and local authorities in addition to the FDA, including the Centers for Medicare and Medicaid Services, other divisions of the U.S. Department of Health and Human Services (e.g., the Office of Inspector General), the Department of Veterans Affairs, the U.S. Department of Justice and individual U.S. Attorney offices within the Department of Justice, and state and local governments. For example, sales, marketing and scientific/educational grant programs must comply with the anti-fraud and abuse provisions of the Social Security Act, the False Claims Act, the privacy provisions of the Health Insurance Portability and Accountability Act, or HIPAA, and similar state laws, each as amended. Pricing and rebate programs must comply with the Medicaid rebate requirements of the Omnibus Budget Reconciliation Act of 1990 and the Veterans Health Care Act of 1992, each as amended. If products are made available to authorized users of the Federal Supply Schedule of the General Services Administration, additional laws and requirements apply. Under the Veterans Health Care Act, or VHCA, drug companies are required to offer certain drugs at a reduced price to a number of federal agencies including U.S.

## **Table of Contents**

Department of Veterans Affairs and U.S. Department of Defense, the Public Health Service and certain private Public Health Service designated entities in order to participate in other federal funding programs including Medicare and Medicaid. Participation under the VHCA requires submission of pricing data and calculation of discounts and rebates pursuant to complex statutory formulas, as well as the entry into government procurement contracts governed by the Federal Acquisition Regulations. In addition, legislative changes may require that discounted prices be offered for certain U.S. Department of Defense purchases for its TRICARE retail pharmacy program via a rebate system.

In order to distribute products commercially, we must comply with state laws that require the registration of manufacturers and wholesale distributors of pharmaceutical products in a state, including, in certain states, manufacturers and distributors who ship products into the state even if such manufacturers or distributors have no place of business within the state. Some states also impose requirements on manufacturers and distributors to establish the pedigree of product in the chain of distribution, including some states that require manufacturers and others to adopt new technology capable of tracking and tracing product as it moves through the distribution chain. Several states have enacted legislation requiring pharmaceutical companies to establish marketing compliance programs, file periodic reports with the state, make periodic public disclosures on sales, marketing, pricing, clinical trials and other activities, and/or register their sales representatives, as well as to prohibit pharmacies and other healthcare entities from providing certain physician prescribing data to pharmaceutical companies for use in sales and marketing, and to prohibit certain other sales and marketing practices.

We must also register our manufacturing establishments and list all of the drugs we manufacture under federal law. All of our activities are potentially subject to federal and state consumer protection and unfair competition laws.

## **Employees**

As of December 31, 2011, we had 220 employees worldwide. None of our employees is represented by a labor union or is covered by a collective bargaining agreement. We consider our relationship with our employees to be good.

## **Legal Proceedings**

We are not currently a party to any material legal proceedings.

## **Research and Development Costs**

Our research and development costs were \$101.7 million in 2011, \$86.3 million in 2010, and \$51.8 million in 2009. These costs consist of the cost of our own independent research and development efforts and the costs associated with collaborative research and development and in-licensing arrangements. Research and development costs, including upfront fees and milestones paid to collaboration partners, are expensed as incurred if the underlying products have not received regulatory approval and have no future alternative use.

## **Segment and Geographic Information**

We view our operations and manage our business in one operating segment and we operate in only the United States.

**Table of Contents****Executive Officers**

The following table lists the positions, names and ages of our executive officers as of March 1, 2012:

***Executive Officers***

Tuan Ha-Ngoc	60	Chief Executive Officer, President and Director
David Johnston	56	Chief Financial Officer
Elan Ezickson	48	Executive Vice President, Chief Operating Officer
William Slichenmyer	54	Chief Medical Officer
Michael P. Bailey	46	Chief Commercial Officer
Jeno Gyuris	52	Senior Vice President, Chief Scientific Officer

***Tuan Ha-Ngoc*** has served as President and Chief Executive Officer of our company and as a member of our Board of Directors since June 2002. From 1999 to 2002, he was co-founder, President and Chief Executive Officer of deNovis, Inc., an enterprise-scale software development company for the automation of healthcare administrative functions. From 1998 to 1999, Mr. Ha-Ngoc was Corporate Vice President of Strategic Development for Wyeth, following Wyeth's acquisition of Genetics Institute, where Mr. Ha-Ngoc served as Executive Vice President with responsibility for corporate development, commercial operations and European and Japanese operations. Mr. Ha-Ngoc serves on the Board of Directors of Human Genome Sciences, Inc. as well as on the boards of a number of academic and nonprofit organizations, including the Harvard School of Dental Medicine, the Tufts School of Medicine, the MIT Koch Institute of Integrative Cancer Research and the International Institute of Boston. Mr. Ha-Ngoc served on the Board of Directors of ArQule, Inc., from 2002 until 2006. He holds an M.B.A. from INSEAD and an M.A. in pharmacy from the University of Paris, France. We believe that Mr. Ha-Ngoc's qualifications to serve on our Board of Directors include his position as our chief executive officer and his significant experience in the cancer research field and corporate strategy development, including his executive leadership roles at global pharmaceutical companies, and his experiences in commercializing potential drug candidates, including his commercialization experience in North America, Europe and Japan.

***David Johnston*** has served as our Chief Financial Officer since October 2007. From 1998 to 2007, he served as Senior Vice President of Corporate Finance at Genzyme Corporation. Mr. Johnston sits on the Board of Directors of Tissue Banks International. Mr. Johnston holds a B.S. from Washington and Lee University and an M.B.A. from the University of Michigan.

***Elan Ezickson*** was named Chief Operating Officer effective February 1, 2012 and has served as our Executive Vice President, Chief Business Officer since July 2010 and our Chief Business Officer since April 2003. From 1994 to 2003, he worked at Biogen in roles that included President of Biogen Canada, Program Executive and Associate General Counsel. Mr. Ezickson holds a B.A. in Political Science from Yale University and a J.D. from the Columbia University School of Law.

***William Slichenmyer*** has served as our Chief Medical Officer since September 2009. Prior to joining our company, Dr. Slichenmyer served as Chief Medical Officer at Merrimack Pharmaceuticals from 2007 to September 2009. From 2000 to 2007, Dr. Slichenmyer worked at Pfizer Inc. in roles that included Vice President and Global Head of Oncology Clinical Development as well as positions in medical affairs and regulatory affairs. Dr. Slichenmyer holds a B.A. and M.D. from Case Western Reserve University and an Sc.M. in clinical investigation from Johns Hopkins Oncology Center.

***Michael P. Bailey*** has served as our Chief Commercial Officer since September 2010. Prior to joining our company, Mr. Bailey served as Senior Vice President, Business Development and Chief Commercial Officer at Synta Pharmaceuticals from 2008 to September 2010. From 1999 to 2008, Mr. Bailey worked at ImClone, leading their commercial organization, most recently as Senior Vice President of Commercial Operations. Prior

## **Table of Contents**

to his role at ImClone, Mr. Bailey managed the cardiovascular development portfolio at Genentech, Inc. from 1997 to 1999. Mr. Bailey started his career in the pharmaceutical industry as part of Smith-Kline Beecham's Executive Marketing Development Program, where he held a variety of commercial roles from 1992 to 1997, including sales, strategic planning, and product management. Mr. Bailey received a B.S. in psychology from St. Lawrence University and an M.B.A. in international marketing from the University of Notre Dame Graduate School of Business.

*Jeno Gyuris* was named Chief Scientific Officer effective February 1, 2012 and oversees all our research activities. Dr. Gyuris joined our company in January 2003 and served as our Vice President, Molecular Technologies until January 2007, as our Senior Vice President, Drug Discovery from January 2007 to January 2010 and our Senior Vice President, Head of Research from January 2010 to January 2012. From 1993 to 2002, Dr. Gyuris worked at GPC Biotech AG, formerly Mitotix Inc., where he held positions of increasing responsibility, most recently Vice President of Molecular Technologies. Dr. Gyuris has received several research fellowships in Europe and the United States, and is the author of numerous patents and publications. Dr. Gyuris received his Ph.D. from University of Szeged, Szeged, Hungary.

## **Available Information**

We file reports and other information with the SEC as required by the Securities Exchange Act of 1934, as amended, which we refer to as the Exchange Act. You can find, copy and inspect information we file at the SEC's public reference room, which is located at 100 F Street, N.E., Room 1580, Washington, DC 20549. Please call the SEC at 1-800-SEC-0330 for more information about the operation of the SEC's public reference room. You can review our electronically filed reports and other information that we file with the SEC on the SEC's web site at <http://www.sec.gov>.

We were incorporated under the laws of the State of Delaware on October 19, 2001 as GenPath Pharmaceuticals, Inc. and changed our name to AVEO Pharmaceuticals, Inc. on March 1, 2005. Our principal executive offices are located at 75 Sidney Street, Cambridge, Massachusetts, 02139, and our telephone number is (617) 299-5000. Our Internet website is <http://www.aveopharma.com>. We make available free of charge through our website our annual report on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and amendments to those reports filed or furnished pursuant to Sections 13(a) and 15(d) of the Exchange Act. We make these reports available through our website as soon as reasonably practicable after we electronically file such reports with, or furnish such reports to, the SEC. In addition, we regularly use our website to post information regarding our business, product development programs and governance, and we encourage investors to use our website, particularly the information in the section entitled "Investors/Media," as a source of information about us.

The foregoing references to our website are not intended to, nor shall they be deemed to, incorporate information on our website into this report by reference.

## **ITEM 1A. Risk Factors**

Our business is subject to numerous risks. We caution you that the following important factors, among others, could cause our actual results to differ materially from those expressed in forward-looking statements made by us or on our behalf in filings with the SEC, press releases, communications with investors and oral statements. Any or all of our forward-looking statements in this Annual Report on Form 10-K and in any other public statements we make may turn out to be wrong. They can be affected by inaccurate assumptions we might make or by known or unknown risks and uncertainties. Many factors mentioned in the discussion below will be important in determining future results. Consequently, no forward-looking statement can be guaranteed. Actual future results may differ materially from those anticipated in forward-looking statements. We undertake no obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise. You are advised, however, to consult any further disclosure we make in our reports filed with the SEC.

## Table of Contents

### **Risks Related to Development, Clinical Testing and Regulatory Approval of Our Drug Candidates**

*We are dependent on the success of our lead drug candidate, tivozanib, for which we intend to file registration applications in the second half of 2012.*

To date, we have invested a significant portion of our efforts and financial resources in the research and development of tivozanib. We recently announced top-line data from our phase 3 registration clinical trial for tivozanib for the treatment of RCC, referred to as TIVO-1, and are conducting additional clinical trials in RCC and other disease indications, many of which focus on tivozanib in combination with other known anti-cancer agents. We estimate that we will submit an NDA with the FDA seeking marketing approval of tivozanib for the treatment of RCC in the third quarter of 2012, and that our partner, Astellas, will submit an MAA with European Medicines Agency in the second half of 2012.

Our near-term prospects, including our ability to finance our company and to generate revenues, will depend heavily on the successful development and commercialization of tivozanib. All of our other potential product candidates, with the exception of ficlatuzumab, are in the preclinical research stage. The clinical and commercial success of tivozanib will depend on a number of factors, including the following:

our ability to demonstrate to the satisfaction of the U.S. Food and Drug Administration, or FDA, or equivalent foreign regulatory agencies, tivozanib's safety and efficacy through current and future clinical and non-clinical trials, including without limitation, the TIVO-1 study;

timely receipt of necessary marketing approvals from the FDA and similar foreign regulatory authorities and, in particular, approval of our planned NDA and MAA seeking to market tivozanib for the treatment of RCC;

achieving and maintaining compliance with all regulatory requirements applicable to tivozanib;

the prevalence and severity of adverse side effects;

the availability, relative cost, safety and efficacy of alternative and competing treatments;

the effectiveness of our marketing, sales and distribution strategies and operations, and those of Astellas, our strategic collaboration partner for development and commercialization of tivozanib;

the ability of our third-party manufacturers to manufacture clinical trial and commercial supplies of tivozanib and to develop, validate and maintain a commercially viable manufacturing process that is compliant with current good manufacturing practices, or cGMP (current good manufacturing practices);

our ability, and the ability of Astellas, to successfully obtain third party reimbursement and generate commercial demand that result in sales of tivozanib, assuming applicable regulatory approvals are obtained;

our ability to avoid third party patent interference or patent infringement claims;

acceptance of tivozanib as safe and effective by patients, the medical community and third-party payors;

## Edgar Filing: AVEO PHARMACEUTICALS INC - Form 10-K

our ability to successfully compete with companies that have developed or are developing VEGF inhibitors and, in particular, companies that are marketing and selling VEGF inhibitors or other therapies to treat RCC;

timely enrollment in, and completion of, our on-going or planned clinical trials; and

a continued acceptable safety profile of the product following approval.

Many of these factors are beyond our control. Accordingly, we cannot assure you that we, or our strategic partner, will ever be able to obtain regulatory approval for, successfully commercialize, or generate revenues

---

**Table of Contents**

through the sale of tivozanib. If we, or our strategic partner, are not successful in commercializing tivozanib, or are significantly delayed in doing so, our business will be materially harmed and the price of our common stock could substantially decline.

*If the results of our phase 3 clinical trial are not sufficient for approval of tivozanib, our business will be adversely affected.*

We recently reported top-line data from our phase 3 clinical trial in which tivozanib demonstrated superiority over Nexavar in the primary endpoint of progression-free survival in patients with RCC. We estimate that we will submit an NDA with the FDA seeking marketing approval of tivozanib for the treatment of RCC in the third quarter of 2012, and that our partner, Astellas, will submit an MAA with the European Medicines Agency in the second half of 2012. The FDA has advised us that the results of the phase 3 clinical trial will need to show not only that patients treated with tivozanib have a statistically significant improvement in progression-free survival as compared to patients treated with Nexavar, but also that the improvement in progression-free survival of patients treated with tivozanib is clinically meaningful in the context of the safety of the drug. It is not clear how much of an improvement in progression-free survival will be required in order for it to be deemed clinically meaningful in the context of the safety of the drug. The FDA and other regulatory authorities will have substantial discretion in evaluating the results of our phase 3 clinical trial, including with respect to what constitutes a clinically meaningful improvement in progression-free survival. Overall survival is a secondary endpoint in our phase 3 clinical trial. Based on our discussions with the FDA, we do not expect the FDA to require that we show a statistically significant improvement in overall survival in patients treated with tivozanib in order to obtain approval by the FDA; however, if the overall survival data are not positive, it may influence how the FDA and other regulatory authorities interpret other data from our phase 3 clinical trial. We did not gather data on overall survival in our phase 2 clinical trial of tivozanib and data on overall survival from the Tivo-1 study is not yet available.

We cannot be certain as to what type and how many clinical trials the FDA, or equivalent foreign regulatory agencies, will require us to conduct before we may successfully gain approval to market tivozanib. Prior to approving a new drug, the FDA generally requires that the efficacy of the drug be demonstrated in two adequate and well-controlled clinical trials. In some situations, the FDA approves drugs on the basis of a single well-controlled clinical trial. Based on our discussions with the FDA and the EMA, we believe we will be required to conduct only a single phase 3 clinical trial of tivozanib in advanced RCC. All of the VEGF inhibitor drugs approved by the FDA and the EMA to date in advanced RCC, have been approved on the basis of a single phase 3 clinical trial. However, if the FDA or EMA determines that our phase 3 clinical trial results are not statistically significant and do not demonstrate a clinically meaningful benefit and an acceptable safety profile, or if the FDA or EMA requires us to conduct additional phase 3 clinical trials of tivozanib in order to gain approval, we will incur significant additional development costs, commercialization of tivozanib would be prevented or delayed and our business would be adversely affected.

*If we do not obtain regulatory approval for tivozanib, ficlatuzumab or any other product candidates, our business will be adversely affected.*

Tivozanib, ficlatuzumab and any other product candidate we seek to develop will be subject to extensive governmental regulations relating to, among other things, development, clinical trials, manufacturing and commercialization. In order to obtain regulatory approval for the commercial sale of any product candidate, we must demonstrate through extensive preclinical studies and clinical trials that the product candidate is safe and effective for use in each target indication, and that our production process yields a consistent and stable product. This process can take many years to complete, requiring the expenditure of substantial resources with highly uncertain results. We or our strategic partners may never obtain regulatory approval for tivozanib, ficlatuzumab or any other product candidate we may develop.

We have completed a phase 2 clinical trial of our lead product candidate, tivozanib, and are currently conducting a phase 3 clinical trial of tivozanib for the treatment of advanced RCC. We are also conducting phase

---

## **Table of Contents**

1b and phase 2 clinical trials of tivozanib in various combinations and dosing regimens in RCC and additional solid tumor indications, including breast cancer and colorectal cancer. In addition to tivozanib, we have a pipeline of monoclonal antibodies derived from our Human Response Platform, a novel method of building preclinical models of human cancer, which are intended to more accurately represent cancer biology in patients. Our first product candidate derived from our Human Response Platform, ficlatuzumab, has entered a phase 2 clinical trial for non-small cell lung cancer. The results to date from preclinical studies, our phase 1, phase 2 and phase 3 clinical trials of tivozanib and our phase 1 clinical trials of ficlatuzumab may not be predictive of results in preclinical studies and clinical trials currently in process or that we may initiate in the future. A failure of one or more preclinical or clinical trials can occur at any stage of testing. Moreover, there can be no assurance that we will demonstrate the required safety and efficacy to obtain regulatory approvals for any of our product candidates.

Even though tivozanib has been generally well-tolerated in the limited number of patients who have been treated with it, there is no guarantee that unacceptable side effects or other risks will not occur with the exposure of a larger number of patients. If tivozanib, ficlatuzumab or any other product candidate is not shown to be safe and effective in humans through clinical trials, we or our strategic partners will not be able to obtain regulatory approval for such product candidate, and the resulting delays in developing other product candidates and conducting related preclinical studies and clinical trials, as well as the potential need for additional financing, would have a material adverse effect on our business, financial condition and results of operations.

***If we are not successful in discovering, developing and commercializing additional product candidates, our ability to expand our business and achieve our strategic objectives would be impaired.***

Although a substantial amount of our efforts will focus on the continued clinical testing and potential approval of tivozanib as well as the continued development of ficlatuzumab, a key element of our strategy is to discover, develop and commercialize a portfolio of antibody-based products. We are seeking to do so through our internal research programs and intend to explore strategic partnerships for the development of new products. All of our other potential product candidates remain in the discovery and preclinical study stages. Research programs to identify product candidates require substantial technical, financial and human resources, whether or not any product candidates are ultimately identified. Our research programs may initially show promise in identifying potential product candidates, yet fail to yield product candidates for clinical development for many reasons, including the following:

the research methodology used may not be successful in identifying potential product candidates;

competitors may develop alternatives that render our product candidates obsolete;

a product candidate may on further study be shown to have harmful side effects or other characteristics that indicate it is unlikely to be effective or otherwise does not meet applicable regulatory criteria;

a product candidate may not be capable of being produced in commercial quantities at an acceptable cost, or at all; and

a product candidate may not be accepted as safe and effective by patients, the medical community or third-party payors.

***Any failure or delay in completing clinical trials for our product candidates may prevent us from obtaining regulatory approval or commercializing product candidates on a timely basis, or at all, which would require us to incur additional costs and delay receipt of any product revenue.***

We cannot predict whether we will encounter problems with any of our ongoing or planned clinical trials that will cause us or regulatory authorities to delay, suspend or terminate those clinical trials. The completion of clinical trials for product candidates may be delayed or halted for many reasons, including:

delays or failure in reaching agreement on acceptable clinical trial contracts or clinical trial protocols with prospective sites;





**Table of Contents**

failure of our third-party contractors or our investigators to comply with regulatory requirements or otherwise meet their contractual obligations in a timely manner;

delays or failure in obtaining the necessary approvals from regulators or institutional review boards in order to commence a clinical trial at a prospective trial site, or their suspension or termination of a clinical trial once commenced;

our inability to manufacture or obtain from third parties materials sufficient to complete our preclinical studies and clinical trials;

delays in patient enrollment, and variability in the number and types of patients available for clinical trials, or high drop-out rates of patients in our clinical trials;

difficulty in maintaining contact with patients after treatment, resulting in incomplete data;

poor effectiveness of our product candidates during clinical trials;

safety issues, including serious adverse events associated with our product candidates;

governmental or regulatory delays and changes in regulatory requirements, policy and guidelines; or

varying interpretations of data by the FDA and similar foreign regulatory agencies.

Clinical trials often require the enrollment of large numbers of patients, and suitable patients may be difficult to identify and recruit. Our ability to enroll sufficient numbers of patients in our clinical trials depends on many factors, including the size of the patient population, the nature of the protocol, the proximity of patients to clinical sites, the eligibility criteria for the trial, competing clinical trials and the availability of approved effective drugs. In addition, patients may withdraw from a clinical trial for a variety of reasons. If we fail to enroll and maintain the number of patients for which the clinical trial was designed, the statistical power of that clinical trial may be reduced which would make it harder to demonstrate that the product candidate being tested in such clinical trial is safe and effective. Additionally, we may not be able to enroll a sufficient number of qualified patients in a timely or cost-effective manner.

We, the FDA, other applicable regulatory authorities or institutional review boards may suspend or terminate clinical trials of a product candidate at any time if we or they believe the patients participating in such clinical trials are being exposed to unacceptable health risks or for other reasons.

Significant clinical trial delays could allow our competitors to obtain marketing approval before we do or shorten the patent protection period during which we may have the exclusive right to commercialize our product candidates. Our product development costs also will increase if we experience delays in completing clinical trials. In addition, it is impossible to predict whether legislative changes will be enacted, or whether FDA regulations, guidance or interpretations will be changed, or what the impact of such changes, if any, may be. If we experience any such problems, we may not have the financial resources to continue development of the product candidate that is affected or the development of any of our other product candidates.

***Even if we receive regulatory approval for any of our product candidates, we will be subject to ongoing FDA requirements and continued regulatory review, which may result in significant additional expense. Additionally, our product candidates, if approved, could be subject to labeling and other restrictions and market withdrawal and we may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our products.***

Any regulatory approvals that we or our strategic partners receive for our product candidates may also be subject to limitations on the approved indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for potentially costly

## Edgar Filing: AVEO PHARMACEUTICALS INC - Form 10-K

post-marketing testing, including phase 4 clinical trials, and surveillance to monitor the safety and efficacy of the product candidate. In addition, if the FDA approves any of our product candidates, the manufacturing processes, labeling, packaging, distribution, adverse

---

## **Table of Contents**

event reporting, storage, advertising, promotion and recordkeeping for the product will be subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, registration, as well as continued compliance with cGMP and good clinical practices, or GCP, for any clinical trials that we conduct post-approval. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with our third-party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in, among other things:

restrictions on the marketing or manufacturing of the product, withdrawal of the product from the market, or voluntary or mandatory product recalls;

finances, warning letters or holds on clinical trials;

refusal by the FDA to approve pending applications or supplements to approved applications filed by us or our strategic partners, or suspension or revocation of product license approvals;

product seizure or detention, or refusal to permit the import or export of products; and

injunctions or the imposition of civil or criminal penalties.

The FDA's policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability, which would adversely affect our business.

### ***Failure to obtain regulatory approval in jurisdictions outside the United States will prevent us from marketing our products abroad.***

We intend to market our products, if approved, in international markets, which will require separate regulatory approvals and compliance with numerous and varying regulatory requirements. The approval procedures vary among countries and may involve requirements for additional testing, and the time required to obtain approval may differ from that required to obtain FDA approval. In addition, in many countries outside the United States, a product candidate must be approved for reimbursement before it can be approved for sale in that country. In some cases, the price that we intend to charge for our product is also subject to approval. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one foreign regulatory authority does not ensure approval by regulatory authorities in other foreign countries or jurisdictions or by the FDA. The foreign regulatory approval process may include all of the risks associated with obtaining FDA approval. We may not obtain foreign regulatory approvals on a timely basis, if at all. We and our strategic partners may not be able to file for regulatory approvals and may not receive necessary approvals to commercialize our products in any market.

### **Risks Related to Our Financial Position and Capital Requirements**

***We anticipate that we will continue to incur significant operating costs for the foreseeable future. We may not be able to sustain profitability, which would depress the market price of our common stock.***

Although we had net income for the year ended December 31, 2011, we have incurred net losses in all prior periods, and as of December 31, 2011, we had an accumulated deficit of \$205.9 million. To date, we have not commercialized any products or generated any revenues from the sale of products, and absent the realization of sufficient revenues from product sales, we will not be able to sustain profitability. Our losses have resulted principally from costs incurred in our discovery and development activities. We anticipate that we will continue to incur significant operating costs over the next several years as we execute our plan to expand our discovery,

---

## **Table of Contents**

research, development and commercialization activities, including planned development activities and commercialization of our lead product candidate, tivozanib, and the continued clinical development of our phase 2 product candidate, ficlatuzumab.

If we do not successfully develop and obtain regulatory approval for our existing and future pipeline product candidates and effectively manufacture, market and sell any product candidates that are approved, we may never generate product sales, and even if we do generate product sales, we may never achieve or sustain profitability on a quarterly or annual basis. Our failure to become and remain profitable would depress the market price of our common stock and could impair our ability to raise capital, expand our business, diversify our product offerings or continue our operations.

***We will require substantial additional financing to achieve our goals, and a failure to obtain this necessary capital when needed could force us to delay, limit, reduce or terminate our product development or commercialization efforts.***

Since our inception, most of our resources have been dedicated to the discovery, preclinical and clinical development of our product candidates. In particular, we are currently conducting multiple phase 1 and phase 2 clinical trials and a phase 3 clinical trial of tivozanib, for which we share expenses with Astellas, and phase 1 clinical trials and a phase 2 clinical trial of ficlatuzumab, and anticipate future clinical trials for AV-203, which will require substantial funds to complete. We believe that we will continue to expend substantial resources for the foreseeable future developing tivozanib, ficlatuzumab and other new and existing antibody product candidates. These expenditures will include costs associated with research and development, acquiring new technologies, conducting preclinical and clinical trials, obtaining regulatory approvals and manufacturing products, as well as marketing and selling any products approved for sale. In addition, other unanticipated costs may arise. Because the outcome of our planned and anticipated clinical trials is highly uncertain, we cannot reasonably estimate the actual amounts necessary to successfully complete the development and commercialization of our product candidates.

We believe that our existing cash and cash equivalents, marketable securities, committed research and development funding and milestone payments that we expect to receive under our existing strategic partnership and license agreements, will allow us to fund our operating plan into the second half of 2013. However, our operating plan may change as a result of many factors currently unknown to us, and we may need to seek additional funds sooner than planned, through public or private equity or debt financings or other sources, such as strategic partnerships. In addition, we may seek additional capital due to favorable market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans.

Our future capital requirements depend on many factors, including:

the number and characteristics of the product candidates we pursue;

the scope, progress, results and costs of researching and developing our product candidates, and conducting preclinical and clinical trials;

the timing of, and the costs involved in, obtaining regulatory approvals for our product candidates;

the cost of commercialization activities if any of our product candidates are approved for sale, including marketing, sales and distribution costs;

the cost of manufacturing our product candidates and any products we successfully commercialize;

our ability to establish and maintain strategic partnerships, licensing or other arrangements and the financial terms of such agreements;

Edgar Filing: AVEO PHARMACEUTICALS INC - Form 10-K

the costs involved in preparing, filing, prosecuting, maintaining, defending and enforcing patent claims, including litigation costs and the outcome of such litigation; and

---

**Table of Contents**

the timing, receipt and amount of sales of, or royalties on, our future products, if any. Additional funds may not be available when we need them, on terms that are acceptable to us, or at all. If adequate funds are not available to us on a timely basis, we may be required to:

delay, limit, reduce or terminate preclinical studies, clinical trials or other development activities for one or more of our product candidates;

delay, limit, reduce or terminate our research and development activities; or

delay, limit, reduce or terminate our establishment of sales and marketing capabilities or other activities that may be necessary to commercialize our product candidates.

***Raising additional capital may cause dilution to our existing stockholders, restrict our operations or require us to relinquish rights to our technologies or product candidates.***

We may seek additional capital through a combination of private and public equity offerings, debt financings, strategic partnerships and alliances and licensing arrangements. To the extent that we raise additional capital through the sale of equity or convertible debt securities, stockholders will be diluted, and the terms may include liquidation or other preferences that adversely affect stockholders' rights. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take certain actions, such as incurring debt, making capital expenditures or declaring dividends. If we raise additional funds through strategic partnerships and alliances and licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies or product candidates, or grant licenses on terms that are not favorable to us. If we are unable to raise additional funds through equity or debt financing when needed, we may be required to delay, limit, reduce or terminate our product development or commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

***A substantial portion of our future revenues may be dependent upon our strategic partnership agreements.***

Our success will depend in significant part on our ability to attract and maintain strategic partners and strategic relationships to support the development and commercialization of our products. We currently expect that a substantial portion of our future revenues may be dependent upon our strategic partnerships with Astellas, OSI, Biogen Idec and Centocor. Under each of these strategic partnerships, our strategic partners have significant development and commercialization responsibilities with respect to anticipated therapeutics to be developed and sold. If these strategic partners were to terminate their agreements with us, fail to meet their obligations or otherwise decrease their level of efforts, allocation of resources or other commitments under these agreements, our future revenues could be negatively impacted and the development and commercialization of product candidates could be interrupted. In addition, if some or any of the development, regulatory and commercial milestones are not achieved or if certain net sales thresholds are not achieved, as set forth in the respective agreements, we will not fully realize the expected economic benefits of the agreements. Further, the achievement of certain of the milestones under these strategic partnership agreements will depend on factors that are outside of our control and most are not expected to be achieved for several years, if at all. Any failure to successfully maintain our strategic partnership agreements could materially and adversely affect our ability to generate revenues.

For a discussion of additional risks that we face with respect to our strategic partnership agreements, see [Item 1A](#). If any of our current strategic partners fails to perform its obligations or terminates its agreement with us, the development and commercialization of the product candidates under such agreement could be delayed or terminated and our business could be substantially harmed [beginning on page 48](#).

## **Table of Contents**

### ***Fluctuations in our quarterly operating results could adversely affect the price of our common stock.***

Our quarterly operating results may fluctuate significantly. Some of the factors that may cause our operating results to fluctuate on a period-to-period basis include:

the status of our preclinical and clinical development programs;

the level of expenses incurred in connection with our preclinical and clinical development programs, including development costs relating to tivozanib, ficlatuzumab and AV-203;

the level of expenses incurred in connection with planned pre-commercialization activities for tivozanib;

any intellectual property infringement lawsuit or other litigation in which we may become involved;

the implementation or termination of collaboration, licensing, manufacturing or other material agreements with third parties, and non-recurring revenue or expenses under any such agreement; and

compliance with regulatory requirements.

Period-to-period comparisons of our historical and future financial results may not be meaningful, and investors should not rely on them as an indication of future performance. Our fluctuating results may fail to meet the expectations of securities analysts or investors. Our failure to meet these expectations may cause the price of our common stock to decline.

### ***Unstable market and economic conditions may have serious adverse consequences on our business, financial condition and stock price.***

As widely reported, global credit and financial markets have been experiencing extreme disruptions over the past several years, including severely diminished liquidity and credit availability, declines in consumer confidence, declines in economic growth, increases in unemployment rates, and uncertainty about economic stability. There can be no assurance that further deterioration in credit and financial markets and confidence in economic conditions will not occur. Our general business strategy may be adversely affected by the current adverse economic conditions and volatile business environment and continued unpredictable and unstable market conditions. If the current equity and credit markets deteriorate further, or do not improve, it may make any necessary debt or equity financing more difficult, more costly, and more dilutive. 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. In addition, 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 could directly affect our ability to attain our operating goals on schedule and on budget.

At December 31, 2011, we had \$275.4 million of cash, cash equivalents and marketable securities consisting of U.S. government agency securities, a foreign government bond, an asset-backed security, and corporate debt securities, including commercial paper. As of the date of this report, we are not aware of any downgrades, material losses, or other significant deterioration in the fair value of our cash equivalents or marketable securities. However, no assurance can be given that further deterioration in conditions of the global credit and financial markets would not negatively impact our current portfolio of cash equivalents or marketable securities or our ability to meet our financing objectives. Further dislocations in the credit market may adversely impact the value and/or liquidity of marketable securities owned by us.

There is a possibility that our stock price may decline, due in part to the volatility of the stock market and general economic downturn.



---

## **Table of Contents**

### **Risks Related to Our Business and Industry**

*We face substantial competition, which may result in others discovering, developing or commercializing products before, or more successfully, than we do.*

Our future success depends on our ability to demonstrate and maintain a competitive advantage with respect to the design, development and commercialization of product candidates. Our objective is to design, develop and commercialize new products with superior efficacy, convenience, tolerability and safety. We expect any product candidate that we commercialize with our strategic partners or on our own will compete with existing, market-leading products. For example, we anticipate that tivozanib, if approved for the treatment of advanced RCC, would compete with angiogenesis inhibitors and mTOR inhibitors that are currently approved for the treatment of advanced RCC, such as Avastin, marketed by Roche Laboratories, Inc., Nexavar, marketed by Onyx Pharmaceuticals, Inc. and Bayer HealthCare AG, Sutent and Inlyta, marketed by Pfizer Inc., Votrient, marketed by GlaxoSmithKline plc, Torisel, marketed by Pfizer, Inc. and Afinitor, marketed by Novartis Pharmaceuticals Corporation, and other therapies in development.

Many of our potential competitors have substantially greater financial, technical and personnel resources than we have and several are already marketing products to treat the same indications, and having the same biological targets, as the product candidates we are developing, including with respect to tivozanib. In addition, many of these competitors have significantly greater commercial infrastructures than we have. We will not be able to compete successfully unless we successfully:

design and develop products that are superior to other products in the market in terms of, among other things, both safety and efficacy;

attract qualified scientific, medical, sales and marketing and commercial personnel;

obtain patent and/or other proprietary protection for our processes and product candidates;

obtain favorable reimbursement, formulary and guideline status;

obtain required regulatory approvals; and

collaborate with others in the design, development and commercialization of new products.

Established competitors may invest heavily to quickly discover and develop novel compounds that could make our product candidates obsolete. In addition, any new product that competes with an approved product must demonstrate compelling advantages in efficacy, convenience, tolerability and safety in order to overcome price competition and to be commercially successful. If we are not able to compete effectively against our current and future competitors, our business will not grow and our financial condition and operations will suffer.

*We may not achieve research, development and commercialization goals in the time frames that we publicly estimate, which could have an adverse impact on our business and could cause our stock price to decline.*

We set goals, and make public statements regarding our expectations, for the timing of certain accomplishments, such as the commencement and completion of preclinical studies, initiation and completion of clinical trials, and other developments and milestones under our research and development programs. The actual timing of these events can vary significantly due to a number of factors including without limitation delays or failures in our and our current and potential future collaborators' preclinical studies or clinical trials, the amount of time, effort and resources committed to our programs by us and our current and potential future collaborators and the uncertainties inherent in the regulatory approval process. As a result, there can be no assurance that our or our current and potential future collaborators' preclinical studies and clinical trials will advance or be completed in the time frames we expect or announce, that we or our current and potential future collaborators will make regulatory submissions or receive regulatory approvals as planned or that we or our current and potential future collaborators will be able to

## Edgar Filing: AVEO PHARMACEUTICALS INC - Form 10-K

adhere to our current schedule for the achievement of key milestones under any of our programs. If we or any collaborators fail to achieve one or more of these milestones as planned, our business could be materially adversely affected and the price of our common stock could decline.

---

## **Table of Contents**

***Because we have a short operating history, there is a limited amount of information about us upon which you can evaluate our business and prospects.***

Our operations began in October 2001 and we have only a limited operating history upon which you can evaluate our business and prospects. In addition, we have limited experience and have not yet demonstrated an ability to successfully overcome many of the risks and uncertainties frequently encountered by companies in new and rapidly evolving fields, particularly in the biopharmaceutical area. For example, to execute our business plan, we will need to successfully:

execute product development activities;

obtain required regulatory approvals for the development and commercialization of our product candidates;

build and maintain a strong intellectual property portfolio;

build and maintain robust sales, distribution, reimbursement and marketing capabilities;

obtain reimbursement and gain market acceptance for our products;

develop and maintain successful strategic relationships and partnerships; and

manage our spending as costs and expenses increase due to clinical trials, regulatory approvals and commercialization.

If we are unsuccessful in accomplishing these objectives, we may not be able to develop product candidates, raise capital, expand our business or continue our operations.

***If we fail to attract and keep senior management and key scientific personnel, we may be unable to successfully develop our product candidates, conduct our clinical trials and commercialize our product candidates.***

Our success depends in part on our continued ability to attract, retain and motivate highly qualified management, clinical and scientific personnel. We are highly dependent upon our senior management, particularly Tuan Ha-Ngoc, our President and Chief Executive Officer, Elan Ezickson, our Executive Vice President and Chief Operating Officer, David Johnston, our Chief Financial Officer, William Slichenmyer, our Chief Medical Officer, Michael Bailey, our Chief Commercial Officer, and Jenő Gyuris, our Senior Vice President, and Chief Scientific Officer, as well as others on our management team. The loss of services of any of these individuals or one or more of our other members of management could delay or prevent the successful development of our product pipeline, completion of our planned clinical trials or the commercialization of our product candidates. We do not carry key person insurance covering any members of our senior management. Although we have entered into an employment agreement and a severance and change in control agreement with Tuan Ha-Ngoc, and severance and change in control agreements with each of Elan Ezickson, David Johnston, William Slichenmyer, Michael Bailey and Jenő Gyuris, these agreements do not provide for a fixed term of service.

Competition for qualified personnel in the biotechnology and pharmaceuticals field is intense. We will need to hire additional personnel as we expand our clinical development and commercial activities. We may not be able to attract and retain quality personnel on acceptable terms.

***Our employees may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements and insider trading.***

We are exposed to the risk of employee fraud or other misconduct. Misconduct by employees could include intentional failures to comply with FDA regulations, to provide accurate information to the FDA, to comply with manufacturing standards we have established, to comply with

federal and state health-care fraud and abuse laws

---

**Table of Contents**

and regulations, to report financial information or data accurately or to disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Employee misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. We have adopted a Code of Business Conduct and Ethics, but it is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant fines or other sanctions.

In addition, during the course of our operations, our directors, executives and employees may have access to material, nonpublic information regarding our business, our results of operations or potential transactions we are considering. Despite the adoption of an Insider Trading Policy, we may not be able to prevent a director, executive or employee from trading in our common stock on the basis of, or while having access to, material, nonpublic information. If a director, executive or employee was to be investigated, or an action was to be brought against a director, executive or employee for insider trading, it could have a negative impact on our reputation and our stock price. Such a claim, with or without merit, could also result in substantial expenditures of time and money, and divert attention of our management team from other tasks important to the success of our business.

***We may encounter difficulties in managing our growth and expanding our operations successfully.***

As we seek to advance our product candidates through clinical trials, we will need to expand our development, regulatory, manufacturing, marketing and sales capabilities or contract with third parties to provide these capabilities for us. As our operations expand, we expect that we will need to manage additional relationships with various strategic partners, suppliers and other third parties. Future growth will impose significant added responsibilities on members of management. Our future financial performance and our ability to commercialize our product candidates and to compete effectively will depend, in part, on our ability to manage any future growth effectively. To that end, we must be able to manage our development efforts and clinical trials effectively and hire, train and integrate additional management, administrative and sales and marketing personnel. We may not be able to accomplish these tasks, and our failure to accomplish any of them could prevent us from successfully growing our company.

***If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of our product candidates.***

We face an inherent risk of product liability as a result of the clinical testing of our product candidates and will face an even greater risk if we commercialize any products. For example, we may be sued if any product we develop allegedly causes injury or is found to be otherwise unsuitable during product testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability, and a breach of warranties. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of our product candidates. Even successful defense could require significant financial and management resources. Regardless of the merits or eventual outcome, liability claims may result in:

decreased demand for our product candidates or products that we may develop;

injury to our reputation;

## **Table of Contents**

withdrawal of clinical trial participants;

costs to defend the related litigation;

diversion of management's time and our resources;

substantial monetary awards to trial participants or patients;

product recalls, withdrawals or labeling, marketing or promotional restrictions;

loss of revenue;

the inability to commercialize our product candidates; and

a decline in our stock price.

Our inability to obtain and retain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the commercialization of products we develop. We currently carry product liability insurance covering our clinical studies in the amount of \$10 million in the aggregate. Although we maintain such insurance, any claim that may be brought against us could result in a court judgment or settlement in an amount that is not covered, in whole or in part, by our insurance or that is in excess of the limits of our insurance coverage. Our insurance policies also have various exclusions, and we may be subject to a product liability claim for which we have no coverage. We will have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient capital to pay such amounts.

***We may incur significant costs complying with environmental laws and regulations, and failure to comply with these laws and regulations could expose us to significant liabilities.***

We use hazardous chemicals and radioactive and biological materials in certain aspects of our business and are subject to a variety of federal, state and local laws and regulations governing the use, generation, manufacture, distribution, storage, handling, treatment and disposal of these materials. Although we believe our safety procedures for handling and disposing of these materials and waste products comply with these laws and regulations, we cannot eliminate the risk of accidental injury or contamination from the use, manufacture, distribution, storage, handling, treatment or disposal of hazardous materials. In the event of contamination or injury, or failure to comply with environmental, occupational health and safety and export control laws and regulations, we could be held liable for any resulting damages and any such liability could exceed our assets and resources. We do not maintain insurance for any environmental liability or toxic tort claims that may be asserted against us.

### **Risks Related to Commercialization of Our Product Candidates**

***We have limited sales, marketing, reimbursement or distribution experience and we will have to invest significant resources to develop those capabilities.***

We have limited sales, marketing, reimbursement or distribution experience. To develop internal sales, reimbursement, distribution and marketing capabilities, we will have to invest significant amounts of financial and management resources, some of which will be committed prior to any confirmation that tivozanib will be approved. For product candidates such as tivozanib, where we will have lead commercialization responsibility in North America under our strategic alliance with Astellas, we could face a number of additional risks in developing our commercial infrastructure, including:

Edgar Filing: AVEO PHARMACEUTICALS INC - Form 10-K

we may not be able to attract and build an effective marketing or sales force;

the cost of establishing a marketing or sales force may not be justifiable in light of the revenues generated by any particular product;  
and

our direct sales and marketing efforts may not be successful.

## **Table of Contents**

Furthermore, we have granted Astellas the rights to commercialize tivozanib in Europe and other areas of the world outside of Asia and, where appropriate, we may elect in the future to utilize strategic partners or contract sales forces to assist in the commercialization of ficlatuzumab, AV-203 and future products, if approved. We may have limited or no control over the sales, marketing and distribution activities of these third parties. Our future revenues may depend heavily on the success of the efforts of these third parties.

*Our commercial success depends upon attaining significant market acceptance of our product candidates, if approved, including tivozanib and ficlatuzumab, among physicians, patients, healthcare payors and, in the cancer market, acceptance by the major operators of cancer clinics.*

Even if tivozanib, ficlatuzumab or any other product candidate that we may develop or acquire in the future obtains regulatory approval, the product may not gain market acceptance among physicians, healthcare payors, patients and the medical community. Market acceptance of any products for which we receive approval depends on a number of factors, including:

the efficacy and safety of the product candidate, as demonstrated in clinical trials;

the clinical indications for which the drug is approved;

acceptance by physicians, major operators of cancer clinics, healthcare payors, physician networks and patients of the drug as a safe and effective treatment;

with respect to tivozanib, the extent to which the results from our phase 3 clinical trial demonstrate that treatment with tivozanib represents a clinically meaningful improvement in care as compared to other available VEGF inhibitors;

the potential and perceived advantages over alternative treatments, including, with respect to tivozanib, advantages over Avastin, Nexavar, Sutent, Inlyta, Votrient or other emerging therapies;

the cost of treatment in relation to alternative treatments;

the availability of adequate reimbursement and pricing by third parties and government authorities;

the continued projected growth of oncology drug markets;

relative convenience and ease of administration;

the prevalence and severity of adverse side effects; and

the effectiveness of our sales and marketing efforts.

If our approved drugs fail to achieve market acceptance, we would not be able to generate significant revenue.

*Reimbursement may be limited or unavailable in certain market segments for our product candidates, which could make it difficult for us to sell our products profitably.*



## Edgar Filing: AVEO PHARMACEUTICALS INC - Form 10-K

Market acceptance and sales of our product candidates will depend significantly on the availability of adequate coverage and reimbursement from third-party payors for any of our product candidates and may be affected by existing and future healthcare reform measures. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which drugs they will pay for and establish reimbursement levels. Reimbursement by a third-party payor may depend upon a number of factors, including the third-party payor's determination that use of a product is:

a covered benefit under its health plan;

safe, effective and medically necessary;

appropriate for the specific patient;

---

**Table of Contents**

cost-effective; and

neither experimental nor investigational.

Obtaining coverage and reimbursement approval for a product from a government or other third party payor is a time consuming and costly process that could require us to provide supporting scientific, clinical and cost-effectiveness data for the use of our products to the payor. We may not be able to provide data sufficient to gain acceptance with respect to coverage and reimbursement. We cannot be sure that coverage or adequate reimbursement will be available for any of our product candidates. Also, we cannot be sure that reimbursement amounts will not reduce the demand for, or the price of, our products. If reimbursement is not available or is available only to limited levels, we may not be able to commercialize certain of our products.

In both the United States and certain foreign jurisdictions, there have been a number of legislative and regulatory changes to the healthcare system that could impact our ability to sell our products profitably. In particular, the Medicare Modernization Act of 2003 revised the payment methodology for many products under Medicare. This has resulted in lower rates of reimbursement. There have been numerous other federal and state initiatives designed to reduce payment for pharmaceuticals.

As a result of legislative proposals and the trend towards managed healthcare in the United States, third-party payors are increasingly attempting to contain healthcare costs by limiting both coverage and the level of reimbursement of new drugs. They may also refuse to provide any coverage of approved products for medical indications other than those for which the FDA has granted market approvals. As a result, significant uncertainty exists as to whether and how much third-party payors will reimburse patients for their use of newly approved drugs, which in turn will put pressure on the pricing of drugs. We expect to experience pricing pressures in connection with the sale of any products we may develop or commercialize due to the trend toward managed healthcare, the increasing influence of health maintenance organizations, additional legislative proposals, as well as country, regional, or local healthcare budget limitations. Any products that we may develop or commercialize may not be considered cost-effective, and coverage and reimbursement may not be available or sufficient to allow us to sell our products on a profitable basis.

***Foreign governments may impose price controls, which may adversely affect our future profitability.***

We and our strategic partners intend to seek approval to market our future products in both the United States and in foreign jurisdictions. If approval is obtained in one or more foreign jurisdictions, we and our strategic partners will be subject to rules and regulations in those jurisdictions relating to our product. In some foreign countries, particularly in countries in the European Union, the pricing of prescription pharmaceuticals and biologics is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product candidate. If reimbursement of our future products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, we may be unable to achieve or sustain profitability.

***Healthcare reform measures could hinder or prevent our product candidates' commercial success.***

The U.S. government and other governments have shown significant interest in pursuing healthcare reform. Any government-adopted reform measures could adversely impact the pricing of healthcare products and services in the U.S. or internationally and the amount of reimbursement available from governmental agencies or other third party payors. The continuing efforts of the U.S. and foreign governments, insurance companies, managed care organizations and other payors of healthcare services to contain or reduce healthcare costs may adversely affect our ability to set prices which we believe are fair for any products we may develop and commercialize, and our ability to generate revenues and achieve and maintain profitability.

New laws, regulations and judicial decisions, or new interpretations of existing laws, regulations and decisions, that relate to healthcare availability, methods of delivery or payment for products and services, or

---

## **Table of Contents**

sales, marketing or pricing, may limit our potential revenue, and we may need to revise our research and development programs. The pricing and reimbursement environment may change in the future and become more challenging due to several reasons, including policies advanced by the U.S. government, new healthcare legislation or fiscal challenges faced by government health administration authorities. Specifically, in both the U.S. and some foreign jurisdictions, there have been a number of legislative and regulatory proposals and initiatives to change the healthcare system in ways that could affect our ability to sell any products we may develop and commercialize profitably. Some of these proposed and implemented reforms could result in reduced reimbursement rates for our potential products, which would adversely affect our business strategy, operations and financial results. For example, in March 2010, President Obama signed into law a legislative overhaul of the U.S. healthcare system, known as the Patient Protection and Affordable Care Act of 2010, as amended by the Healthcare and Education Affordability Reconciliation Act of 2010, or the PPACA, which may have far reaching consequences for life science companies like us. As a result of this new legislation, substantial changes could be made to the current system for paying for healthcare in the United States, including changes made in order to extend medical benefits to those who currently lack insurance coverage. Extending coverage to a large population could substantially change the structure of the health insurance system and the methodology for reimbursing medical services, drugs and devices. These structural changes could entail modifications to the existing system of private payors and government programs, such as Medicare and Medicaid, creation of a government-sponsored healthcare insurance source, or some combination of both, as well as other changes. Restructuring the coverage of medical care in the United States could impact the reimbursement for prescribed drugs, biopharmaceuticals, medical devices, or our product candidates. If reimbursement for our approved product candidates, if any, is substantially less than we expect in the future, or rebate obligations associated with them are substantially increased, our business could be materially and adversely impacted.

Further federal and state proposals and healthcare reforms could limit the prices that can be charged for the product candidates that we develop and may further limit our commercial opportunity. Our results of operations could be materially adversely affected by the PPACA, by Medicare prescription drug coverage legislation, by the possible effect of such current or future legislation on amounts that private insurers will pay and by other healthcare reforms that may be enacted or adopted in the future.

### **Risks Related to Our Dependence on Third Parties**

*If any of our current strategic partners fails to perform its obligations or terminates its agreement with us, the development and commercialization of the product candidates under such agreement could be delayed or terminated and our business could be substantially harmed.*

We currently have strategic partnerships in place relating to certain of our product candidates and technologies as follows:

We have entered into a strategic partnership with Astellas in connection with which we and Astellas have agreed to develop and commercialize tivozanib in North America and Europe and have exclusively licensed to Astellas rights to develop and commercialize tivozanib in the rest of the world other than Asia.

We have entered into an exclusive license agreement with Centocor for the worldwide development and commercialization of our internally-discovered antibodies targeting the RON receptor (Recepteur d'Origine Nantais).

We have entered into a strategic partnership with OSI, under which we licensed rights to OSI to research, develop, manufacture and commercialize products related to targets involved in the processes of epithelial-mesenchymal transition or mesenchymal-epithelial transition in cancer.

We have entered into an exclusive option and license agreement with Biogen Idec regarding the development and commercialization of our ErbB3-targeted antibodies for the potential treatment and diagnosis of cancer and other diseases outside of the United States, Canada and Mexico.

## Table of Contents

These strategic partnerships may not be scientifically or commercially successful due to a number of important factors, including the following:

Each of our strategic partners has significant discretion in determining the efforts and resources that it will apply to their strategic partnership with us. The timing and amount of any cash payments, related royalties and milestones that we may receive under such strategic partnerships will depend on, among other things, the efforts, allocation of resources and successful development and commercialization of our product candidates by our strategic partners under their respective agreements. For instance, under our collaboration with Astellas, we must agree on all development and commercialization plans and strategies for North America and Europe before initiating such activities. If we cannot agree with Astellas with respect to specific development or commercialization initiatives, the program may be delayed or unsuccessful.

Our strategic partners may change the focus of their development and commercialization efforts or pursue higher-priority programs.

Our strategic partners may, under specified circumstances, terminate their strategic partnership with us on short notice and for circumstances outside of our control, which could make it difficult for us to attract new strategic partners or adversely affect how we are perceived in the scientific and financial communities. For example, Astellas can terminate its agreement with us after February 2013 with six months notice and can terminate the entire agreement with us in connection with a material breach of the agreement by us that remains uncured for a specified cure period. OSI can terminate its agreement with us, with respect to any or all collaboration targets and all associated products, upon written notice to us and can terminate the entire agreement with us in connection with a material breach of the agreement by us that remains uncured for a specified cure period. Biogen Idec may not elect to exercise its option to develop and commercialize products relating to our ErbB3 program and, after exercise of its option, may terminate its agreement with us for convenience with respect to any product(s) by providing us with three months prior written notice, or due to a material breach of the agreement by us that is not cured within a short time period or if all of our assets are acquired by, or we merge with, another entity, and the other entity is independently developing or commercializing a product containing an ErbB3 antibody and fails to divest the ErbB3 product within a specified time period. Centocor has the right to terminate its license agreement with us upon 90 days written notice to us prior to the filing of an investigational new drug application or, thereafter, upon 180 days written notice to us.

Our strategic partnership agreements with OSI, Biogen Idec and Centocor permit our strategic partners wide discretion in deciding which product candidates to advance through the clinical trial process. For example, under our strategic partnership with OSI, it is possible for the strategic partner to reject product candidates at any point in the research, development and clinical trial process, without triggering a termination of the strategic partnership agreement. In the event of any such decision, our business and prospects may be adversely affected due to our inability to progress such candidates ourselves.

OSI or Biogen Idec may develop and commercialize, either alone or with others, products that are similar to or competitive with the product candidates that are the subject of their strategic partnerships with us.

Our strategic partners may enter into one or more transactions with third parties, including a merger, consolidation, reorganization, sale of a substantial amount of its assets, sale of a substantial amount of its stock or change in control, which could divert the attention of a strategic partner's management and adversely affect a strategic partner's ability to retain and motivate key personnel who are important to the continued development of the programs under the applicable strategic partnership with us. In addition, the third-party in such a transaction with our strategic partner could determine to reprioritize the strategic partner's development programs such that the strategic partner ceases to diligently pursue the development of our programs and/or cause the respective strategic partnership with us to terminate.

## **Table of Contents**

Certain of our strategic partners may have the first right to maintain or defend our intellectual property rights and, although we may have the right to assume the maintenance and defense of our intellectual property rights if our strategic partners do not, our ability to do so may be compromised by our strategic partners' acts or omissions.

Our strategic partners may utilize our intellectual property rights in such a way as to invite litigation that could jeopardize or invalidate our intellectual property rights or expose us to potential liability.

Our strategic partners may not comply with all applicable regulatory requirements, or fail to report safety data in accordance with all applicable regulatory requirements.

If Astellas, OSI or Centocor breaches or terminates its arrangement with us, or if Biogen Idec does not elect to exercise its option to participate in development of our ErbB3 antibody candidate, the development and commercialization of the affected product candidate could be delayed, curtailed or terminated because we may not have sufficient financial resources or capabilities to continue development and commercialization of the product candidate on our own.

Our strategic partners may not have sufficient resources necessary to carry the product candidate through clinical development or may not obtain the necessary regulatory approvals.

If one or more of our strategic partners fails to develop or effectively commercialize product candidates for any of the foregoing reasons, we may not be able to replace the strategic partner with another partner to develop and commercialize a product candidate under the terms of the strategic partnership. We may also be unable to obtain, on terms acceptable to us, a license from such strategic partner to any of its intellectual property that may be necessary or useful for us to continue to develop and commercialize a product candidate. Any of these events could have a material adverse effect on our business, results of operations and our ability to achieve future profitability, and could cause our stock price to decline.

***We may not be successful in establishing and maintaining additional strategic partnerships, which could adversely affect our ability to develop and commercialize products.***

In addition to our current strategic partnerships, a part of our strategy is to enter into additional strategic partnerships in the future, including alliances with major biotechnology or pharmaceutical companies. We face significant competition in seeking appropriate strategic partners and the negotiation process is time-consuming and complex. Moreover, we may not be successful in our efforts to establish a strategic partnership or other alternative arrangements for any future product candidates and programs because our research and development pipeline may be insufficient, our product candidates and programs may be deemed to be at too early of a stage of development for collaborative effort and/or third parties may not view our product candidates and programs as having the requisite potential to demonstrate safety and efficacy. Even if we are successful in our efforts to establish new strategic partnerships, the terms that we agree upon may not be favorable to us and we may not be able to maintain such strategic partnerships if, for example, development or approval of a product candidate is delayed or sales of an approved product are disappointing. Any delay in entering into new strategic partnership agreements related to our product candidates could delay the development and commercialization of our product candidates and reduce their competitiveness even if they reach the market.

Moreover, if we fail to establish and maintain additional strategic partnerships related to our product candidates:

the development of certain of our current or future product candidates may be terminated or delayed;

our cash expenditures related to development of certain of our current or future product candidates would increase significantly and we may need to seek additional financing;

## Edgar Filing: AVEO PHARMACEUTICALS INC - Form 10-K

we may be required to hire additional employees or otherwise develop expertise, such as sales and marketing expertise, for which we have not budgeted; and

we will bear all of the risk related to the development of any such product candidates.

## **Table of Contents**

In addition, if we fail to establish and maintain additional strategic partnerships involving our Human Response Platform, we would not realize its potential as a means of identifying and validating targets for new cancer therapies in collaboration with strategic partners or of identifying biomarkers to aid in the development of our strategic partners' drug candidates.

*We rely on third-party manufacturers to produce our preclinical and clinical drug supplies and we intend to rely on third parties to produce commercial supplies of any approved product candidates. Any failure by a third-party manufacturer to produce supplies for us may delay or impair our ability to complete our clinical trials or commercialize our product candidates.*

We have relied upon a small number of third-party manufacturers for the manufacture of our product candidates for preclinical and clinical testing purposes and intend to continue to do so in the future, including for commercial purposes. For instance, we rely on one supplier for the drug substance for tivozanib. Currently, a separate contract manufacturer manufactures, packages and distributes the drug product for clinical supplies of tivozanib. While we believe that our existing supplier of drug substance and our existing supplier of drug product, or an alternative supplier, would be capable of producing drug substance and drug product, as the case may be, in commercial quantities, we will need to fully validate their ability to produce drug substance and drug product on a commercial scale. If we are unable to validate our third party manufacturing sources' ability to supply on a commercial basis, we may not be able to successfully produce and market tivozanib or could be delayed in doing so.

If the amounts of ficlatuzumab we currently have in our inventory are insufficient to complete our current clinical trials, or if we are unsuccessful in implementing the manufacturing technology transferred to us from Merck, future clinical trials and any commercial production of ficlatuzumab could be adversely affected.

As with tivozanib and ficlatuzumab, we also expect to rely upon third parties to produce materials required for the clinical and commercial production of any other product candidates. If we are unable to arrange for third-party manufacturing sources, or to do so on commercially reasonable terms, we may not be able to complete development of such other product candidates or market them.

Reliance on third-party manufacturers entails risks to which we would not be subject if we manufactured product candidates ourselves, including reliance on the third party for regulatory compliance and quality assurance, the possibility of breach of the manufacturing agreement by the third party because of factors beyond our control (including a failure to synthesize and manufacture our product candidates in accordance with our product specifications), failure of the third party to accept orders for supply of drug substance or drug product and the possibility of termination or nonrenewal of the agreement by the third party, based on its own business priorities, at a time that is costly or damaging to us. In addition, the FDA and other regulatory authorities require that our product candidates be manufactured according to cGMP and similar foreign standards. Any failure by our third-party manufacturers to comply with cGMP or failure to scale up manufacturing processes, including any failure to deliver sufficient quantities of product candidates in a timely manner, could lead to a delay in, or failure to obtain, regulatory approval of any of our product candidates. In addition, such failure could be the basis for action by the FDA to withdraw approvals for product candidates previously granted to us and for other regulatory action, including recall or seizure, fines, imposition of operating restrictions, total or partial suspension of production or injunctions.

We rely on our manufacturers to purchase from third-party suppliers the materials necessary to produce our product candidates for our clinical studies. There are a small number of suppliers for certain capital equipment and raw materials that we use to manufacture our drugs. Such suppliers may not sell these raw materials to our manufacturers at the times we need them or on commercially reasonable terms. We do not have any control over the process or timing of the acquisition of these raw materials by our manufacturers. Moreover, we currently do not have any agreements for the commercial production of these raw materials. Although we generally do not begin a clinical trial unless we believe we have a sufficient supply of a product candidate to complete the clinical

## **Table of Contents**

trial, any significant delay in the supply of a product candidate or the raw material components thereof for an ongoing clinical trial due to the need to replace a third-party manufacturer could considerably delay completion of our clinical studies, product testing and potential regulatory approval of our product candidates. If our manufacturers or we are unable to purchase these raw materials after regulatory approval has been obtained for our product candidates, the commercial launch of our product candidates would be delayed or there would be a shortage in supply, which would impair our ability to generate revenues from the sale of our product candidates.

Because of the complex nature of many of our early stage compounds and product candidates, our manufacturers may not be able to manufacture such compounds and product candidates at a cost or in quantities or in a timely manner necessary to develop and commercialize related products. If we successfully commercialize any of our drugs, we may be required to establish or access large-scale commercial manufacturing capabilities. In addition, as our drug development pipeline increases and matures, we will have a greater need for clinical trial and commercial manufacturing capacity. We do not own or operate manufacturing facilities for the production of clinical or commercial quantities of our product candidates and we currently have no plans to build our own clinical or commercial scale manufacturing capabilities. To meet our projected needs for commercial manufacturing, third parties with whom we currently work will need to increase their scale of production or we will need to secure alternate suppliers.

***We rely on third parties to conduct preclinical and clinical trials for our product candidates, and if they do not properly and successfully perform their obligations to us, we may not be able to obtain regulatory approvals for our product candidates.***

We design the clinical trials for our product candidates, but we rely on contract research organizations and other third parties to assist us in managing, monitoring and otherwise carrying out many of these trials. We compete with larger companies for the resources of these third parties.

Although we rely on these third parties to conduct many of our clinical trials, we are responsible for ensuring that each of our clinical trials is conducted in accordance with its general investigational plan and protocol. Moreover, the FDA and foreign regulatory agencies require us to comply with regulations and standards, commonly referred to as good clinical practices, for designing, conducting, monitoring, recording, analyzing, and reporting the results of clinical trials to assure that the data and results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. Our reliance on third parties that we do not control does not relieve us of these responsibilities and requirements.

The third parties on whom we rely generally may terminate their engagements with us at any time. If we are required to enter into alternative arrangements because of any such termination the introduction of our product candidates to market could be delayed.

If these third parties do not successfully carry out their duties under their agreements with us, if the quality or accuracy of the data they obtain is compromised due to their failure to adhere to our clinical trial protocols or regulatory requirements, or if they otherwise fail to comply with clinical trial protocols or meet expected deadlines, our clinical trials may not meet regulatory requirements. If our clinical trials do not meet regulatory requirements or if these third parties need to be replaced, our preclinical development activities or clinical trials may be extended, delayed, suspended or terminated. If any of these events occur, we may not be able to obtain regulatory approval of our product candidates and our reputation could be harmed.

### **Risks Related to Our Intellectual Property Rights**

***We could be unsuccessful in obtaining adequate patent protection for one or more of our product candidates.***

We cannot be certain that patents will be issued or granted with respect to applications that are currently pending, or that issued or granted patents will not later be found to be invalid and/or unenforceable. The patent position of biotechnology and pharmaceutical companies is generally uncertain because it involves complex legal



## **Table of Contents**

and factual considerations. The standards applied by the United States Patent and Trademark Office and foreign patent offices in granting patents are not always applied uniformly or predictably. For example, there is no uniform worldwide policy regarding patentable subject matter or the scope of claims allowable in biotechnology and pharmaceutical patents. Consequently, patents may not issue from our pending patent applications. As such, we do not know the degree of future protection that we will have on our proprietary products and technology. The scope of patent protection that the U.S. Patent and Trademark Office will grant with respect to the antibodies in our antibody product pipeline is uncertain. It is possible that the U.S. Patent and Trademark Office will not allow broad antibody claims that cover closely related antibodies as well as the specific antibody. Upon receipt of FDA approval, competitors would be free to market antibodies almost identical to ours, thereby decreasing our market share.

### ***Issued patents covering one or more of our products could be found invalid or unenforceable if challenged in court.***

If we or one of our corporate partners were to initiate legal proceedings against a third party to enforce a patent covering one of our products, the defendant could counterclaim that our patent is invalid and/or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, for example, lack of novelty, obviousness or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the U.S. Patent and Trademark Office, or made a misleading statement, during prosecution. Although we have conducted due diligence on patents we have exclusively in-licensed, and we believe that we have conducted our patent prosecution in accordance with the duty of candor and in good faith, the outcome following legal assertions of invalidity and unenforceability during patent litigation is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which we and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, we would lose at least part, and perhaps all, of the patent protection on one of our products or certain aspects of our Human Response Platform. Such a loss of patent protection could have a material adverse impact on our business.

### ***Claims that our platform technologies, our products or the sale or use of our products infringe the patent rights of third parties could result in costly litigation or could require substantial time and money to resolve, even if litigation is avoided.***

We cannot guarantee that our platform technologies, our products, or the use of our products, do not infringe third party patents. Third parties might allege that we are infringing their patent rights or that we have misappropriated their trade secrets. Such third parties might resort to litigation against us. The basis of such litigation could be existing patents or patents that issue in the future.

It is also possible that we failed to identify relevant third party patents or applications. For example, applications filed before November 29, 2000 and certain applications filed after that date that will not be filed outside the United States remain confidential until patents issue. Patent applications in the United States and elsewhere are published approximately 18 months after the earliest filing, which is referred to as the priority date. Therefore, patent applications covering our products or platform technology could have been filed by others without our knowledge. Additionally, pending patent applications which have been published can, subject to certain limitations, be later amended in a manner that could cover our platform technologies, our products or the use of our products.

With regard to tivozanib, we are aware of a third party United States patent, and corresponding foreign counterparts, that contain broad claims related to use of an organic compound, that, among other things, inhibits the tyrosine phosphorylation of a VEGF receptor caused by VEGF binding to such VEGF receptor. Additionally, tivozanib falls within the scope of certain pending patent applications that have broad generic disclosure and

## **Table of Contents**

disclosure of certain compounds possessing structural similarities to tivozanib. Although we believe it is unlikely that such applications will lead to issued claims that would cover tivozanib and still be valid in view of the prior art, patent prosecution is inherently unpredictable. We are also aware of third party United States patents that contain broad claims related to the use of a tyrosine kinase inhibitor in combination with a DNA damaging agent such as chemotherapy or radiation and we have received written notice from the owners of such patents indicating that they believe we may need a license from them in order to avoid infringing their patents. With regard to ficlatuzumab, we are aware of two separate families of United States patents, United States patent applications and foreign counterparts, with each of the two families being owned by a different third party, that contain broad claims related to anti-HGF antibodies having certain binding properties and their use. We are also aware of a United States patent that contains claims related to a method of treating a tumor by administering an agent that blocks the ability of HGF to promote angiogenesis in the tumor. With regard to AV-203, we are aware of a third party United States patent that contains broad claims relating to anti-ErbB3 antibodies. Based on our analyses, if any of the above third party patents were asserted against us, we do not believe our proposed products or activities would be found to infringe any valid claim of these patents. If we were to challenge the validity of any issued United States patent in court, we would need to overcome a statutory presumption of validity that attaches to every United States patent. This means that in order to prevail, we would have to present clear and convincing evidence as to the invalidity of the patent's claims. There is no assurance that a court would find in our favor on questions of infringement or validity.

In order to avoid or settle potential claims with respect to any of the patent rights described above or any other patent rights of third parties, we may choose or be required to seek a license from a third party and be required to pay license fees or royalties or both. These licenses may not be available on acceptable terms, or at all. Even if we or our strategic partners were able to obtain a license, the rights may be nonexclusive, which could result in our competitors gaining access to the same intellectual property. Ultimately, we could be prevented from commercializing a product, or be forced to cease some aspect of our business operations, if, as a result of actual or threatened patent infringement claims, we are unable to enter into licenses on acceptable terms. This could harm our business significantly.

Defending against claims of patent infringement or misappropriation of trade secrets could be costly and time consuming, regardless of the outcome. Thus, even if we were to ultimately prevail, or to settle at an early stage, such litigation could burden us with substantial unanticipated costs. In addition, litigation or threatened litigation could result in significant demands on the time and attention of our management team, distracting them from the pursuit of other company business.

### ***Unfavorable outcomes in intellectual property litigation could limit our research and development activities and/or our ability to commercialize certain products.***

If third parties successfully assert intellectual property rights against us, we might be barred from using aspects of our technology platform, or barred from developing and commercializing related products. Prohibitions against using specified technologies, or prohibitions against commercializing specified products, could be imposed by a court or by a settlement agreement between us and a plaintiff. In addition, if we are unsuccessful in defending against allegations of patent infringement or misappropriation of trade secrets, we may be forced to pay substantial damage awards to the plaintiff. There is inevitable uncertainty in any litigation, including intellectual property litigation. There can be no assurance that we would prevail in any intellectual property litigation, even if the case against us is weak or flawed. If litigation leads to an outcome unfavorable to us, we may be required to obtain a license from the patent owner in order to continue our research and development programs or to market our product(s). It is possible that the necessary license will not be available to us on commercially acceptable terms, or at all. This could limit our research and development activities, our ability to commercialize specified products, or both.

Most of our competitors are larger than we are and have substantially greater resources. They are, therefore, likely to be able to sustain the costs of complex patent litigation longer than we could. In addition, the

## **Table of Contents**

uncertainties associated with litigation could have a material adverse effect on our ability to raise the funds necessary to continue our clinical trials, continue our internal research programs, in-license needed technology, or enter into strategic partnerships that would help us bring our product candidates to market.

In addition, any future patent litigation, interference or other administrative proceedings will result in additional expense and distraction of our personnel. An adverse outcome in such litigation or proceedings may expose us or our strategic partners to loss of our proprietary position, expose us to significant liabilities, or require us to seek licenses that may not be available on commercially acceptable terms, if at all.

***Intellectual property litigation may lead to unfavorable publicity that harms our reputation and causes the market price of our common stock to decline.***

During the course of any patent litigation, there could be public announcements of the results of hearings, rulings on motions, and other interim proceedings in the litigation. If securities analysts or investors regard these announcements as negative, the perceived value of our products, programs, or intellectual property could be diminished. Accordingly, the market price of our common stock may decline.

***Tivozanib and certain aspects of our platform technology are protected by patents exclusively licensed from other companies. If the licensors terminate the licenses or fail to maintain or enforce the underlying patents, our competitive position and our market share in the markets for any of our approved products will be harmed.***

We are a party to several license agreements under which certain aspects of our business depend on patents and/or patent applications owned by other companies or institutions. In particular, we hold exclusive licenses from Kyowa Hakko Kirin for tivozanib and the Dana-Farber Cancer Institute for our MaSS screen, which is a method of using our models to screen for, and identify, novel targets for new cancer drugs. We are likely to enter into additional license agreements as part of the development of our business in the future. Our licensors may not successfully prosecute certain patent applications under which we are licensed and on which our business depends. Even if patents issue from these applications, our licensors may fail to maintain these patents, may decide not to pursue litigation against third party infringers, may fail to prove infringement, or may fail to defend against counterclaims of patent invalidity or unenforceability. In addition, in spite of our best efforts, our licensors might conclude that we have materially breached our license agreements and might therefore terminate the license agreements, thereby removing our ability to obtain regulatory approval and to market products covered by these license agreements. If these in-licenses are terminated, or if the underlying patents fail to provide the intended market exclusivity, competitors would have the freedom to seek regulatory approval of, and to market, products identical to ours. This could have a material adverse effect on our competitive business position and our business prospects.

***We could be unsuccessful in obtaining patent protection on one or more components of our technology platform.***

We believe that an important factor in our competitive position relative to other companies in the field of targeted oncology therapeutics is our proprietary Human Response Platform. This platform is useful for identifying new targets for drug discovery, confirming that newly-identified drug targets actually play a role in cancer, testing new compounds for effectiveness as drugs, and identifying traits useful for predicting which patients will respond to which drugs. We own issued U.S. patents covering our chimeric model technology and directed complementation technology. We have exclusively in-licensed certain patent rights covering a method of using our inducible cancer models to identify new targets for cancer drugs. However, patent protection on other aspects of our technology platform, such as our reconstituted human breast tumor model, is still pending. There is no guarantee that any of such pending patent applications, in the United States or elsewhere, will result in issued patents, and, even if patents eventually issue, there is no certainty that the claims in the eventual patents will have adequate scope to preserve our competitive position. Third parties might invent alternative technologies

## **Table of Contents**

that would substitute for our technology platform while being outside the scope of the patents covering our platform technology. By successfully designing around our patented technology, third parties could substantially weaken our competitive position in oncology research and development.

***Confidentiality agreements with employees and third parties may not prevent unauthorized disclosure of trade secrets and other proprietary information.***

In addition to patents, we rely on trade secrets, technical know-how, and proprietary information concerning our business strategy in order to protect our competitive position in the field of oncology. In the course of our research, development and business activities, we often rely on confidentiality agreements to protect our proprietary information. Such confidentiality agreements are used, for example, when we talk to vendors of laboratory or clinical development services or potential strategic partners. In addition, each of our employees is required to sign a confidentiality agreement upon joining our company. We take steps to protect our proprietary information, and we seek to carefully draft our confidentiality agreements to protect our proprietary interests. Nevertheless, there can be no guarantee that an employee or an outside party will not make an unauthorized disclosure of our proprietary confidential information. This might happen intentionally or inadvertently. It is possible that a competitor will make use of such information, and that our competitive position will be compromised, in spite of any legal action we might take against persons making such unauthorized disclosures.

Trade secrets are difficult to protect. Although we use reasonable efforts to protect our trade secrets, our employees, consultants, contractors, or outside scientific collaborators might intentionally or inadvertently disclose our trade secret information to competitors. Enforcing a claim that a third party illegally obtained and is using any of our trade secrets is expensive and time consuming, and the outcome is unpredictable. In addition, courts outside the United States sometimes are less willing than U.S. courts to protect trade secrets. Moreover, our competitors may independently develop equivalent knowledge, methods and know-how.

Our research and development strategic partners may have rights to publish data and other information to which we have rights. In addition, we sometimes engage individuals or entities to conduct research relevant to our business. The ability of these individuals or entities to publish or otherwise publicly disclose data and other information generated during the course of their research is subject to certain contractual limitations. These contractual provisions may be insufficient or inadequate to protect our confidential information. If we do not apply for patent protection prior to such publication, or if we cannot otherwise maintain the confidentiality of our proprietary technology and other confidential information, then our ability to obtain patent protection or to protect our trade secret information may be jeopardized.

***Intellectual property rights do not necessarily address all potential threats to our competitive advantage.***

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations, and may not adequately protect our business, or permit us to maintain our competitive advantage. The following examples are illustrative:

Others may be able to make compounds that are similar to our product candidates but that are not covered by the claims of the patents that we own or have exclusively licensed.

We or our licensors or strategic partners might not have been the first to make the inventions covered by the issued patent or pending patent application that we own or have exclusively licensed.

We or our licensors or strategic partners might not have been the first to file patent applications covering certain of our inventions.

Others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights.

It is possible that our pending patent applications will not lead to issued patents.



## **Table of Contents**

Issued patents that we own or have exclusively licensed may not provide us with any competitive advantages, or may be held invalid or unenforceable, as a result of legal challenges by our competitors.

Our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets.

We may not develop additional proprietary technologies that are patentable.

The patents of others may have an adverse effect on our business.

***Changes in U.S. patent law could diminish the value of patents in general, thereby impairing our ability to protect our products.***

As is the case with other biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharma industry involve both technological complexity and legal complexity. Therefore, obtaining and enforcing biopharma patents is costly, time-consuming and inherently uncertain. In addition several recent events have increased uncertainty with regard to our ability to obtain patents in the future and the value of patents once obtained. Among these, in September 2011, patent reform legislation passed by Congress was signed into law. The new patent law introduces changes including a first-to-file system for determining which inventors may be entitled to receive patents, and a new post-grant review process that allows third parties to challenge newly issued patents. It remains to be seen how the biopharma industry will be affected by such changes in the patent system. In addition, the Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in specified circumstances or weakening the rights of patent owners in specified situations. Depending on decisions by the U.S. Congress, the federal courts, and the U.S. Patent and Trademark Office, the laws and regulations governing patents could change in unpredictable ways that could weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future.

## **Risks Related to Ownership of Our Common Stock**

***The market price of our common stock has been, and may continue to be, highly volatile, and could fall below the price you paid.***

The trading price of our common stock has been, and is likely to continue to be, highly volatile and could be subject to wide fluctuations in price in response to various factors, many of which are beyond our control, including:

new products, product candidates or new uses for existing products introduced or announced by our strategic partners, or our competitors, including Roche's Avastin, Pfizer's Sutent and Inlyta, Onyx's Nexavar, GSK's Votrient and the timing of these introductions or announcements;

actual or anticipated results from and any delays in our clinical trials, including our phase 3 clinical trial of tivozanib;

results of regulatory reviews relating to the approval of our product candidates;

the results of our efforts to discover, develop, acquire or in-license additional product candidates or products;

disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;

Edgar Filing: AVEO PHARMACEUTICALS INC - Form 10-K

announcements by us or our competitors of significant acquisitions, strategic partnerships, joint ventures and capital commitments;

additions or departures of key scientific or management personnel;

## Table of Contents

conditions or trends in the biotechnology and biopharmaceutical industries;

actual or anticipated changes in earnings estimates, development timelines or recommendations by securities analysts;

general economic and market conditions and other factors that may be unrelated to our operating performance or the operating performance of our competitors, including changes in market valuations of similar companies; and

sales of common stock by us or our stockholders in the future, as well as the overall trading volume of our common stock.

In addition, the stock market in general and the market for biotechnology and biopharmaceutical companies in particular have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of those companies. These broad market and industry factors may seriously harm the market price of our common stock, regardless of our operating performance. In the past, following periods of volatility in the market, securities class-action litigation has often been instituted against companies. Such litigation, if instituted against us, could result in substantial costs and diversion of management's attention and resources, which could materially and adversely affect our business and financial condition.

***Our executive officers, directors, entities affiliated with such executive officers and directors, and certain other significant stockholders own a significant percentage of our stock and may be able to exercise significant influence over matters subject to stockholder approval.***

To our knowledge, as of December 31, 2011, our executive officers, directors, entities affiliated with such executive officers and directors, and certain other significant stockholders, owned approximately 39% of our common stock, including shares subject to outstanding options and warrants that are exercisable within 60 days after December 31, 2011. These stockholders, acting together or individually, may be able to exert influence over our management and affairs and over matters requiring stockholder approval, including the election of our board of directors and approval of significant corporate transactions. This concentration of ownership could have the effect of delaying or preventing a change in control of our company or otherwise discouraging a potential acquirer from attempting to obtain control of us, which in turn could have a material and adverse effect on the fair market value of our common stock.

***Future sales of shares of our common stock, including shares issued upon the exercise of currently outstanding options and warrants, could negatively affect our stock price.***

A substantial portion of our outstanding common stock can be traded without restriction at any time. Some of these shares are currently restricted as a result of securities laws, but will be able to be sold, subject to any applicable volume limitations under federal securities laws with respect to affiliate sales, in the near future. As such, sales of a substantial number of shares of our common stock in the public market could occur at any time. These sales, or the perception in the market that the holders of a large number of shares intend to sell such shares, could reduce the market price of our common stock. In addition, we have a significant number of shares that are subject to outstanding options and warrants. The exercise of these options and warrants and the subsequent sale of the underlying common stock could cause a further decline in our stock price. These sales also might make it difficult for us to sell equity securities in the future at a time and at a price that we deem appropriate.

***Provisions in our certificate of incorporation, our by-laws or Delaware law might discourage, delay or prevent a change in control of our company or changes in our management and, therefore, depress the trading price of our common stock.***

Provisions of our certificate of incorporation, our by-laws or Delaware law may have the effect of deterring unsolicited takeovers or delaying or preventing a change in control of our company or changes in our



## **Table of Contents**

management, including transactions in which our stockholders might otherwise receive a premium for their shares over then current market prices. In addition, these provisions may limit the ability of stockholders to approve transactions that they may deem to be in their best interest. These provisions include:

advance notice requirements for stockholder proposals and nominations;

the inability of stockholders to act by written consent or to call special meetings;

the ability of our board of directors to make, alter or repeal our by-laws; and

the ability of our board of directors to designate the terms of and issue new series of preferred stock without stockholder approval, which could be used to institute a rights plan, or a poison pill, that would work to dilute the stock ownership of a potential hostile acquirer, likely preventing acquisitions that have not been approved by our board of directors.

In addition, Section 203 of the Delaware General Corporation Law prohibits a publicly-held Delaware corporation from engaging in a business combination with an interested stockholder, generally a person which together with its affiliates owns, or within the last three years has owned, 15% of our voting stock, for a period of three years after the date of the transaction in which the person became an interested stockholder, unless the business combination is approved in a prescribed manner.

The existence of the foregoing provisions and anti-takeover measures could limit the price that investors might be willing to pay in the future for shares of our common stock. They could also deter potential acquirers of our company, thereby reducing the likelihood that a stockholder could receive a premium for shares of our common stock held by a stockholder in an acquisition.

### ***Our business could be negatively affected as a result of the actions of activist shareholders.***

Proxy contests have been waged against many companies in the biopharmaceutical industry over the last few years. If faced with a proxy contest, we may not be able to successfully respond to the contest, which would be disruptive to our business. Even if we are successful, our business could be adversely affected by a proxy contest because:

responding to proxy contests and other actions by activist shareholders may be costly and time-consuming, and may disrupt our operations and divert the attention of management and our employees;

perceived uncertainties as to the potential outcome of any proxy contest may result in our inability to consummate potential acquisitions, collaborations or in-licensing opportunities and may make it more difficult to attract and retain qualified personnel and business partners; and

if individuals that have a specific agenda different from that of our management or other members of our board of directors are elected to our board as a result of any proxy contest, such an election may adversely affect our ability to effectively and timely implement our strategic plan and create additional value for our stockholders.

### ***We have limited experience complying with public company obligations.***

We face increased legal, accounting, administrative and other costs and expenses as a public company. Compliance with the Sarbanes-Oxley Act of 2002, the federal securities laws, as well as other rules of the SEC and NASDAQ, will result in significant costs to us as well as ongoing increases in our legal, audit and financial compliance costs.



## **Table of Contents**

***Failure to maintain effective internal controls in accordance with Section 404 of the Sarbanes-Oxley Act could have a material adverse effect on our ability to produce accurate financial statements and on our stock price.***

Section 404 of the Sarbanes-Oxley Act of 2002 requires us, on an annual basis beginning in 2011, to review and evaluate our internal controls, and requires our independent registered public accounting firm to attest to the effectiveness of our internal controls. Despite our efforts, we can provide no assurance as to our, or our independent registered public accounting firm's, conclusions with respect to the effectiveness of our internal control over financial reporting under Section 404. There is a risk that neither we nor our independent registered public accounting firm will be able to continue to conclude within the prescribed timeframe that our internal control over financial reporting is effective as required by Section 404. This could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

***We do not expect to pay any cash dividends for the foreseeable future.***

You should not rely on an investment in our common stock to provide dividend income. We do not anticipate that we will pay any cash dividends to holders of our common stock in the foreseeable future. Instead, we plan to retain any earnings to maintain and expand our existing operations. In addition, our ability to pay cash dividends is currently prohibited by the terms of our debt financing arrangements, and any future debt financing arrangement may contain terms prohibiting or limiting the amount of dividends that may be declared or paid on our common stock. Accordingly, investors must rely on sales of their common stock after price appreciation, which may never occur, as the only way to realize any return on their investment. As a result, investors seeking cash dividends should not purchase our common stock.

***Our management has broad discretion over the use of the cash available for our operations and working capital requirements and might not spend available cash in ways that increase the value of your investment.***

Our management has broad discretion on where and how to use our cash and you will be relying on the judgment of our management regarding the application of our available cash to fund our operations. Our management might not apply our cash in ways that increase the value of your investment. We expect to use a substantial portion of our cash to fund our existing and future clinical trials for tivozanib, ficlatuzumab and AV-203, as well as pre-commercialization activities for tivozanib, with the balance, if any, to be used for working capital and other general corporate purposes, which may in the future include investments in, or acquisitions of, complementary businesses, joint ventures, partnerships, services or technologies. Our management might not be able to yield a significant return, if any, on any investment of this cash. You will not have the opportunity to influence our decisions on how to use our cash reserves.

### **ITEM 1B. Unresolved Staff Comments**

None

### **ITEM 2. Properties**

We sublease our principal facilities, which consist of approximately 55,200 square feet of research and office space located at 75 Sidney Street, Cambridge, Massachusetts, which sublease expires in February 2014, approximately 7,407 square feet of office space located at 64 Sidney Street, Cambridge, Massachusetts, which sublease expires in February 2014, and approximately 25,714 square feet of office space located at 12 Emily Street, Cambridge, Massachusetts, under subleases expiring in February 2014 and May 2015, respectively. We believe that our existing facilities are sufficient for our current needs for the foreseeable future.

### **ITEM 3. Legal Proceedings**

None.

### **ITEM 4. Mine Safety Disclosures**

Not applicable.



**Table of Contents****PART II****ITEM 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities**  
**MARKET PRICE INFORMATION**

Our common stock began trading on the NASDAQ Global Market on March 12, 2010 under the symbol AVEO. Prior to that time, there was no established public trading market for our common stock. The following table sets forth the high and low sale prices per share for our common stock on the NASDAQ Global Market for the period indicated:

	<b>High</b>	<b>Low</b>
<b>2010</b>		
First Quarter (beginning March 12, 2010)	\$ 9.02	\$ 8.16
Second Quarter	\$ 9.91	\$ 6.90
Third Quarter	\$ 11.23	\$ 6.01
Fourth Quarter	\$ 17.93	\$ 11.24
<b>2011</b>		
First Quarter	\$ 16.00	\$ 13.05
Second Quarter	\$ 21.00	\$ 13.00
Third Quarter	\$ 21.55	\$ 15.02
Fourth Quarter	\$ 17.65	\$ 14.01

**HOLDERS**

At February 29, 2012, there were approximately 108 holders of record of our common stock. We believe that the number of beneficial owners of our common stock at that date was substantially greater.

**DIVIDENDS**

We have never declared or paid any cash dividends on our common stock and our ability to pay cash dividends is currently prohibited by the terms of our debt financing arrangements. We currently intend to retain earnings, if any, for use in our business and do not anticipate paying cash dividends on our common stock in the foreseeable future. Payment of future dividends, if any, on our common stock will be at the discretion of our board of directors after taking into account various factors, including our financial condition, operating results, anticipated cash needs, and plans for expansion.

**RECENT SALES OF UNREGISTERED EQUITY SECURITIES**

Set forth below is information regarding certain shares of common stock issued by us during 2011 that were not registered under the Securities Act of 1933, as amended, which we refer to as the Securities Act. Also included is the consideration, if any, received by us for such shares and information relating to the section of the Securities Act, or rule of the SEC, under which exemption from registration was claimed.

On May 31, 2011, we entered into a definitive agreement with respect to the sale of 438,340 shares of our unregistered common stock at \$17.11 per share to Johnson & Johnson Development Corporation. We completed the private placement on May 31, 2011, resulting in approximately \$7.5 million in net proceeds to us. No underwriters were involved in the transaction and the shares were issued in reliance upon the exemption from the registration requirements of the Securities Act set forth in Section 4(2) of the Securities Act. In connection with the issuance, Johnson & Johnson Development Corporation represented to us that it was an accredited investor, it

**Table of Contents**

was acquiring the applicable securities for investment and not distribution and it could bear the risks of the investment. Johnson & Johnson Development Corporation received written disclosures that the securities had not been registered under the Securities Act and that any resale must be made pursuant to a registration or an available exemption from such registration. The shares issued to Johnson & Johnson Development Corporation were deemed restricted securities for purposes of the Securities Act. The certificate issued representing the shares included appropriate legends setting forth that the shares had not been registered and the applicable restrictions on transfer.

**USE OF PROCEEDS FROM REGISTERED SECURITIES**

Our initial public offering of common stock was effected through Registration Statements on Form S-1 (File Nos. 333-163778 and 333-165412), that were declared effective by the SEC on March 11, 2010. As of December 31, 2011, we estimate that we have used all of the net proceeds from the initial public offering to fund the clinical development of tivozanib and for working capital, capital expenditures and other general corporate purposes. There was no material change in the use of proceeds from the initial public offering from that described in the final prospectus filed with the SEC on March 12, 2010.

**Comparative Stock Performance Graph**

The information included under the heading Comparative Stock Performance Graph in this Item 5 of Part II of this Annual Report on Form 10-K shall not be deemed to be soliciting material or subject to Regulation 14A or 14C, shall not be deemed filed for purposes of Section 18 of the Exchange Act, or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act.

Set forth below is a graph comparing the total cumulative returns of AVEO, the NASDAQ Composite Index and the NASDAQ Biotechnology Index. The graph assumes \$100 was invested on March 12, 2010 in our common stock and each of the indices and that all dividends, if any, are reinvested.

	3/12/10	3/31/10	6/30/10	9/30/10	12/31/10	3/31/11	6/30/11	9/30/11	12/31/11
AVEO Pharmaceuticals	\$ 100.00	\$ 100.11	\$ 78.64	\$ 123.92	\$ 162.63	\$ 148.16	\$ 229.25	\$ 171.19	\$ 191.32
NASDAQ Composite Index	\$ 100.00	\$ 101.28	\$ 89.09	\$ 100.04	\$ 112.05	\$ 117.46	\$ 117.14	\$ 102.02	\$ 110.03
NASDAQ Biotechnology Index	\$ 100.00	\$ 100.23	\$ 85.39	\$ 95.57	\$ 103.56	\$ 111.10	\$ 118.31	\$ 103.50	\$ 115.78

**Table of Contents****ITEM 6. Selected Financial Data**

The following selected consolidated financial data should be read in conjunction with our Consolidated Financial Statements and the Notes thereto and Management's Discussion and Analysis of Financial Condition and Results of Operations included elsewhere in this Annual Report on Form 10-K. The Balance Sheet Data at December 31, 2011 and 2010 and the Statement of Operations Data for each of the three years ended December 31, 2011 have been derived from our audited Consolidated Financial Statements for such years, included elsewhere in this Annual Report on Form 10-K. The Balance Sheet Data at December 31, 2009, 2008 and 2007, and the Statement of Operations Data for each of the two years in the period ended December 31, 2008 have been derived from the audited Consolidated Financial Statements for such years not included in this Annual Report on Form 10-K. Please refer to the Critical Accounting Policies and Significant Judgments and Estimates section in Management's Discussion and Analysis of Financial Condition and Results of Operations for discussion of the impact of our adoption of Accounting Standards Update, or ASU, 2009-13 on the selected data below.

Our historical results for any prior period are not necessarily indicative of results to be expected in any future period.

	2011	2010	Years Ended December 31, 2009		2008	2007
	(in thousands, except per share data)					
<b>Statement of operations data:</b>						
Revenue	\$ 164,849	\$ 44,682	\$ 20,719	\$ 19,660	\$ 11,034	
Operating expenses:						
Research and development	101,735	86,345	51,792	41,820	29,248	
General and administrative	29,167	14,763	10,120	9,165	6,502	
Total operating expenses	130,902	101,108	61,912	50,985	35,750	
Income (loss) from operations	33,947	(56,426)	(41,193)	(31,325)	(24,716)	
Other income and expense:						
Other income (expense), net	10	900	(333)	(230)		
Interest expense	(3,836)	(3,389)	(2,811)	(2,086)	(2,437)	
Interest income	527	126	144	1,168	2,171	
Other expense, net	(3,299)	(2,363)	(3,000)	(1,148)	(266)	
Net income (loss) before benefit for income taxes	30,648	(58,789)	(44,193)	(32,473)	(24,982)	
Benefit for income taxes			100			
Net income (loss)	\$ 30,648	\$ (58,789)	\$ (44,093)	\$ (32,473)	\$ (24,982)	
Net income (loss) per share - basic	\$ 0.77	\$ (2.30)	\$ (27.43)	\$ (21.08)	\$ (17.89)	
Weighted average number of common shares used in net income (loss) per share calculation - basic						
	39,715	25,582	1,607	1,541	1,396	
Net income (loss) per share - diluted	\$ 0.74	\$ (2.30)	\$ (27.43)	\$ (21.08)	\$ (17.89)	
Weighted average number of common shares and dilutive common share equivalents used in net income (loss) per share calculation - diluted						
	41,473	25,582	1,607	1,541	1,396	

**Table of Contents**

	2011	2010	As of December 31, 2009 (in thousands)	2008	2007
<b>Balance sheet data:</b>					
Cash, cash equivalents, and marketable securities	\$ 275,440	\$ 140,198	\$ 51,301	\$ 32,364	\$ 61,742
Working capital	199,786	103,360	18,789	16,073	42,542
Total assets	295,050	151,048	59,844	40,087	67,654
Loans payable, including current portion, net of discount	24,170	23,402	19,745	21,055	15,078
Preferred stock warrant liability			1,459	1,211	905
Convertible preferred stock			156,705	123,720	123,720
Accumulated deficit	(205,866)	(236,514)	(177,725)	(133,631)	(101,158)
Total stockholders' equity (deficit)	223,541	71,770	(170,291)	(128,688)	(98,458)



**Table of Contents****ITEM 7. Management's Discussion and Analysis of Financial Condition and Results of Operations**

*You should read the following discussion and analysis of our financial condition and results of operations together with our financial statements and the related notes appearing elsewhere in this report. Some of the information contained in this discussion and analysis or set forth elsewhere in this report, including information with respect to our plans and strategy for our business and related financing, includes forward-looking statements that involve risks and uncertainties. You should read the Risk Factors section in Part 1 Item 1A. of this report for a discussion of important factors that could cause actual results to differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.*

**Overview**

We are a cancer therapeutics company committed to discovering, developing and commercializing targeted cancer therapies to impact patients lives. Our product candidates are directed against important mechanisms, or targets, known or believed to be involved in cancer. Our proprietary Human Response Platform, a novel method of building preclinical models of human cancer, provides us with unique insights into cancer biology and is being leveraged in the discovery and clinical development of our cancer therapeutics.

Tivozanib, our lead product candidate, which we partnered with Astellas Pharma Inc., or Astellas, in 2011, is a potent, selective, long half-life inhibitor of all three vascular endothelial growth factor, or VEGF, receptors that is designed to optimize VEGF blockade while minimizing off-target toxicities. Our clinical trials of tivozanib to date have demonstrated a favorable safety and efficacy profile for tivozanib. In January 2012, we announced top-line data from our global, phase 3 clinical trial comparing the efficacy and safety of tivozanib with Nexavar® (sorafenib), an approved therapy for first-line treatment in renal cell carcinoma, or RCC, which we refer to as the TIVO-1 study. The TIVO-1 study is being conducted in patients with advanced clear cell RCC who have undergone a prior nephrectomy (kidney removal) and who have not received any prior VEGF- and mTOR-targeted therapy. In this trial, we measured, among other things, each patient's progression-free survival, or PFS, which refers to the period of time that began when a patient entered the clinical trial and ended when either the patient died or the patient's cancer had grown by a specified percentage or spread to a new location in the body. PFS is the primary endpoint in the TIVO-1 study. In the TIVO-1 study, tivozanib demonstrated a statistically significant improvement in PFS with a median PFS of 11.9 months compared to a median PFS of 9.1 months for Nexavar in the overall study population. Tivozanib also demonstrated a statistically significant improvement in PFS with a median PFS of 12.7 months compared to a median PFS of 9.1 months for Nexavar in the pre-specified subpopulation of patients who received no prior systemic anti-cancer therapy for metastatic disease, a subpopulation that comprised approximately 70% of the total study population. In the TIVO-1 study, tivozanib demonstrated a well-tolerated safety profile consistent with the results from our tivozanib phase 2 clinical trial in patients with advanced RCC; the most commonly reported side effect was hypertension, a well established on-target and manageable effect of VEGF receptor inhibitors. The most common treatment-related side effects seen in the phase 2 clinical trial were hypertension (44.9%) and dysphonia, or hoarseness of voice (21.7%). Additionally, the incidence of other side effects in the phase 2 clinical trial that are commonly associated with other VEGF receptor inhibitors, such as diarrhea, rash, mucositis, stomatitis, fatigue, and hand-foot syndrome, was relatively low.

In addition to the TIVO-1 study, we are evaluating tivozanib in multiple phase 1 and phase 2 clinical trials including our BATON (Biomarker Assessment of Tivozanib in ONcology) program, a series of clinical trials assessing tivozanib biomarkers in solid tumors. The BATON trials include BATON-RCC, a phase 2 exploratory biomarker study in patients with advanced RCC, which completed enrollment in early 2012. The second BATON study underway is BATON-CRC, a phase 2 clinical trial evaluating tivozanib in combination with modified FOLFOX6 (mFOLFOX6) compared to Avastin® (bevacizumab) in combination with mFOLFOX6 as first-line therapy in patients with advanced metastatic colorectal cancer, or CRC. Additionally, we expect to initiate further clinical evaluation of tivozanib in breast cancer in 2012 as part of our BATON program.

---

**Table of Contents**

We expect that the results of all of our phase 1 and phase 2 trials will help to inform our clinical development plans for tivozanib as a monotherapy and in combination with other anti-cancer therapies in multiple cancer indications.

We acquired exclusive rights to develop and commercialize tivozanib worldwide outside of Asia pursuant to a license agreement we entered into with Kirin Brewery Co. Ltd. (now Kyowa Hakko Kirin), or KHK, in 2006. Under the license agreement, we obtained an exclusive license to research, develop, manufacture and commercialize tivozanib, pharmaceutical compositions thereof and associated biomarkers for the diagnosis, prevention and treatment of any and all human diseases and conditions outside of Asia. KHK has retained all rights to tivozanib in Asia. We have obligations to make milestone and royalty payments to KHK. The royalty rates range from the low to mid-teens as a percentage of our net sales of tivozanib. We are also obligated to pay a specified percentage of certain amounts we receive from any third party sublicensees, including Astellas. As discussed below under the heading Strategic Partnerships, we entered into a strategic collaboration with Astellas in which we have agreed to share responsibility, including all profits and losses, with Astellas for continued development and commercialization of tivozanib in North America and Europe. Throughout the rest of the world, outside of North America, Europe and Asia, we granted Astellas an exclusive, royalty-bearing license to develop and commercialize tivozanib.

In addition to tivozanib, we have a pipeline of monoclonal antibodies derived from our proprietary Human Response Platform. Ficlatusumab, our next most advanced product candidate, is an antibody which binds to hepatocyte growth factor, or HGF, thereby blocking its function. We have completed two phase 1 clinical trials of ficlatusumab demonstrating the ability to combine ficlatusumab with epidermal growth factor receptor, or EGFR, inhibitors Tarceva® and Iressa®. In May 2010, we initiated a phase 2 clinical trial evaluating ficlatusumab in patients with non-small cell lung cancer. This is a first-line study comparing ficlatusumab in combination with Iressa versus Iressa monotherapy. We anticipate announcing data from the ficlatusumab phase 2 trial in the second half of 2012.

We have also identified a number of other promising targets for the development of novel cancer therapeutics using our Human Response Platform. We have preclinical and discovery antibody programs underway focused on targets that appear to be important drivers of tumor growth, including our third clinical candidate AV-203, which targets the ErbB3 receptor (partnered with Biogen Idec, Inc., or Biogen Idec), as well as programs directed toward the RON receptor (Recepteur d'Origine Nantais) (partnered with Centocor Ortho Biotech Inc., or Centocor). We expect to initiate clinical development with AV-203 in the first half of 2012.

Our proprietary Human Response Platform was designed to overcome many of the limitations of traditional approaches to modeling human cancer. The traditional method of modeling human cancer uses a model referred to as a xenograft. A xenograft model is created by adapting cells from a human tumor to grow in a petri dish, and then injecting these cells in a mouse, where they grow into tumors. However, the resulting tumors differ from the original tumor in important respects, and, accordingly, xenograft models are often poor predictors of the success of cancer drugs in human clinical trials. In our Human Response Platform, we use patented genetic engineering techniques to grow populations of spontaneous tumors in animals containing human-relevant, cancer-causing mutations and tumor variation akin to what is seen in populations of human tumors. Because we believe that these populations of tumors better replicate what is seen in human cancer, we believe that our Human Response Platform provides us with unique insights into cancer biology and mechanisms of drug response and resistance, and represents a significant improvement over traditional approaches. We are utilizing this Human Response Platform alone and with our strategic partners to (i) identify and validate target genes which drive tumor growth, (ii) evaluate drugs which can block the function of these targets and (iii) identify biomarkers, which are indicators of drug response and resistance in patients, in an effort to evaluate which patients are most likely to respond favorably to treatment with such drugs. The potential identification and development of relevant biomarkers through our Human Response Platform is a core component of our oncology drug development efforts. Our goal is to utilize the biomarker data from BATON-CRC and other BATON clinical trials to further inform our clinical development strategy.

## **Table of Contents**

We have devoted substantially all of our resources to our drug discovery efforts comprising research and development, conducting clinical trials for our product candidates, protecting our intellectual property and the general and administrative support of these operations. We have generated no revenue from product sales through December 31, 2011, and have principally funded our operations through:

\$303.7 million of non-dilutive capital in the form of license fees, milestone payments and research and development funding received from our strategic partners;

\$15.0 million of gross proceeds in connection with the license agreement with Centocor executed in May 2011, which includes \$7.5 million of gross proceeds from the sale of common stock to Johnson & Johnson Development Corporation, an affiliate of Centocor (recorded at \$8.0 million, the fair market value on the date of issuance), and \$7.5 million of non-dilutive capital in the form of license fees (recorded net of the discount on sale of common stock as \$7.0 million of revenue);

\$169.6 million of funding from the sale of convertible preferred stock to our investors, including \$77.5 million of equity sales to our strategic partners;

\$89.7 million of gross proceeds from the sale of common stock in connection with the completion of our initial public offering;

\$25.0 million of loan proceeds in connection with our loan agreement with Hercules Technology II, L.P. and Hercules Technology III, L.P.;

\$60.8 million of gross proceeds from the private placement of 4.5 million shares of our unregistered common stock at \$13.50 per share to a group of institutional and accredited investors in November 2010; and

\$111.2 million of gross proceeds from the sale of common stock in connection with a follow-on offering of our common stock in June 2011.

We do not have a history of being profitable and, as of December 31, 2011, we had an accumulated deficit of \$205.9 million. We anticipate that we will continue to incur significant operating costs over the next several years as we advance our plan to expand our discovery, research, development and commercialization activities, including the phase 3 clinical development and planned commercialization of our lead product candidate, tivozanib, the continued clinical development of our phase 2 product candidate, ficlatuzumab, as well as anticipated clinical trials for AV-203. We will need additional financing to support our operating activities.

## **Strategic Partnerships**

### ***Kyowa Hakko Kirin***

In December 2006, we entered into a license agreement with KHK under which we obtained an exclusive license, with the right to grant sublicenses subject to certain restrictions, to research, develop, manufacture and commercialize tivozanib, pharmaceutical compositions thereof and associated biomarkers. Our exclusive license covers all territories in the world, except for Asia. KHK has retained rights to tivozanib in Asia. Under the license agreement, we obtained exclusive rights in our territory under certain KHK patents, patent applications and know-how related to tivozanib, to research, develop, make, have made, use, import, offer for sale, and sell tivozanib for the diagnosis, prevention and treatment of any and all human diseases and conditions. Upon entering into the license agreement with KHK, we made a one-time cash payment in the amount of \$5.0 million.

Under our license agreement with KHK, we may be required to

## Edgar Filing: AVEO PHARMACEUTICALS INC - Form 10-K

make up to an aggregate of \$50.0 million in future milestone payments upon the achievement of specified regulatory milestones,

pay tiered royalty payments on net sales we make of tivozanib in our territory ranging from the low to mid teens as a percentage of our net sales of tivozanib, and

---

**Table of Contents**

pay 30% of certain amounts we receive under our collaboration and license agreement with Astellas, which we describe below, in connection with Astellas' development and commercialization activities outside of North America and Asia related to tivozanib, other than amounts we receive in respect of research and development funding or equity investments, subject to certain limitations.

In March 2010, we made a \$10.0 million milestone payment to KHK in connection with the dosing of the first patient in our phase 3 clinical trial of tivozanib.

We also recorded \$22.5 million of research and development expense in the year ended December 31, 2011 associated with the payment made to KHK related to the up-front license payment received under the collaboration and license agreement with Astellas which we entered into in February 2011.

***Astellas Pharma***

In February 2011, we entered into a collaboration and license agreement with Astellas and certain of its indirect wholly-owned subsidiaries in connection with which we and Astellas will develop and commercialize tivozanib for the treatment of a broad range of cancers, including RCC, and breast and colorectal cancers. Under the terms of the collaboration agreement, we and Astellas will share responsibility for continued development and commercialization of tivozanib in the United States, Mexico and Canada, or North America, and in Europe under the joint development plan and joint commercialization plan, respectively. Throughout the rest of the world (which excludes North America, Europe and Asia), which we refer to as the royalty territory, Astellas has an exclusive, royalty-bearing license to develop and commercialize tivozanib. Our plan to commercialize tivozanib in collaboration with Astellas, as described herein, is subject to our and Astellas' receipt of necessary regulatory approvals from the Food and Drug Administration, or FDA, and foreign regulatory authorities based upon favorable results in clinical trials. There can be no assurance that such approvals will be obtained.

Assuming successful approvals of tivozanib by applicable regulatory agencies, we will hold all marketing authorizations in North America, including any new drug application in the United States, and Astellas will hold all marketing authorizations in the rest of the world, other than Asia.

Assuming successful approvals of tivozanib by applicable regulatory agencies, we, as the lead commercialization party in North America, will have lead responsibility for formulating the commercialization strategy for North America under the joint commercialization plan, with each of us and Astellas responsible for conducting fifty percent (50%) of the sales efforts and medical affairs activities in North America. Astellas will have lead responsibility for commercialization activities in Europe under the joint commercialization plan, and we will be responsible for conducting fifty percent (50%) of the medical affairs activities in the major European countries. All costs associated with each party's conduct of development and commercialization activities (including clinical manufacturing and commercial manufacturing costs, if any) in North America (including any regulatory milestones and royalties associated with tivozanib in North America which may become payable by us to KHK under our license agreement with KHK), and any resulting profits or losses, will be shared equally between the parties. All costs associated with each party's conduct of development and commercialization activities (including clinical manufacturing and commercial manufacturing costs, if any) in Europe, and any resulting profits or losses, will be shared equally between the parties. As between the parties, we will remain responsible for complying with our sublicense revenue sharing obligations, if any, to KHK under our license agreement with KHK in connection with the development and commercialization of tivozanib outside of North America.

We are responsible for manufacturing, through our third party manufacturer, all of Astellas' requirements for tivozanib pursuant to a clinical supply agreement which we have entered into with Astellas, and a commercial supply agreement which the parties are currently negotiating.

---

**Table of Contents**

Each party is obligated to use commercially reasonable efforts to develop and commercialize tivozanib in each of the United States, Mexico and Canada, and to develop and commercialize tivozanib in each European country specified in the agreement. Astellas is also obligated to use commercially reasonable efforts to develop and commercialize tivozanib in each country in the royalty territory.

During the term of the agreement, neither party nor its controlled affiliates may commercialize anywhere in North America, Europe or the royalty territory any product that has a specified mechanism of action (as further defined in the collaboration agreement) for any oncology indication, except that Astellas may commercialize specified compounds for hematological cancer. Astellas may also commercialize products (other than tivozanib) in the royalty territory, on a country-by-country basis, upon expiration of the applicable royalty term, and in North America and Europe upon expiration of all valid claims under the licensed patents.

In connection with the agreement, we received an initial cash payment of \$125 million, comprised of a \$75 million license fee and \$50 million in research and development funding, both of which are non-creditable and non-refundable against any amounts due under the collaboration agreement. We retained net proceeds of approximately \$97.6 million of the initial cash payment from Astellas, after payments to KHK and strategic, legal and financial advisors. We are also eligible to receive an aggregate of approximately \$1.3 billion in potential milestone payments, comprised of (i) up to \$85 million in substantive milestone payments upon achievement of specified clinical and development milestone events, (ii) up to \$490 million in substantive milestone payments upon achievement of specified regulatory milestone events, including up to \$90 million in milestone payments in connection with specified regulatory filings, and receipt of marketing approvals, for tivozanib to treat RCC in the United States and Europe, and (iii) up to \$780 million in milestone payments upon the achievement of specified commercial sales events. The first anticipated clinical and development milestone is due to us upon initiation of our next phase 3 clinical trial. The timing of this milestone is uncertain, as we have not finalized plans for our future trials. We have elected to recognize all milestone payments as revenue once the milestones have been triggered if the milestone is deemed to be substantive. Significant potential near-term regulatory milestones include acceptance by the FDA of the first filing of an NDA for RCC (monotherapy) (\$15 million) and acceptance by the European Medicines Agency, or EMA of the first filing of a Marketing Authorization Application (\$15 million). In addition, if tivozanib is successfully developed and launched in the royalty territory, Astellas will be required to pay to us tiered, double digit royalties on net sales of tivozanib in the royalty territory, if any, subject to offsets under certain circumstances. We are required to pay KHK low to mid-teen royalties on our net sales in North America, and 30% of certain amounts we may receive from Astellas in connection with Astellas' development and commercialization activities in Europe and the royalty territory, including up-front license fees, milestone payments and royalties.

Unless terminated earlier in accordance with its terms, the collaboration agreement with Astellas expires (a) with respect to the royalty territory, on a country by-country basis, upon the latest to occur of: (i) the expiration of the last-to-expire valid claim of an AVEO patent or joint patent covering the composition of tivozanib, (ii) the expiration of the last-to-expire valid claim of an AVEO patent or joint patent covering the use of tivozanib, but only for so long as no generic competition exists in such country, and (iii) twelve years from first commercial sale of tivozanib in such country, and (b) with respect to North America and Europe as a whole, upon the expiration of all payment obligations between the parties related to development and commercialization of tivozanib in North America and Europe. After the second anniversary of the effective date of the collaboration agreement, Astellas has the right to terminate the collaboration agreement, in its entirety or solely with respect to the royalty territory, at any time upon 180 days prior written notice to us. Either party may terminate the collaboration agreement with respect to a specified territory or country as set forth in the collaboration agreement, if the other party fails to cure a material breach related to such territory or country, as applicable. We may also terminate the collaboration agreement in its entirety upon a patent-related challenge by Astellas, its affiliates or sublicensees, if such patent-related challenge is not withdrawn within 30 days following our notice to Astellas of such termination.

---

**Table of Contents**

We are accounting for the joint development and commercialization activities in North America and Europe as a joint risk sharing collaboration in accordance with Accounting Standards Codification, or ASC, 808 *Collaborative Arrangements*. In addition, these activities were not deemed to be separate deliverables under the agreement with Astellas.

Payments from Astellas with respect to Astellas' share of research and development costs incurred by us are recorded as a reduction to expense due to the joint risk sharing provisions of the agreement in North America and Europe. As a result of the cost-sharing provisions in our agreement with Astellas, we reduced research and development expense by \$26.7 million during the year ended December 31, 2011, and general and administrative expense by \$1.2 million during the year ended December 31, 2011. The net amount due to us from Astellas pursuant to the cost-sharing provisions is \$6.4 million at December 31, 2011.

Activities under the agreement with Astellas outside of the joint development and commercialization activities in North America and Europe were evaluated under ASC 605-25 *Revenue Recognition - Multiple Element Arrangements*, or ASC 605-25, to determine if they represented a multiple element revenue arrangement. The agreement with Astellas includes the following deliverables outside of the joint development and commercialization activities in North America and Europe: a co-exclusive license to develop and commercialize tivozanib in North America and Europe, a royalty-bearing license to develop and commercialize tivozanib in the royalty-bearing territory, which includes our obligation to provide access to clinical and regulatory information resulting from the activities in North America and Europe to Astellas for its development and commercialization of tivozanib in the royalty-bearing territory, and our obligation to supply clinical material to Astellas for development of tivozanib in the royalty-bearing territory. The co-exclusive license in North America and Europe is not sublicensable. Astellas has the right to sublicense the exclusive royalty-bearing license to develop tivozanib in the royalty-bearing territory. Our obligation to provide access to clinical and regulatory information as part of the royalty territory deliverable includes the obligation to provide access, upon request, to all clinical data, regulatory filings, safety data and manufacturing data to Astellas for use in the development of tivozanib in the royalty-bearing territory. The obligation to supply clinical material to Astellas for development in the royalty-bearing territory includes supplying such clinical material in accordance with current good manufacturing practices applicable to clinical materials and other relevant regulatory authority requirements, upon request, for the development of tivozanib in the royalty-bearing territory. All of these deliverables were deemed to have stand-alone value and to meet the criteria to be accounted for as separate units of accounting under ASC 605-25. ASC 605-25 establishes a selling price hierarchy for determining the selling price of a deliverable, which includes: (1) vendor-specific objective evidence if available; (2) third-party evidence if vendor-specific objective evidence is not available; and (3) estimated selling price if neither vendor-specific objective evidence nor third-party evidence is available. We allocated the up-front consideration of \$125 million to the deliverables based on our best estimate of selling price of each deliverable using the relative selling price method as we did not have vendor specific objective evidence or third party evidence for such deliverables. Our best estimate of selling price considered discounted cash flow models, the key assumptions of which included the market opportunity for commercialization of tivozanib in North America and Europe and in the royalty-bearing territory, the development costs and market opportunity for the expansion of tivozanib into other solid tumor types, and the time to commercialization of tivozanib for all potential oncology indications. We allocated \$120.2 million of the up-front consideration from Astellas to the co-exclusive license in North America and Europe and \$4.8 million of the up-front consideration from Astellas to the combined deliverable representing a royalty-bearing license to develop and commercialize tivozanib in the royalty-bearing territory along with our obligation to provide access to clinical and regulatory information resulting from the activities in North America and Europe to Astellas for its use in the royalty-bearing territory. The relative selling price for our obligation to supply clinical material to Astellas for development in the royalty-bearing territory had de minimus value.

We recorded the \$120.2 million relative selling price of the co-exclusive license granted in North America and Europe as collaboration revenue during the three months ended March 31, 2011 upon delivery of the license, and deferred approximately \$4.8 million of revenue representing the relative selling price of the royalty-bearing license to develop and commercialize tivozanib in the royalty-bearing territory along with our obligation to

---

**Table of Contents**

provide access to clinical and regulatory information resulting from the activities in North America and Europe to Astellas for its use in the royalty-bearing territory. We are recording the \$4.8 million ratably over our period of performance through April 2022, the remaining patent life of tivozanib. We estimated the period of performance considering that we plan to develop tivozanib with Astellas in several indications outside of RCC, including in breast cancer and colorectal cancer and potentially in other cancer indications. The clinical development of tivozanib in these indications is in earlier stages of development and, as a result, the clinical development timeline is uncertain and is expected to change as we obtain additional clinical data in these indications. As a result, we estimated the period of performance as the remaining patent life of tivozanib as it represents the longest period over which development of tivozanib could occur. We reassess the period of performance at each reporting period. We recorded approximately \$376,000 of revenue during the year ended December 31, 2011 associated with the royalty territory deliverable.

***Centocor Ortho Biotech***

In May 2011, we entered into an exclusive license agreement with Centocor for the worldwide development and commercialization of our internally-discovered antibodies targeting the RON receptor, including the grant to Centocor of an exclusive, worldwide license to our proprietary RON-driven tumor models. We also granted Centocor a nonexclusive, non-sublicensable, worldwide license to our proprietary list of human genes intended to predict correlation of response to RON-targeted antibodies, or our RON index. Centocor is responsible for all clinical development, manufacturing and commercialization activities and costs. Subject to an agreed-upon research plan and budget, Centocor will also fund certain research for a three-year term to be conducted by us, including translational research studies using our proprietary Human Response Platform to identify biomarkers for patients most likely to benefit from treatment with RON targeted antibodies.

In connection with the Centocor license agreement, we received a one-time cash payment in the amount of \$7.5 million and a separate equity investment in the amount of approximately \$7.5 million through the purchase by Johnson & Johnson Development Corporation, an affiliate of Centocor, of 438,340 newly issued shares of our common stock at a purchase price of \$17.11 per share. Centocor also agreed to fund certain research and development activities. Milestone payments for the successful development and commercialization of a RON-targeted antibody, if all approvals in multiple indications and all sales milestones are achieved, could total, in the aggregate, \$540 million, comprised of (i) up to \$40 million in substantive milestone payments upon achievement of specified clinical and development milestone events, (ii) up to \$165 million in substantive milestone payments upon achievement of specified regulatory milestone events in connection with specified regulatory filings, and receipt of marketing approvals, and (iii) up to \$335 million in milestone payments upon the achievement of specified sales events. We could earn the first clinical and development milestone of \$2.0 million under the Centocor license agreement upon the selection of a lead antibody for entry into pre-clinical studies, with respect to the first licensed product under the agreement. We expect to achieve this milestone during the year ending December 31, 2012. Upon commercialization, we are eligible to receive tiered double-digit royalty payments on Centocor's net sales of any RON-targeted antibody, as a percentage of net sales. Centocor's royalty obligations in a particular country begin on the date of first commercial sale of a product in that country, and end on the later of 10 years after the date of first commercial sale of the product in that country or the date of the last to expire of the issued patents covering the product in that country. All milestone payments and royalties will be reduced by a specified percentage if Centocor develops or commercializes a RON-targeted antibody which has incorporated significant, meaningful improvements made after a specified period by Centocor to the antibodies delivered by us. The royalties will also be reduced by a specified percentage on a country-by-country basis upon the entry of a generic competitor.

The Centocor license agreement will remain in effect until the expiration of all of Centocor's royalty obligations to us, determined on a product-by-product and country-by-country basis. Prior to the filing of an investigational new drug application with the FDA, or a similar application filed with another regulatory authority outside of the United States (which we refer to as IND submission), Centocor has the right to terminate the Centocor license agreement at will upon 90 days written notice to us. After IND submission, Centocor may



---

**Table of Contents**

terminate the Centocor license agreement at will upon 180 days written notice to us. Either party has the right to terminate the Centocor license agreement in connection with an insolvency event involving the other party or a material breach of the Centocor license agreement by the other party that remains uncured for a specified cure period. In the event that Centocor terminates the Centocor license agreement at will, or if we terminate the Centocor license agreement due to Centocor's material breach or insolvency, worldwide rights to the development, manufacture, and commercialization of RON-targeted antibodies revert back to us.

As noted above, Johnson & Johnson Development Corporation paid \$7.5 million for 438,340 shares of our common stock at a purchase price of \$17.11 per share, which reflected the average of the daily volume weighted average prices for our common stock for the 30 consecutive trading days ending on May 26, 2011. This weighted average sales price of \$17.11 per share resulted in a \$1.22 per share discount from the May 31, 2011 closing price of \$18.33 per share, or a discount of \$534,775 from the fair market value of the common stock on the effective date of the Centocor license agreement. We determined this transaction was not within the scope of ASC 605-25 and, accordingly, we recorded the sale of common stock to Johnson & Johnson Development Corporation at fair value based on the closing price of our stock on May 31, 2011 of \$18.33 per share.

The remaining activities under the Centocor license agreement were evaluated under ASC 605-25 to determine if they represented a multiple element revenue arrangement. We determined that the Centocor license agreement included the following deliverables:

Exclusive, sublicensable commercialization and development license related to RON antibodies;

Non-exclusive license to use our RON index; and

Our obligation to provide research services.

We determined that each deliverable had stand-alone value upon delivery and therefore represents a separate unit of accounting. Factors considered in this determination included, among other things, the subject of the licenses and the research and development and commercial capabilities of Centocor.

We excluded the fair value of the common stock purchased by Johnson & Johnson Development Corporation from the arrangement consideration to be allocated to the identified deliverables and allocated the remaining \$7.0 million of up-front consideration attributable to the deliverables based on the relative selling price method. We determined the estimated selling price for the license related to the RON antibodies and the license to the RON index based on management's best estimate of selling price as we did not have vendor-specific objective evidence or third-party evidence of selling price for those deliverables. In determining our best estimate of selling price for the RON license and the RON Index license, we considered market conditions as well as entity-specific factors, including those factors contemplated in negotiating the Centocor license agreement and internally developed revenue models. Our best estimate of selling price for the license related to the RON antibodies and license to the RON index considered discounted cash flow models, the key assumptions of which included the market opportunity for commercialization of a potential product candidate using the RON receptor worldwide, an estimate of costs related to phase 1, 2 and 3 clinical studies with certain multiplication factors related to the probability of success, and the time to commercialization of a potential product candidate. This analysis used various assumptions that are typical for similarly staged monoclonal antibodies and other cost assumptions we believed to be reasonable in determining research and development, and sales, general and administrative costs. More specifically, our estimate of peak revenues was consistent with what might be expected from an approved antibody product. Other key assumptions included: cost of goods sold, which was assumed to be a specified percentage of revenues based on estimated cost of goods sold of a typical oncology antibody product; clinical trial costs, which were based on estimated clinical costs for a single phase 1 safety study, followed by phase 2 and 3 studies for a single oncology indication; and sales and marketing costs, which were based on the costs required to field an oncology sales force and marketing group, including external costs required to promote an oncology product. The factors used to estimate the probability of success and the time to commercialization of a product candidate were based on standard industry averages for antibodies being

## **Table of Contents**

developed for oncology indications. The results of our analysis indicated an estimated selling price for the licenses of approximately \$39 million. The analysis used a weighted average cost of capital of 15% derived from returns on equity for comparable companies.

With respect to the research services, we considered the nature of the research services to be provided (basic translational research related to a pre-clinical, antibody-based technology) and the fact that other vendors could provide the research services. As a result, we concluded that third party evidence of selling price exists for the research services deliverable. In supporting third party evidence of selling price, we considered the nature of the research services, the rates charged by vendors in the marketplace for similar services and rates charged by us for other non-complex, pre-clinical research services in our other license and development agreements.

As the relative selling price of the license related to the RON antibodies and license to the RON index (the delivered items) exceeds the up-front consideration attributable to the deliverables of \$7.0 million, the entire up-front payment was recognized as revenue upon delivery of the licenses during the three months ended June 30, 2011. We concluded that a change in the assumptions used to determine estimated selling price for the units of accounting would not have a significant effect on the allocation of arrangement consideration.

We will record revenue related to research and development services as the services are delivered at the contractual rate, which approximates fair value for those services.

We may be entitled to receive future milestone payments totaling \$540 million. We have elected to recognize all milestone payments as revenue once the milestones have been triggered if the milestone is deemed to be substantive. We believe the clinical and development, and regulatory milestones that may be received under the Centocor license agreement are consistent with the definition of a milestone included in ASU 2010-17, *Revenue Recognition - Milestone Method*, or ASU 2010-17, and, accordingly, we will recognize payments related to the achievement of such milestones, if any, as revenue when such milestone is achieved. Factors considered in this determination included scientific and regulatory risks that must be overcome to achieve each milestone, the level of effort and investment required to achieve each milestone, and the monetary value attributed to each milestone.

We did not recognize any milestone payments under this arrangement during the year ended December 31, 2011.

### ***OSI Pharmaceuticals***

In September 2007, we entered into a collaboration and license agreement with OSI Pharmaceuticals, Inc., (a wholly-owned subsidiary of Astellas US Holding Inc., a holding company owned by Astellas Pharma Inc.) or OSI. This strategic partnership is primarily focused on the identification and validation of genes and targets involved in the processes of epithelial-mesenchymal transition or mesenchymal-epithelial transition, in cancer. The research program portion of our strategic partnership with OSI, which concluded in June 2011, focused on the development of proprietary target-driven tumor models for use in target validation, drug screening and biomarker identification to support OSI's drug discovery and development activities. In connection with the terms of our agreement, OSI elected to obtain exclusive rights, with the right to grant sublicenses, under certain aspects of our intellectual property, to research, develop, make, sell and import drug products and associated diagnostics directed to 16 targets identified and/or validated under the agreement. OSI has sole responsibility and is required to use commercially reasonable efforts to develop and commercialize drugs and associated diagnostics directed to the targets to which it has obtained rights. In July 2009, we expanded our strategic partnership with OSI and we granted OSI a non-exclusive license to use our proprietary bioinformatics platform, and non-exclusive, perpetual licenses to use bioinformatics data and to use a proprietary gene index related to a specific target pathway. Further, as part of our expanded strategic partnership, we granted OSI an option to receive non-exclusive perpetual rights to certain elements of our Human Response Platform, including the right to obtain certain of our tumor models and tumor archives.

---

**Table of Contents**

In September 2007, OSI paid us an up-front payment of \$7.5 million, which was recorded in deferred revenue and was amortized over our period of substantial involvement, which ended in July 2011. OSI also paid us \$2.5 million for the first year of research program funding, which was recorded in deferred revenue and was recognized as revenue over the performance period and, thereafter, made sponsored research payments of \$625,000 per quarter through July 2009. In addition, OSI purchased 1,833,334 shares of our series C convertible preferred stock, at a per share price of \$3.00, resulting in gross proceeds to us of \$5.5 million. We determined that the price paid of \$3.00 per share by OSI represented a premium of \$0.50 over the price per share for shares of our series D convertible preferred stock sold in April 2007; accordingly, we recognized the premium of \$917,000 as additional license revenue on a straight-line basis over the period of substantial involvement. In connection with the initial public offering we consummated in March 2010 and the related 1:4 reverse stock split of our common stock, each four shares of outstanding series C convertible preferred stock were converted into one share of common stock.

In July 2009 under the amended agreement, OSI paid us an up-front payment of \$5.0 million, which was recorded in deferred revenue and was amortized over our remaining period of substantial involvement, which ended in July 2011. OSI also agreed to fund research costs through June 30, 2011. In addition, OSI purchased 3,750,000 shares of our series E convertible preferred stock at a per share price of \$4.00, resulting in gross proceeds to us of \$15.0 million. We determined that the price of \$4.00 per share paid by OSI represented a premium of \$1.04 per share over the fair value of the series E convertible preferred stock of \$2.96 as calculated by us in our retrospective stock valuation; accordingly, we recognized the premium of \$3.9 million as additional license revenue on a straight-line basis over the period of substantial involvement, which ended in July 2011. In connection with the initial public offering we consummated in March 2010 and the related 1:4 reverse stock split of our common stock, each four shares of outstanding series E convertible preferred stock were converted into one share of common stock.

In November 2010, OSI exercised its option under the July 2009 expansion of the agreement to license certain elements of our proprietary technology platform, including components of the Human Response Platform for the identification/characterization of novel epithelial-mesenchymal transition agents and proprietary patient selection biomarkers, in support of OSI's clinical development programs. We did not consider the option granted to OSI in July 2009 as a deliverable as there was significant uncertainty that this option would ultimately be exercised. In connection with the exercise of the option, OSI was obligated to pay us \$25 million in license expansion fees. We received \$12.5 million upon delivery of the notice of option exercise, and we received the remaining \$12.5 million in July 2011 in connection with the successful transfer of the applicable technology. We deferred the initial \$12.5 million payment, and recognized the full \$25 million relating to the option exercise by OSI over the period of substantial involvement, which ended in July 2011.

Under the July 2009 expanded agreement, if all applicable milestones are achieved, payments for the successful achievement of discovery, development and commercialization milestones under the agreement could total, in the aggregate, over \$94.0 million for each target and its associated products, comprised of (i) up to \$17.6 million in substantive milestone payments upon achievement of specified clinical and development milestone events, (ii) up to \$41.3 million in substantive milestone payments upon achievement of specified regulatory milestone events, (iii) up to \$35.0 million in milestone payments upon the achievement of specified sales events, and (iv) up to \$250,000 in patent related milestones. The first milestone we may receive pursuant to this agreement is either a patent related milestone of \$250,000 upon filing of a patent application, or a clinical and development milestone of \$750,000 for commencement of GLP toxicology studies. The timing of these milestones is uncertain.

In March 2011, we earned \$1.5 million related to deliverables and research milestones under the agreement. In addition, we are eligible to receive up to \$24.0 million in biomarker related milestones. Upon commercialization of products which were part of the research program under the agreement, we are eligible to receive tiered royalty payments on sales of products by OSI, its affiliates and sublicensees. All milestones earned to date are for selection of targets, delivery of models, delivery of tumor archives or delivery of cell lines. These milestones are not considered to be substantive and at risk, therefore, the milestone payments were deferred and

---

**Table of Contents**

were recognized on a straight-line basis over the remaining estimated period of substantial involvement, which ended in July 2011. The next regulatory milestone we may receive pursuant to this agreement is \$7.0 million to be achieved for the filing of the NDA with the FDA. We do not expect to achieve this milestone in the year ending December 31, 2012. Upon commercialization of products which were part of the research program under the agreement, we are eligible to receive tiered royalty payments on sales of products by OSI, its affiliates and sublicensees. All milestones earned to date are for selection of targets, delivery of models or delivery of cell lines.

We believe the application of the provisions of ASU 2009-13 to this arrangement would not change the units of accounting under the arrangement or the manner in which we recognize revenue for the arrangement.

***Biogen Idec***

In March 2009, we entered into an exclusive option and license agreement with Biogen Idec International GmbH, a subsidiary of Biogen Idec Inc., which we collectively refer to herein as Biogen Idec, regarding the development and commercialization of our discovery-stage ErbB3-targeted antibodies for the potential treatment and diagnosis of cancer and other diseases outside of the United States, Canada and Mexico. Under the agreement, we are responsible for developing ErbB3 antibodies through completion of the first phase 2 clinical trial designed in a manner that, if successful, will generate data sufficient to support advancement to a phase 3 clinical trial. Within a specified time period after we complete this phase 2 clinical trial and deliver to Biogen Idec a detailed data package containing the results thereof, Biogen Idec may elect to obtain (1) a co-exclusive (with us), worldwide license, including the right to grant sublicenses, under our relevant intellectual property to develop and manufacture ErbB3 antibody products, and (2) an exclusive license, including the right to grant sublicenses, under our relevant intellectual property, to commercialize ErbB3 antibody products in all countries in the world other than the United States, Canada and Mexico. We retain the exclusive right to commercialize ErbB3 antibody products in the United States, Canada and Mexico.

We account for the Biogen Idec arrangement pursuant to ASC 605-25. The deliverables under the arrangement include an option for a co-exclusive, world-wide license to develop and manufacture ErbB3 antibody products and an option for an exclusive license to commercialize ErbB3 antibody products in all countries in the world other than the United States, Canada and Mexico. We determined that these deliverables did not have standalone value due to the fact that the program was still in preclinical development and required our experience to advance development of the product. As such, we determined that the agreement should be accounted for as one unit of accounting.

Under the terms of the agreement, Biogen Idec paid us an upfront cash payment of \$5.0 million in March 2009, which is being amortized over our period of substantial involvement, defined as the patent life of the development candidate. In addition, Biogen Idec purchased 7,500,000 shares of series E convertible preferred stock at a per share price of \$4.00, resulting in gross proceeds to us of \$30.0 million. We determined that the price of \$4.00 paid by Biogen Idec represented a premium of \$1.09 per share over the fair value of the series E convertible preferred stock of \$2.91 as calculated by us in our retrospective stock valuation; accordingly, we are recognizing the premium of \$8.2 million as revenue on a straight-line basis over the period of substantial involvement. In connection with the initial public offering we consummated in March 2010 and the related 1:4 reverse stock split of our common stock, each four shares of outstanding series E convertible preferred stock were converted into one share of common stock.

In June 2009, we received a \$5.0 million milestone payment for achievement of the first pre-clinical discovery milestone under the agreement. Since the \$5.0 million milestone payment received in June 2009 was a near term milestone and not considered to be substantive, the revenue is being amortized as additional license revenue over our period of substantial involvement. We also earned a second \$5.0 million milestone payment upon selection of a development candidate in March 2010 and a third \$5.0 million milestone payment based on achieving the GLP toxicology initiation milestone in June 2011. These milestones were considered substantive and were included in revenue for the quarters ended March 31, 2010 and June 30, 2011, respectively. We could also receive an option exercise fee of \$5.0 million and regulatory milestone payments of up to \$45.0 million in

---

## **Table of Contents**

the aggregate if Biogen Idec exercises its option to obtain exclusive rights to commercialize ErbB3 antibody products in its territory. The first regulatory milestone we may receive pursuant to this agreement of \$25.0 million is due upon the receipt of the first regulatory approval of a licensed product from the EMA. We do not expect to achieve this milestone during the year ending December 31, 2012.

### ***Schering-Plough Corporation (now Merck)***

In March 2007, we entered into an agreement with Schering-Plough Corporation (now Merck & Co., Inc., or Merck), through its subsidiary Schering Corporation, acting through its Schering-Plough Research Institute division, under which we granted Merck exclusive, worldwide rights to develop and commercialize all of our monoclonal antibody antagonists of hepatocyte growth factor, or HGF, including ficlatuzumab, for therapeutic and prophylactic use in humans and for veterinary use. We also granted Merck an exclusive, worldwide license to related biomarkers for diagnostic use. Merck was responsible for all costs related to the clinical development of ficlatuzumab and clinical and commercial manufacturing.

As of December 27, 2010, the effective date of the termination of our collaboration with Merck relating to ficlatuzumab, we became responsible for all process development and all manufacturing of ficlatuzumab for future development and commercialization.

Under the agreement, Merck paid us an up-front payment of \$7.5 million in May 2007, which was being amortized over our period of substantial involvement, which was initially estimated to be through completion of the first phase 2 proof-of-concept trial for ficlatuzumab (which was expected to be the first half of 2012), but was adjusted to reflect the termination of the agreement effective on December 27, 2010. In addition, Merck purchased 4,000,000 shares of our series D convertible preferred stock, at a per share price of \$2.50, resulting in gross proceeds to us of \$10.0 million. The amount paid for the series D convertible preferred stock represented fair value as it was the same as the amounts paid by unrelated investors in March and April 2007. In connection with the initial public offering which we consummated in March 2010, and the related 1:4 reverse stock split of our common stock, each four shares of outstanding series D convertible preferred stock were converted into one share of common stock.

In June 2010, we earned and received an \$8.5 million milestone payment in connection with the enrollment of patients in our phase 2 clinical trial of ficlatuzumab under the agreement. Since the \$8.5 million milestone payment earned in June 2010 was considered substantive, it was included in revenue for the year ended December 31, 2010.

In March 2011, in connection with the transition of responsibility for the ficlatuzumab program from Merck back to us, we made a \$10.2 million payment to Merck for the purchase of a supply of ficlatuzumab to support ongoing clinical studies and have expensed such payment during the year ended December 31, 2011, as title passed to us.

## **Financial Overview**

### ***Revenue***

To date, we have not generated any revenue from product sales. All of our revenue to date has been derived from license fees, milestone payments, and research and development payments received from our strategic partners.

In the future, we may generate revenue from a combination of product sales, license fees, milestone payments and research and development payments in connection with strategic partnerships, and royalties resulting from the sales of products developed under licenses of our intellectual property. We expect that any revenue we generate will fluctuate from quarter to quarter as a result of the timing and amount of license fees, research and development reimbursements, milestone and other payments received under our strategic partnerships, and the amount and timing of payments that we receive upon the sale of our products, to the extent any are successfully commercialized. We do not expect to generate revenue from product sales until 2013 at the

---

**Table of Contents**

earliest. If we or our strategic partners fail to complete the development of our drug candidates in a timely manner or obtain regulatory approval for them, our ability to generate future revenue, and our results of operations and financial position, would be materially adversely affected.

***Research and Development Expenses***

Research and development expenses consist of expenses incurred in connection with the discovery and development of our product candidates. These expenses consist primarily of:

employee-related expenses, which include salaries and benefits;

expenses incurred under agreements with contract research organizations, investigative sites and consultants that conduct our clinical trials and a substantial portion of our preclinical studies;

the cost of acquiring and manufacturing clinical trial materials;

facilities, depreciation and other allocated expenses, which include direct and allocated expenses for rent and maintenance of facilities and equipment, and depreciation of fixed assets;

license fees for, and milestone payments related to, in-licensed products and technology;

stock-based compensation expense to employees and non-employees; and

costs associated with non-clinical activities, regulatory approvals and medical affairs.

We expense research and development costs as incurred. Nonrefundable advance payments for goods and services that will be used in future research and development activities are expensed when the activity has been performed or when the goods have been received rather than when the payment is made.

Research and development expenses are net of amounts reimbursed under our agreement with Astellas for Astellas' share of development costs incurred by us under our joint development plan with Astellas.

Conducting a significant amount of research and development is central to our business model. Product candidates in later stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later stage clinical trials. We plan to increase our research and development expenses for the foreseeable future as we seek to complete development of our most advanced product candidate, tivozanib, and to further advance ficlatuzumab and our earlier-stage research and development projects.

We track external development expenses and personnel expense on a program-by-program basis and allocate common expenses, such as scientific consultants and lab supplies, to each program based on the personnel resources allocated to such program. Facilities, depreciation, stock-based compensation, research and development management and research and development support services are not allocated and are considered overhead. Below is a summary of our research and development expenses for the years ended December 31, 2011, 2010 and 2009:

Years Ended December 31,		
2011	2010	2009

Edgar Filing: AVEO PHARMACEUTICALS INC - Form 10-K

	(in thousands)		
Tivozanib	\$ 48,158	\$ 52,653	\$ 23,399
Ficlatuzumab	24,165	9,855	6,498
AV-203 program	6,362	3,044	1,763
Platform collaborations	2,632	3,259	2,960
Antibody pipeline	6,653	6,044	5,523
Other research and development	1,367	1,299	2,358
Overhead	12,398	10,191	9,291
 Total research and development expenses	 \$ 101,735	 \$ 86,345	 \$ 51,792

---

**Table of Contents***Tivozanib*

In January 2012, we announced top-line data from our global, phase 3 clinical trial comparing the efficacy and safety of tivozanib with Nexavar, an approved therapy for first-line treatment in RCC, which we refer to as the TIVO-1 study. The TIVO-1 study is being conducted in patients with advanced clear cell RCC who have undergone a prior nephrectomy (kidney removal) and who have not received any prior VEGF-targeted therapy. We are also evaluating tivozanib in multiple phase 1 and phase 2 clinical trials including BATON-RCC, a phase 2 exploratory biomarker study in patients with advanced RCC which completed enrollment in early 2012, and BATON-CRC, a phase 2 clinical trial evaluating tivozanib in combination with mFOLFOX6 compared to Avastin in combination with mFOLFOX6 as first-line therapy in patients with advanced metastatic colorectal cancer, or CRC. Future research and development costs for the tivozanib program are not reasonably certain because such costs are dependent on a number of variables, including the cost and design of any additional clinical trials including additional trials in combination with other drugs and the timing of the regulatory process. We entered into a collaboration and license agreement with Astellas in February 2011, pursuant to which we and Astellas share responsibility for tivozanib, including expenses for continued development and commercialization of tivozanib, in North America and Europe. Astellas is responsible for continued development and commercialization of tivozanib outside of North America, Europe and Asia. All costs associated with each party's conduct of development and commercialization activities in North America and Europe, and any resulting profits or losses, are shared equally between the parties pursuant to a joint development plan. We have included \$26.7 million in research and development cost reimbursements as a reduction in tivozanib related expenses for the year ended December 31, 2011. Our current estimate for future costs related to our phase 3 clinical program is approximately \$23.0 million, excluding the effect of our cost sharing arrangement with Astellas. Upon entering into the license agreement with Astellas, we made a cash payment in the amount of \$5.0 million to KHK. In the first quarter of 2010, we paid KHK a \$10.0 million milestone in connection with the initiation of our phase 3 clinical trial of tivozanib. We may also be required to make up to an aggregate of \$50.0 million in milestone payments to KHK upon the achievement of specified regulatory milestones. Further, we are required to pay KHK tiered royalty payments on net sales we make of tivozanib in North America, which range from the low to mid-teens as a percentage of net sales. In connection with the execution of our collaboration agreement with Astellas, we paid KHK 30% of the license fee received from Astellas and are required to pay certain amounts we may receive from Astellas in connection with Astellas' development and commercialization activities outside of North America and Asia related to tivozanib, other than amounts we receive in respect of research and development funding or equity investments, subject to certain limitations. In the first quarter of 2011, we recorded \$22.5 million of expense for amounts owed to KHK related to the up-front license payment received under the collaboration agreement with Astellas.

*Ficlatuzumab*

In March 2007, we entered into a license agreement related to ficlatuzumab with Merck (formerly Schering-Plough) pursuant to which Merck was responsible for all expenses relating to development of ficlatuzumab in accordance with an agreed-upon budget. We recorded revenue and expenses on a gross basis under this arrangement. We have completed a phase 1 clinical trial of ficlatuzumab and completed enrollment of a phase 2 clinical trial. We earned an \$8.5 million milestone payment from Merck upon initiation of the phase 2 clinical trial in the second quarter of 2010. As of December 27, 2010, the date of termination of the collaboration agreement by Merck, we became responsible for the performance and funding of all future research, development, manufacturing and commercialization activities for ficlatuzumab. In connection with the transition of responsibility for the ficlatuzumab program, we purchased supply of ficlatuzumab from Merck for \$10.2 million to support ongoing clinical trials of ficlatuzumab. We have taken title to all of this material as of December 31, 2011 and, pursuant to the provisions of ASC 730, *Research and Development*, have recognized this amount as research and development expense during the year ended December 31, 2011. In November 2011, we entered into an agreement with Boehringer Ingelheim for large-scale process development and clinical manufacturing of ficlatuzumab. Boehringer Ingelheim will produce ficlatuzumab for clinical trials at its biopharmaceutical site in Fremont, California. We have retained all rights to the development and commercialization of ficlatuzumab. Due to the unpredictable nature of preclinical and clinical development, we are unable to estimate with any certainty the costs we will incur in the future development of the ficlatuzumab program.



---

## **Table of Contents**

### *AV-203: Anti-ErbB3 Antibody Program*

Our AV-203 program is focused on identifying inhibitors of ErbB3. In 2010, we nominated our lead development candidate, AV-203, which is currently in preclinical development. We have granted Biogen Idec an exclusive option to co-develop (with us) and commercialize our ErbB3-targeted antibodies for the potential treatment and diagnosis of cancer and other diseases outside of the United States, Canada and Mexico. Upon the selection of AV-203 as a development candidate in the first quarter of 2010, we earned a \$5.0 million milestone payment from Biogen Idec, and we earned an additional \$5.0 million milestone payment in June 2011 based on initiation of a GLP toxicology study. Through our discovery efforts, we have identified antibodies that have been shown to be potent and selective inhibitors of ErbB3 in preclinical studies. In preclinical testing, these antibodies have significantly inhibited the growth of a number of different tumors, including breast, prostate and pancreatic cancers. We have commenced manufacturing of our lead development candidate for human clinical trials. We anticipate initiating phase 1 development with AV-203 in 2012. Due to the unpredictable nature of preclinical and clinical development and given the early stage of this program, we are unable to estimate with any certainty the costs we will incur in the future development of any candidate identified from this program.

### *Platform Collaborations*

We have performed research services for OSI Pharmaceuticals using our Human Response Platform under a collaboration and license agreement with OSI that concluded in July 2011. The related expenses, including personnel and related expenses, are captured as a cost of the agreement with OSI Pharmaceuticals. Expenses incurred under the agreement with OSI Pharmaceuticals were fully supported by the revenue from that agreement. We also perform research services for Centocor under the Centocor license agreement. Centocor funds certain research for a three-year term, including translational research studies using our proprietary Human Response Platform to identify biomarkers for patients most likely to benefit from treatment with RON targeted antibodies. The related expenses are captured as a cost of the agreement with Centocor.

### *Antibody Pipeline*

We expect that the expenses related to our antibody pipeline will continue to increase as we seek to identify additional targets for preclinical research. Future research and development costs for our antibody pipeline are not reasonably certain because such costs are dependent on a number of variables, including the success of preclinical studies on these antibodies and the identification of other potential candidates across multiple oncology indications.

### *Other Research and Development*

Other research and development includes expenses related to our Human Response Platform, which is not specifically related to a particular product candidate or a specific strategic partnership, and in 2010 and 2009 included expenses related to AV-412, a product candidate for which we have decided not to pursue further development. AV-412 was the subject of a license agreement with Mitsubishi Pharma Corporation. We terminated the license agreement with Mitsubishi Pharma effective January 26, 2010. We do not expect to incur further costs for this product candidate.

### *Uncertainties of Estimates Related to Research and Development Expenses*

The process of conducting preclinical studies and clinical trials necessary to obtain FDA approval for each of our product candidates is costly and time consuming. The probability of success for each product candidate and clinical trial may be affected by a variety of factors, including, among others, the quality of the product candidate's early clinical data, investment in the program, competition, manufacturing capabilities and commercial viability.

At this time, we cannot reasonably estimate or know the nature, specific timing and estimated costs of the efforts that will be necessary to complete the remainder of the development of our product candidates, or the

## **Table of Contents**

period, if any, in which material net cash inflows may commence from our product candidates. This is due to the numerous risks and uncertainties associated with developing drugs, including the uncertainty of:

the progress and results of our clinical trials;

the scope, progress, results and costs of preclinical development, laboratory testing and clinical trials for any other product candidate;

the costs, timing and outcome of regulatory review of our product candidates;

our ability to establish and maintain strategic partnerships, the terms of those strategic partnerships and the success of those strategic partnerships, if any, including the timing and amount of payments that we might receive from strategic partners;

the emergence of competing technologies and products and other adverse market developments; and

the costs of preparing, filing and prosecuting patent applications and maintaining, enforcing and defending intellectual property-related claims.

As a result of the uncertainties discussed above, we are unable to determine the duration and completion costs of current or future clinical stages of our product candidates (except for the estimates we have made for the cost of our phase 3 clinical trial of tivozanib) or when, or to what extent, we will generate revenues from the commercialization and sale of any of our product candidates. Development timelines, probability of success and development costs vary widely. We anticipate that we will make determinations as to which additional programs to pursue and how much funding to direct to each program on an ongoing basis in response to the scientific and clinical success of each product candidate, as well as ongoing assessment of the product candidate's commercial potential. We plan to develop additional product candidates internally which will significantly increase our research and development expenses in future periods. We will need to raise additional capital in the future in order to commercialize tivozanib and to fund the development of ficlatuzumab, AV-203 and our other product candidates.

### ***General and Administrative Expenses***

General and administrative expenses consist principally of salaries and related costs for personnel in executive, finance, business development, marketing, information technology, legal and human resources functions. Other general and administrative expenses include facility costs not otherwise included in research and development expenses, patent filing, prosecution and defense costs and professional fees for legal, consulting, pre-commercialization activities, auditing and tax services.

We anticipate that our general and administrative expenses will increase for, among others, the following reasons:

the need to support our research and development activities, which we expect to expand as we continue the development of our product candidates;

we incur expenses related to the anticipated commercial launch of tivozanib before we receive regulatory approval, including expanding our commercial infrastructure; and

as a result of increased payroll, and higher consulting, legal and accounting costs associated with the anticipated commercial launch of tivozanib.

*Interest Income and Interest Expense*

Interest income consists of interest earned on our cash, cash equivalents and marketable securities. The primary objective of our investment policy is capital preservation.

Interest expense consists primarily of interest, amortization of debt discount, and amortization of deferred financing costs associated with our loans payable.

## **Table of Contents**

### ***Income Taxes***

We calculate our provision for income taxes on ordinary income based on our projected annual tax rate for the year. We recorded net income for the first time during the year ended December 31, 2011. We have utilized certain of our net operating loss carryforwards to offset taxable income, which resulted in an effective tax rate of 0% for the year ended December 31, 2011. As such, we have not recorded an income tax provision for the year ended December 31, 2011.

### **Critical Accounting Policies and Significant Judgments and Estimates**

Our discussion and analysis of our financial condition and results of operations are based on our condensed consolidated financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States. The preparation of these financial statements requires us to make estimates and judgments that affect the reported amounts of assets, liabilities, revenues and expenses and the disclosure of contingent assets and liabilities in our financial statements. On an ongoing basis, we evaluate our estimates and judgments, including those related to revenue recognition, accrued clinical expenses, and stock-based compensation. We base our estimates on historical experience, known trends and events and various other factors that are believed 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 from these estimates under different assumptions or conditions.

Our significant accounting policies are described in more detail in the notes to our consolidated financial statements appearing elsewhere in this report. We believe the following accounting policies to be most critical to the judgments and estimates used in the preparation of our consolidated financial statements.

### ***Revenue Recognition***

Our revenues are generated primarily through collaborative research, development and commercialization agreements. The terms of these agreements generally contain multiple elements, or deliverables, which may include (i) licenses, or options to obtain licenses, to our technology, (ii) research and development activities to be performed on behalf of the collaborative partner and (iii) in certain cases, services in connection with the manufacturing of pre-clinical and clinical material. Payments to us under these arrangements typically include one or more of the following: non-refundable, up-front license fees; option exercise fees; funding of research and/or development efforts; milestone payments; and royalties on future product sales.

We exercise our judgment in determining whether an agreement contains multiple elements and, if so, how much revenue is allocable to each element. In addition, we exercise our judgment in determining when our significant obligations have been met under such agreements and the specific time periods over which we recognize revenue, such as non-refundable, up-front license fees and other payments. To the extent that actual facts and circumstances differ from our initial judgments, our revenue recognition with respect to such transactions would change accordingly and any such change could affect our reported operating results.

Effective January 1, 2011, we adopted ASU 2009-13, which amends ASC 605-25. When evaluating multiple element arrangements in accordance with ASC 602-25, as amended by ASU 2009-13, we consider whether the deliverables under the arrangement represent separate units of accounting. This evaluation requires subjective determinations and requires management to make judgments about the individual deliverables and whether such deliverables are separable from the other aspects of the contractual relationship. In determining the units of accounting, management evaluates certain criteria, including whether the deliverables have standalone value, based on the consideration of the relevant facts and circumstances for each arrangement. The consideration received is allocated among the separate units of accounting using the relative selling price method, and the applicable revenue recognition criteria are applied to each of the separate units.

---

**Table of Contents**

We determine the estimated selling price for deliverables within each agreement using vendor-specific objective evidence, or VSOE, of selling price, if available, third-party evidence, or TPE, of selling price if VSOE is not available, or best estimate of selling price if neither VSOE nor TPE is available. Determining the best estimate of selling price for a deliverable requires significant judgment. We typically use best estimate of selling price to estimate the selling price for licenses to our proprietary technology, since we often do not have VSOE or TPE of selling price for these deliverables. In those circumstances where we utilize best estimate of selling price to determine the estimated selling price of a license to our proprietary technology, we consider market conditions as well as entity-specific factors, including those factors contemplated in negotiating the agreements as well as internally developed models that include assumptions related to the market opportunity, estimated development costs, probability of success and the time needed to commercialize a product candidate pursuant to the license. In validating our best estimate of selling price, we evaluate whether changes in the key assumptions used to determine the best estimate of selling price will have a significant effect on the allocation of arrangement consideration between multiple deliverables.

We typically receive up-front, non-refundable payments when licensing our intellectual property in conjunction with a research and development agreement. When management believes the license to our intellectual property has stand-alone value, we generally recognize revenue attributed to the license upon delivery. When management believes the license to our intellectual property does not have stand-alone value from the other deliverables to be provided in the arrangement, we generally recognize revenue attributed to the license on a straight-line basis over our contractual or estimated performance period, which is typically the term of our research and development obligations. If management cannot reasonably estimate when our performance obligation ends, then revenue is deferred until management can reasonably estimate when the performance obligation ends. The periods over which revenue should be recognized are subject to estimates by management and may change over the course of the research and development agreement. Such a change could have a material impact on the amount of revenue we record in future periods.

Payments or reimbursements resulting from our research and development efforts for those arrangements where such efforts are considered as deliverables are recognized as the services are performed and are presented on a gross basis so long as there is persuasive evidence of an arrangement, the fee is fixed or determinable, and collection of the related receivable is reasonably assured. Amounts received prior to satisfying the above revenue recognition criteria are recorded as deferred revenue in the accompanying balance sheets.

In addition, effective January 1, 2011, we adopted ASU 2010-17. Under ASU 2010-17, at the inception of each agreement that includes milestone payments, we evaluate whether each milestone is substantive on the basis of the contingent nature of the milestone. This evaluation includes an assessment of whether (a) the consideration is commensurate with either (1) the entity's performance to achieve the milestone, or (2) the enhancement of the value of the delivered item(s) as a result of a specific outcome resulting from the entity's performance to achieve the milestone, (b) the consideration relates solely to past performance and (c) the consideration is reasonable relative to all of the deliverables and payment terms within the arrangement. We evaluate factors such as the scientific, regulatory, commercial and other risks that must be overcome to achieve the respective milestone, the level of effort and investment required to achieve the respective milestone and whether the milestone consideration is reasonable relative to all deliverables and payment terms in the arrangement in making this assessment. We aggregate our milestones into four categories: (i) clinical and development milestones, (ii) regulatory milestones, (iii) commercial milestones, and (iv) patent related milestones. We have concluded that the clinical and development, regulatory and patent related milestones pursuant to our research and development arrangements are substantive.

Clinical and development milestones are typically payable when a product candidate advances into a defined phase of clinical research or completes such phase. For example, a milestone may be due upon the initiation of the phase 3 clinical trial in a new indication, the last phase of clinical development, which if the product candidate is proven to be safe and effective, may lead to ultimate marketing approval by the FDA or other global regulatory authorities. Regulatory milestones are typically payable upon acceptance of the

---

## **Table of Contents**

submission for marketing approval of a product candidate or upon approval to market the product candidate by the FDA or other global regulatory authorities. For example, a milestone may be due to us upon the FDA's acceptance of an NDA. Commercial milestones are typically payable when an approved pharmaceutical product reaches certain defined levels of net sales by the licensee. For example, when a product first achieves global sales of a specified amount, or when a product first achieves annual sales of a specified amount. Patent related milestones are typically payable when a patent application is filed or issued with respect to certain intellectual property related to the applicable collaboration.

Revenues from clinical and development, regulatory and patent related milestones, if they are nonrefundable and deemed substantive, are recognized upon successful accomplishment of the milestones. Milestones that are not considered substantive are accounted for as license payments and recognized on a straight-line basis over the remaining period of performance. Commercial milestones are accounted for similar to royalties and are recorded as revenue upon achievement of the milestone, assuming all other revenue recognition criteria are met.

### ***Accrued Clinical Expenses***

As part of the process of preparing our financial statements, we are required to estimate our accrued expenses. This process involves reviewing open contracts and purchase orders, communicating with our applicable personnel to identify services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of actual cost. The majority of our service providers invoice us monthly in arrears for services performed. We make estimates of our accrued expenses as of each balance sheet date in our financial statements based on facts and circumstances known to us at that time. We periodically confirm the accuracy of our estimates with the service providers and make adjustments if necessary. Examples of estimated accrued clinical expenses include:

fees paid to contract research organizations in connection with clinical studies;

fees paid to investigative sites in connection with clinical studies;

fees paid to contract manufacturers in connection with the production of clinical trial materials; and

fees paid to vendors in connection with preclinical development activities.

We base our expenses related to clinical studies on our estimates of the services received and efforts expended pursuant to contracts with multiple research institutions and contract research organizations that conduct and manage clinical studies on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. Payments under some of these contracts depend on factors such as the successful enrollment of patients and the completion of clinical trial milestones. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from our estimate, we adjust the accrual accordingly. Although we do not expect our estimates to be materially different from amounts actually incurred, our understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and may result in us reporting amounts that are too high or too low in any particular period. Based on our level of clinical trial expenses as of December 31, 2011, if our estimates are too high or too low by 5%, this may result in an adjustment to our accrued clinical trial expenses in future periods of approximately \$337,000.

### ***Stock-Based Compensation***

We apply the fair value recognition provisions of ASC 718, *Accounting for Stock Based Compensation*, which we refer to as ASC 718, to our share-based payment awards. All awards granted are recognized in our statements of operations on a straight-line basis over the requisite service periods based on their grant date fair values as calculated using the measurement and recognition provisions of ASC 718. All stock-based awards

**Table of Contents**

granted to non-employees are accounted for at their fair value in accordance with ASC 718 and ASC 505, *Accounting for Equity Instruments that are Issued to Other Than Employees for Acquiring, or in Conjunction with Selling, Goods or Services*, under which compensation expense is generally recognized over the vesting period of the award. Determining the amount of stock-based compensation to be recorded requires us to develop estimates of fair values of stock options as of the grant date. Calculating the fair value of stock-based awards requires that we make highly subjective assumptions. We use the Black-Scholes option pricing model to value our stock option and restricted stock awards. Our expected stock price volatility is based on an average of several peer companies. We utilized a weighted average method of using our own volatility data for the quarters that we have been public, along with data we obtained from our peer companies. For purposes of identifying peer companies, we considered characteristics such as industry, length of trading history, similar vesting terms and in-the-money option status. For periods prior to 2009, we used an average of several peer companies with the characteristics described above to calculate our expected term given our limited history. For 2009 and for all periods thereafter, due to lack of available quarterly data for these peer companies, we elected to use the simplified method for plain vanilla options to estimate the expected term of the stock option grants. Under this approach, the weighted-average expected life is presumed to be the average of the vesting term and the contractual term of the option. We utilize a dividend yield of zero based on the fact that we have never paid cash dividends and have no present intention to pay cash dividends. The risk-free interest rate used for each grant is based on the U.S. Treasury yield curve in effect at the time of grant for instruments with a similar expected life.

During the years ended December 31, 2011, 2010 and 2009, respectively, the assumptions used in the Black-Scholes pricing model for new grants were as follows:

	<b>Years Ended December 31,</b>		
	<b>2011</b>	<b>2010</b>	<b>2009</b>
Volatility	64.37%-65.56%	63.92%-66.81%	70.35%-72.04%
Expected Term (in years)	5.50-6.25	5.50-6.25	5.50-6.25
Risk-Free Interest Rates	1.09%-2.57%	1.59%-2.92%	1.98%-3.04%
Dividend Yield			

We recognized stock-based compensation expense of approximately \$5.9 million, \$4.1 million and \$2.4 million for the years ended December 31, 2011, 2010, and 2009, respectively, in accordance with ASC 718. As of December 31, 2011, we had approximately \$9.6 million of total unrecognized stock-based compensation expense related to stock options granted under our 2002 Stock Incentive Plan and 2010 Stock Incentive Plan, net of related forfeiture estimates, which we expect to recognize over a weighted-average period of approximately 2.7 years.

As of December 31, 2011, there was \$0.3 million of total unrecognized stock-based compensation expense related to restricted stock awards granted under our 2002 Stock Incentive Plan and 2010 Stock Incentive Plan. We expect to recognize the expense over a weighted-average period of 0.6 years.

Under ASC 718, we are also required to estimate the level of forfeitures expected to occur and record compensation expense only for those awards that we ultimately expect will vest. We have performed a historical analysis of option awards that were forfeited prior to vesting and recorded total stock option expense that reflected this estimated forfeiture rate.

We have historically granted stock options at exercise prices not less than the fair market value of our common stock. Prior to our initial public offering in March 2010, the fair value of our common stock was determined by our board of directors, with input from management, as there was no public market for our common stock at that time. Prior to our initial public offering, our board of directors had historically determined the estimated fair value of our common stock on the date of grant based on a number of objective and subjective factors, including external market conditions affecting the biotechnology industry sector, the prices at which we sold shares of convertible preferred stock, the superior rights and preferences of securities senior to our common

**Table of Contents**

stock at the time of each grant, the results of operations, financial position, status of our research and development efforts, our stage of development and business strategy and the likelihood of achieving a liquidity event such as an initial public offering, or IPO, or sale of our company.

Our valuation models used the Market Approach and the Probability Weighted Expected Return Method as outlined in the AICPA Technical Practice Aid, *Valuation of Privately-Held-Company Equity Securities Issued as Compensation*, or Practice Aid. The exercise prices for stock options granted were determined by the results of our contemporaneous valuations completed in November 2008, January 2009, March 2009, June 2009, September 2009, December 2009 and January 2010, respectively.

In connection with the preparation of the consolidated financial statements for the year ended December 31, 2009 and in preparing for an IPO, we reexamined the contemporaneous valuations of our common stock during the period November 2008 to September 2009 to support the fair value of our common stock prior to our initial public offering.

**Results of Operations****Comparison of Years Ended December 31, 2011 and 2010**

The following tables summarize the results of our operations for each of the years ended December 31, 2011 and 2010, together with the changes in those items in dollars and as a percentage:

	Years Ended December 31,		Increase/ (decrease)	%
	2011	2010	(in thousands)	
Revenue	\$ 164,849	\$ 44,682	\$ 120,167	269%
Operating expenses:				
Research and development	101,735	86,345	15,390	18%
General and administrative	29,167	14,763	14,404	98%
Total operating expenses	130,902	101,108	29,794	29%
Income (loss) from operations	33,947	(56,426)	90,373	(160)%
Other income, net	10	900	(890)	(99)%
Interest expense	(3,836)	(3,389)	(447)	13%
Interest income	527	126	401	318%
Net income (loss)	\$ 30,648	\$ (58,789)	\$ 89,437	(152)%

	Years Ended December 31,		Increase/ (decrease)	%
	2011	2010	(in thousands)	
Revenue				
Strategic Partner:				
Astellas	\$ 120,576		\$ 120,576	
OSI	29,576	\$ 16,186	13,390	83%
Centocor	8,810		8,810	
Biogen Idec	5,863	5,757	106	2%
Merck		22,561	(22,561)	(100)%
Other	24	178	(154)	(87)%
	\$ 164,849	\$ 44,682	\$ 120,167	269%





---

**Table of Contents**

**Revenue.** Revenue for the year ended December 31, 2011 was \$164.8 million compared to \$44.7 million for the year ended December 31, 2010, an increase of approximately \$120.2 million, or 269%. The increase is primarily attributable to \$120.6 million in revenue recognized in connection with our agreement with Astellas; an increase of \$13.4 million in revenue from OSI primarily related to the recognition of revenue related to OSI's option exercise in November 2010 under our research and license agreement; \$7.0 million in revenue recognized in connection with the up-front license payment from Centocor related to the RON program; and \$1.8 million in research and development funding from Centocor. These increases were partially offset by a decrease of \$22.6 million in revenue earned under our license agreement with Merck due to its termination in December 2010.

**Research and development.** Research and development expenses for the year ended December 31, 2011 were \$101.7 million compared to \$86.3 million for the year ended December 31, 2010, an increase of \$15.4 million, or 18%. The increase is primarily attributable to a \$13.1 million increase in contract manufacturing costs primarily due to a \$10.2 million payment to Merck for the purchase of a supply of ficlatuzumab to support ongoing clinical studies; a net increase in licensing costs of \$12.6 million resulting primarily from a \$22.5 million sublicense revenue payment to KHK related to the up-front license payment received under our agreement with Astellas during the first quarter of 2011, compared to a \$10.0 million milestone payment to KHK in connection with the initial dosing of patients in our phase 3 clinical trial of tivozanib during the same period last year; a \$7.5 million increase in salaries, benefits and contract labor primarily due to an increase in personnel hired to support development activities for tivozanib; a \$3.7 million increase in outsourcing costs primarily related to an increase in medical affairs activities related to tivozanib, as well as an increase in development costs related to ficlatuzumab and AV-203; a \$1.4 million increase in clinical trial costs primarily related to an increase in ficlatuzumab clinical trial costs, partially offset by a decrease in clinical trial costs related to tivozanib; an increase of \$1.3 million in consulting costs primarily related to the development of tivozanib; a \$1.0 million increase in facility costs primarily due to our expansion to an additional location at 12 Emily Street; a \$0.7 million increase in stock-based compensation; and an increase in travel expenses of \$0.6 million primarily due to an increase in personnel. These increases were partially offset by the net reimbursement of \$26.7 million of tivozanib development costs pursuant to our agreement with Astellas.

Included in research and development expenses were stock-based compensation expenses of approximately \$2.5 million and \$1.8 million for the years ended December 31, 2011 and 2010, respectively.

**General and administrative.** General and administrative expenses for the year ended December 31, 2011 were \$29.2 million compared to \$14.8 million for the year ended December 31, 2010, an increase of \$14.4 million, or 98%. The increase is primarily the result of a \$4.25 million payment to a financial advisor in connection with the consummation of our agreement with Astellas; an increase of \$3.6 million in salaries and benefits primarily due to an overall increase in personnel hired to support our pre-commercialization activities for tivozanib as well as an increase in hiring to support our growth of operations; an increase of \$2.4 million for pre-commercialization activities for tivozanib; an increase of \$1.2 million in consulting costs and other outsourced costs due to a growth of the business; a \$1.1 million increase in stock-based compensation expense; a \$1.1 million increase in legal costs incurred primarily due to patent prosecution and trademark costs and advice related to the collaboration agreement with Astellas; an increase of \$0.9 million for recruiting and relocation costs due to an overall increase in hiring; and an increase of \$0.5 million in facility costs due to an increase in personnel and our expansion to an additional location at 12 Emily Street. These increases were partially offset by the net reimbursement of \$1.2 million of tivozanib commercialization costs pursuant to our agreement with Astellas.

Included in general and administrative expenses were stock-based compensation expenses of approximately \$3.4 million and \$2.3 million for the years ended December 31, 2011 and 2010, respectively.

**Other income, net.** Other income, net for the year ended December 31, 2011 was \$10,000 compared to \$900,000 for the year ended December 31, 2010, a decrease of \$890,000, or 99%. The income for the year ended December 31, 2010 was largely a result of income of \$0.7 million related to a decrease in the value of warrants to

**Table of Contents**

purchase preferred stock resulting from a decrease in the value of the underlying stock and income of \$0.7 million related to a qualifying therapeutic discovery grant from the Internal Revenue Service. There was no warrant valuation adjustment for the year ended December 31, 2011 as the warrants converted to warrants to purchase common stock in connection with our initial public offering in March 2010. The income for the year ended December 31, 2011 was primarily related to foreign currency exchange rates.

**Interest expense.** Interest expense for the year ended December 31, 2011 was \$3.8 million compared to \$3.4 million for the year ended December 31, 2010, an increase of \$0.4 million, or 13%. The increase in interest expense is due to the refinancing of our loan agreement with Hercules Technology Growth Capital Inc., or Hercules Technology Growth, and Comerica Bank, in May 2010, resulting in a higher average loan balance outstanding during the year ended December 31, 2011 compared to the year ended December 31, 2010.

**Interest income.** Interest income for the year ended December 31, 2011 was \$527,000 compared to \$126,000 for the year ended December 31, 2010, an increase of \$401,000, or 318%. The increase in interest income is primarily due to an overall higher average cash balance during the year ended December 31, 2011 compared to the year ended December 31, 2010.

**Comparison of Years Ended December 31, 2010 and 2009**

The following tables summarize the results of our operations for each of the years ended December 31, 2010 and 2009, together with the changes in those items in dollars and as a percentage:

	Years Ended December 31,		Increase/ (decrease)	%
	2010	2009	(in thousands)	
Revenue	\$ 44,682	\$ 20,719	\$ 23,963	116%
Operating expenses:				
Research and development	86,345	51,792	34,553	67%
General and administrative	14,763	10,120	4,643	46%
Total operating expenses	101,108	61,912	39,196	63%
Loss from operations	(56,426)	(41,193)	(15,233)	37%
Other income (expense), net	900	(333)	1,233	(370)%
Interest expense	(3,389)	(2,811)	(578)	21%
Interest income	126	144	(18)	(13)%
Net loss before benefit for income taxes	(58,789)	(44,193)	(14,596)	33%
Benefit for income taxes		100	(100)	(100)%
Net loss	\$ (58,789)	\$ (44,093)	\$ (14,696)	33%

	Years Ended December 31,		Increase/ (decrease)	%
	2010	2009	(in thousands)	
Revenue				
Strategic Partner:				
Merck	\$ 22,561	\$ 10,853	\$ 11,708	108%
OSI	16,186	9,788	6,398	65%
Biogen Idec	5,757		5,757	
Other	178	78	100	128%

\$ 44,682      \$ 20,719      \$ 23,963      116%

---

**Table of Contents**

**Revenue.** Revenue for the year ended December 31, 2010 was \$44.7 million compared to \$20.7 million for the year ended December 31, 2009, an increase of \$24.0 million, or 116%. The increase is attributable to a \$8.5 million milestone payment from Merck earned in May 2010 for commencing enrollment of patients in our phase 2 clinical trial of ficlatuzumab; an increase in amortization of deferred revenue associated with the amended OSI agreement in the amount of \$5.3 million, which includes \$3.6 million of revenue related to OSI's exercise of its option to license certain elements of our proprietary technology platform; a \$5.0 million milestone payment from Biogen Idec earned in March 2010 for selection of the development candidate for our AV-203 program; additional research and development funding from Merck related to ficlatuzumab in the amount of \$2.1 million; an increase in research revenue earned under the OSI agreement of \$1.1 million; an increase in amortization of previously deferred revenue related to the cancellation of the license agreement with Merck related to ficlatuzumab of \$1.1 million; and an increase of \$0.8 million associated with amortization of previously deferred Biogen Idec license revenue which began in the first quarter of 2010.

**Research and development.** Research and development expenses for the year ended December 31, 2010 were \$86.3 million compared to \$51.8 million for the year ended December 31, 2009, an increase of \$34.6 million, or 67%. The increase is primarily attributable to an increase in clinical trial costs of \$17.1 million resulting primarily from an increase in costs due to the phase 3 clinical trial of tivozanib, including an \$11.6 million purchase of Nexavar, the comparator drug for the clinical trial, partially offset by a reduction in costs of the phase 2 clinical trial of tivozanib as it winds down; an increase in licensing costs of \$10.2 million, resulting primarily from a \$10.0 million milestone payment to Kyowa Hakko Kirin in connection with the initial dosing of patients in our phase 3 clinical trial of tivozanib; a \$3.5 million increase in salaries and benefits mainly due to an increase in personnel primarily supporting development activities for tivozanib; a \$3.5 million increase in development costs related to ficlatuzumab, which were reimbursed by Merck but recorded on a gross basis; a \$1.5 million increase in contract manufacturing for tivozanib to support an increasing number of clinical trials; and a \$0.6 million increase in stock-based compensation expense. These increases were partially offset by a decrease of \$1.5 million for preclinical studies as we wind down certain preclinical activities primarily related to toxicology; a decrease in scientific advisory board fees of \$0.5 million; and a decrease of \$0.4 million for outsourcing costs due to timing of work performed on certain projects.

Included in research and development expenses were stock-based compensation expenses of approximately \$1.8 million and \$1.2 million for the years ended December 31, 2010 and 2009, respectively.

**General and administrative.** General and administrative expenses for the year ended December 31, 2010 were \$14.8 million compared to \$10.1 million for the year ended December 31, 2009, an increase of \$4.6 million or 46%. The increase is primarily the result of a \$1.1 million increase in stock-based compensation expense principally related to grants of annual individual performance options and milestone-based options to our officers in February 2010; a \$1.1 million increase in costs related to market development for tivozanib; an increase of \$1.0 million for costs related to being a public company, such as directors and officers liability insurance premiums, public relations, audit services, and an increase in board of directors' compensation; a \$0.6 million increase in salaries and benefits mainly due to an overall increase in hiring; an increase in recruiting and relocation costs of \$0.4 million due to our hiring of additional personnel; and an increase in legal fees of \$0.3 million.

Included in general and administrative expenses were stock-based compensation expenses of approximately \$2.3 million and \$1.1 million for the years ended December 31, 2010 and 2009, respectively.

**Other income (expense), net.** Other income (expense), net for the year ended December 31, 2010 was \$0.9 million compared to \$(0.3) million for the year ended December 31, 2009, an increase of \$1.2 million. The increase is principally due to income of \$0.7 million related to the decrease in the value of warrants to purchase preferred stock resulting from a decrease in value of the underlying stock and income of \$0.7 million related to a qualifying therapeutic discovery grant from the Internal Revenue Service. Other expense for the year ended December 31, 2009 resulted from a charge from the increase in the value of warrants to purchase preferred stock resulting from an increase in value of the underlying stock.

**Table of Contents**

**Interest expense.** Interest expense for the year ended December 31, 2010 was \$3.4 million compared to \$2.8 million for the year ended December 31, 2009, an increase of \$0.6 million or 21%. The increase is a result of our overall debt increasing in 2010 due to the refinancing of our outstanding debt with Hercules Technology Growth and Comerica Bank in May 2010.

**Interest income.** Interest income for the year ended December 31, 2010 was \$126,000 compared to \$144,000 for the year ended December 31, 2009, a decrease of \$18,000 or 13%. Although average cash balances were higher for the year ended December 31, 2010 compared to the same period in 2009, interest rates remained low at slightly above 0% in 2010, causing the decrease in interest income.

**Liquidity and Capital Resources**

We have funded our operations principally through the sale of equity securities sold in connection with our public offerings, private placements of equity securities, revenue and expense reimbursements from strategic partnerships, debt financing and interest income. As of December 31, 2011, we have received gross proceeds of \$89.7 million from the sale of common stock in our initial public offering, \$60.8 million from our private placement of shares of our common stock to a group of institutional and accredited investors, \$111.2 million from our follow-on offering of shares of our common stock, \$169.6 million from the sale of convertible preferred stock prior to becoming a public company, and \$7.5 million from the sale of common stock to Johnson & Johnson Development Corporation in connection with the Centocor license agreement. As of December 31, 2011, we had received an aggregate of \$311.2 million in cash from each of our three agreements with Merck and our agreements with OSI Pharmaceuticals, Biogen Idec, Astellas, Centocor and Eli Lilly, and \$25.0 million in funding from our debt financing with Hercules Technology Growth and certain of its affiliates. As of December 31, 2011, we had cash, cash equivalents and marketable securities of approximately \$275.4 million. Currently, our funds are invested in a money market fund, U.S. Government agency securities, a foreign government bond, an asset-backed security, and corporate debt securities, including commercial paper. The following table sets forth the primary sources and uses of cash for each of the periods set forth below:

	2011	Years Ended December 31, 2010 (in thousands)	2009
Net cash provided by (used in) operating activities	\$ 26,451	\$ (51,825)	\$ (9,973)
Net cash (used in) provided by investing activities	(144,103)	(90,506)	3,414
Net cash provided by financing activities	115,367	142,832	31,035
Net (decrease) increase in cash and cash equivalents	\$ (2,285)	\$ 501	\$ 24,476

During the years ended December 31, 2011, 2010 and 2009, our operating activities provided (used) cash of \$26.5 million, \$(51.8) million and \$(10.0) million, respectively. The cash provided by operations for the year ended December 31, 2011 was due primarily to our net income adjusted for non-cash items offset by a decrease in deferred revenue of \$12.2 million related to, in part, the recognition of previously deferred revenue related to our research and license agreement with OSI, as well as an increase in accounts receivable of \$6.8 million primarily due from Astellas for reimbursement of development expenses. The use of cash during the years ended December 31, 2010 and 2009, respectively, primarily resulted from our net losses adjusted for non-cash items. The cash used in operations for the year ended December 31, 2010 was due primarily to our net loss adjusted for non-cash items as well as a \$3.6 million increase in prepaid expenses primarily associated with advance payments for our clinical trials, and a decrease in deferred revenue of \$1.9 million related to the recognition of previously deferred revenue, offset by an increase in accounts payable and accrued expenses of \$4.5 million primarily related to development expenses. The cash used in operating activities for the year ended December 31, 2009 was primarily the result of our net loss adjusted for non-cash items and an increase in deferred revenue of \$22.0 million related to up-front license payments, near term milestones and equity premiums from our agreements with Biogen and OSI entered into in 2009, and an increase in accounts payable and accrued expenses

---

**Table of Contents**

of \$7.6 million primarily related to our phase 2 clinical trial of tivozanib and costs in preparation for our phase 3 clinical trial of tivozanib.

During the years ended December 31, 2011, 2010 and 2009, our investing activities (used) provided cash of \$(144.1) million, \$(90.5) million and \$3.4 million, respectively. The cash used in investing activities for the years ended December 31, 2011 and 2010 was primarily the net result of more purchases of marketable securities than the proceeds from maturities and sales, in addition to purchases of property and equipment of \$2.6 million, and \$1.7 million, respectively. The cash provided by investing activities for the year ended December 31, 2009 was primarily the result of fewer purchases of marketable securities than the proceeds from maturities and sales, in addition to purchases of property and equipment of \$1.7 million.

During the years ended December 31, 2011, 2010 and 2009, our financing activities provided \$115.4 million, \$142.8 million and \$31.0 million, respectively. The cash provided by financing activities for the year ended December 31, 2011 was primarily due to the sale and issuance of 6,352,119 shares of common stock at a price of \$17.50 per share in our follow-on public offering in June 2011 with net proceeds of \$104.2 million, the sale and issuance of 438,340 shares of common stock at a price of \$17.11 per share in connection with the Centocor license agreement, as well as stock option exercises of \$3.2 million. The cash provided by financing activities during the year ended December 31, 2010 was due to the sale and issuance of 9,000,000 shares of common stock at a price of \$9.00 per share in our initial public offering with net proceeds of \$72.2 million, the exercise of the option to purchase an additional 968,539 shares of common stock by the underwriters in the initial public offering resulting in net proceeds of \$8.1 million, the sale and issuance of 4,500,000 shares of common stock at a price of \$13.50 to a group of institutional and accredited investors related to our private placement resulting in net proceeds of \$56.6 million, stock option exercises of \$1.6 million, and net proceeds of \$7.6 million from the refinancing of loans payable from our loan agreement entered in to with affiliates of Hercules Technology Growth, offset partially by principal payments on loans payable in the amount of \$3.3 million. The cash provided by financing activities in 2009 was due to the sale and issuance of 11,250,000 shares of series E convertible preferred stock resulting in net proceeds of \$32.9 million, and stock option exercises of \$0.2 million, offset partially by the principal payments on loans payable of \$2.0 million.

**Credit Facilities.** On May 28, 2010, we entered into a loan and security agreement with Hercules Technology II, L.P. and Hercules Technology III, L.P., affiliates of Hercules Technology Growth, referred to as the new loan agreement, pursuant to which we received a loan in the aggregate principal amount of \$25.0 million. In connection with the new loan agreement, we paid off the remaining outstanding principal and interest of \$17.4 million under our prior loan agreement with Hercules Technology Growth and Comerica Bank. We are required to repay the aggregate principal balance of the loan that is outstanding under the new loan agreement in 30 equal monthly installments of principal starting on January 1, 2012. The new loan agreement requires a deferred charge of \$1.25 million to be paid in May 2012 related to the termination of the prior loan agreement. This amount is included in current liabilities at December 31, 2011. The new loan agreement also includes an obligation to pay an additional deferred charge of \$1.24 million due upon the maturity of the loan which has been recorded as a loan discount and is being amortized to interest expense over the term of the new loan agreement using the effective interest rate method. We recorded a long-term liability for the full amount of the charge since the payment of such amount is not contingent on any future event. Per annum interest is payable at the greater of 11.9% and an amount equal to 11.9% plus the prime rate of interest minus 4.75%, provided however, that the per annum interest shall not exceed 15.0%. We must make interest payments on the loan each month following the date of borrowing under the new loan agreement. The unpaid principal balance and all accrued but unpaid interest, plus the end of term payment in the amount of approximately \$1.24 million, will be due and payable on June 1, 2014.

The loan is secured by a lien on all of our personal property, as of, or acquired after, the date of the new loan agreement, except for intellectual property. As of December 31, 2011, the principal balance outstanding was \$25.0 million.

---

## **Table of Contents**

**Operating Capital Requirements.** Assuming we obtain requisite regulatory approvals, we anticipate commercializing tivozanib for advanced RCC in 2013 at the earliest. We anticipate that we will continue to incur significant operating costs for the next several years as we incur expenses to build commercial capabilities for and potentially commercialize tivozanib for RCC, continue to advance our clinical trial programs for tivozanib, ficlatuzumab and AV-203, develop our antibody pipeline and expand our corporate infrastructure. We believe that our existing cash and cash equivalents, marketable securities, committed research and development funding and milestone payments that we expect to receive under our existing strategic partnership and license agreements, will allow us to fund our operating plan into the second half of 2013.

If our available cash and cash equivalents are insufficient to satisfy our liquidity requirements, or if we identify additional opportunities to do so, we may seek to sell additional equity or debt securities or obtain a credit facility. The sale of additional equity and debt securities may result in additional dilution to our shareholders. If we raise additional funds through the issuance of debt securities or preferred stock, these securities could have rights senior to those of our common stock and could contain covenants that would restrict our operations. We may require additional capital beyond our currently forecasted amounts. Any such required additional capital may not be available on reasonable terms, if at all. If we were unable to obtain additional financing, we may be required to reduce the scope of, delay or eliminate some or all of our planned research, development and commercialization activities, which could harm our business.

Because of the numerous risks and uncertainties associated with research, development and commercialization of pharmaceutical products, we are unable to estimate the exact amounts of our working capital requirements. Our future funding requirements will depend on many factors, including, but not limited to:

the number and characteristics of the product candidates we pursue;

the scope, progress, results and costs of researching and developing our product candidates, and conducting preclinical and clinical trials;

the timing of, and the costs involved in, obtaining regulatory approvals for our product candidates;

the cost of commercialization activities if any of our product candidates are approved for sale, including marketing, sales and distribution costs;

the cost of manufacturing our product candidates and any products we successfully commercialize;

our ability to establish and maintain strategic partnerships, licensing or other arrangements and the financial terms of such agreements;

the costs involved in preparing, filing, prosecuting, maintaining, defending and enforcing patent claims, including litigation costs and the outcome of such litigation; and

the timing, receipt and amount of sales of, or royalties on, our future products, if any.

### **Contractual Obligations and Commitments**

The following table summarizes our contractual obligations at December 31, 2011:



Edgar Filing: AVEO PHARMACEUTICALS INC - Form 10-K

Contractual Obligations	Total	Payment due by period			
		Less than 1 Year	1 to 3 Years (in thousands)	3 to 5 Years	More than 5 Years
Short and long-term debt (including interest)	\$ 31,588	\$ 12,860	\$ 18,728		
License Agreement <sup>(1)</sup>	16,500	16,500			
Operating lease obligations	7,930	3,306	4,383	\$ 241	
Other License Agreements <sup>(2)</sup>	675	575	50	25	\$ 25
<b>Total contractual cash obligations</b>	<b>\$ 56,693</b>	<b>\$ 33,241</b>	<b>\$ 23,161</b>	<b>\$ 266</b>	<b>\$ 25</b>

---

**Table of Contents**

- (1) Under our license agreement with Kyowa Hakko Kirin, we are required to make certain milestone payments upon the achievement of specified regulatory milestones and pay a specified percentage of certain amounts we may receive under our collaboration agreement with Astellas. Although we believe in 2012 we may be required to make a milestone payment of \$16.5 million to Kyowa Hakko Kirin in connection with our NDA submission for tivozanib with the FDA and for submission for marketing authorization with the European regulatory agencies, we have not included any additional milestone payments in the table above as we are not able to make a reasonable estimate of the probability and timing of such payments, if any.
- (2) As discussed in Note 7 to our audited consolidated financial statements, we have executed license agreements for patented technology and other technology related to research projects, including technology to humanize ficlatuzumab and other antibody product candidates. The license agreements required us to pay non-refundable license fees upon execution, and in certain cases, require milestone payments upon the achievement of defined development goals. The license agreements also require us to pay annual maintenance payments totaling a maximum of \$325,000 per year. We have not included any additional milestone payments in the table above as we are not able to make a reasonable estimate of the probability and timing of such payments, if any. Including amounts in the table above, these agreements include sales and development milestones of up to \$22.5 million, \$6.3 million and \$4.2 million per product, and single digit royalties as a percentage of sales.

**Off-Balance Sheet Arrangements**

We did not have, during the periods presented, and we do not currently have, any off-balance sheet arrangements, as defined under SEC rules.

**New Accounting Pronouncements**

In December 2011, the Financial Accounting Standards Board, or the FASB, issued ASU 2011-11, *Balance Sheet: Disclosures about Offsetting Assets and Liabilities*, or ASU 2011-11. This newly issued accounting standard requires an entity to disclose both gross and net information about instruments and transactions eligible for offset in the statement of financial position as well as instruments and transactions executed under a master netting or similar arrangement and was issued to enable users of financial statements to understand the effects or potential effects of those arrangements on its financial position. This ASU is required to be applied retrospectively and is effective for fiscal years, and interim periods within those years, beginning on or after January 1, 2013. The adoption of this standard is not expected to have an impact on our financial position or results of operations.

In June 2011, the FASB issued ASU 2011-05, *Comprehensive Income: Presentation of Comprehensive Income*, or ASU 2011-05. This newly issued accounting standard (1) eliminates the option to present the components of other comprehensive income as part of the statement of changes in stockholders' equity; (2) requires the consecutive presentation of the statement of net income and other comprehensive income; and (3) requires an entity to present reclassification adjustments on the face of the financial statements from other comprehensive income to net income. The amendments in this ASU do not change the items that must be reported in other comprehensive income or when an item of other comprehensive income must be reclassified to net income nor do the amendments affect how earnings per share is calculated or presented. In December 2011, the FASB issued ASU No. 2011-12, *Deferral of the Effective Date for Amendments to the Presentation of Reclassifications of Items Out of Accumulated Other Comprehensive Income in Accounting Standards Update No. 2011-05*, which defers the requirement within ASU 2011-05 to present on the face of financial statements the effects of reclassifications out of accumulated other comprehensive income on the components of net income and other comprehensive income for all periods presented. During the deferral, entities should continue to report reclassifications out of accumulated other comprehensive income consistent with the presentation requirements in effect prior to the issuance of ASU 2011-05. These ASUs are required to be applied retrospectively and are effective for fiscal years, and interim periods within those years, beginning after December 15, 2011. The adoption of these standards is not expected to have an impact on our financial position or results of operations.

**Table of Contents**

In May 2011, the FASB issued ASU 2011-04, *Amendments to Achieve Common Fair Value Measurement and Disclosure Requirements in U.S. GAAP and IFRS*, or ASU 2011-04. ASU 2011-04 amends ASC 820, *Fair Value Measurement*, to ensure that fair value has the same meaning in U.S. GAAP and International Financial Reporting Standards, or IFRS, and improves the comparability of the fair value measurement and disclosure requirements in U.S. GAAP and IFRS. ASU 2011-04 applies to all entities that measure assets, liabilities or instruments classified in shareholder's equity at fair value, or provide fair value disclosures for items not recorded at fair value. ASU 2011-04 results in common fair value measurement and disclosure requirements in U.S. GAAP and IFRS. Consequently, ASU 2011-04 changes the wording used to describe many of the requirements in U.S. GAAP for measuring fair value and for disclosing information about fair value measurements. For many of the requirements, ASU 2011-04 will not result in a change in the application of the requirements in ASC 820. Some of the requirements in ASU 2011-04 clarify the FASB's intent about the application of existing fair value measurement requirements. Other requirements change a particular principle or requirement for measuring fair value or for disclosing information about fair value measurements. ASU 2011-04 is effective for public companies for interim and annual periods beginning after December 15, 2011 and should be applied prospectively. Early application is not permitted. The adoption of this standard is not expected to have an impact on our financial position or results of operations.

Effective January 1, 2011, we adopted ASU 2009-13, which amended ASC 605-25 to eliminate the residual method of allocation for multiple-deliverable revenue arrangements and required that arrangement consideration be allocated at the inception of an arrangement to all deliverables using the relative selling price method. ASU 2009-13 also established a selling price hierarchy for determining the selling price of a deliverable, which includes: (1) vendor-specific objective evidence, or VSOE, if available; (2) third-party evidence, or TPE, if VSOE is not available; and (3) estimated selling price if neither VSOE nor TPE is available.

Prior to the adoption of ASU 2009-13, ASC 605-25 required that the fair value of an undelivered item be determined by reference to VSOE or TPE. This was difficult to determine when a deliverable was not individually sold because of its unique features. Prior to the adoption of ASU 2009-13, if the fair value of the undelivered elements in the arrangement was not determinable, then revenue was generally deferred and recognized over the delivery period of the longest deliverable or when fair value was determined for the undelivered elements. We prospectively applied the provisions of ASU 2009-13 to all multiple-deliverable revenue arrangements entered into or materially modified after January 1, 2011. The adoption of ASU 2009-13 had a material impact on our financial position and results of operations for the year ended December 31, 2011 as discussed further in our footnotes to the Financial Statements.

On January 1, 2011, we adopted ASU 2010-17, which codified a method of revenue recognition that has been common practice. This guidance concluded that the milestone method is a valid application of the proportional performance model when applied to research or development arrangements. Accordingly, an entity can make an accounting policy election to recognize a payment that is contingent upon the achievement of a substantive milestone in its entirety in the period in which the milestone is achieved. Because our revenue recognition policy for milestone payments is generally consistent with ASU 2010-17, the adoption of this standard did not have a material effect on our condensed consolidated financial position, results of operations or cash flows for the year ended December 31, 2011. This standard may impact our accounting for any milestone payments received in future periods.

**ITEM 7A. Quantitative and Qualitative Disclosures About Market Risk**

We are exposed to market risk related to changes in interest rates. As of December 31, 2011 and December 31, 2010, we had cash and cash equivalents and marketable securities of \$275.4 million and \$140.2 million, respectively, consisting of money market funds, a U.S. treasury security, U.S. government agency securities, a foreign government agency security, a foreign government bond, an asset-backed security, and corporate debt, including commercial paper. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates, particularly because our investments are

**Table of Contents**

in short-term marketable securities. Our marketable securities are subject to interest rate risk and will fall in value if market interest rates increase. Due to the short-term duration of our investment portfolio and the low risk profile of our investments, an immediate 10% change in interest rates would not have a material effect on the fair market value of our portfolio. We have the ability to hold our marketable securities until maturity, and therefore we would not expect our operating results or cash flows to be affected to any significant degree by the effect of a change in market interest rates on our investments. We do not currently have any auction rate securities.

Our long-term debt bears interest at variable rates. In May 2010, we entered into a new loan agreement with affiliates of Hercules Technology Growth Capital pursuant to which we received a loan in the aggregate principal amount of \$25.0 million. Per annum interest is payable at the greater of 11.9% and 11.9% plus the prime rate of interest minus 4.75%, not to exceed 15%. As a result of the 15% maximum per annum interest rate under the new loan agreement, we have limited exposure to changes in interest rates on borrowings under this loan. For every 1% increase in prime over 4.75% on the outstanding debt amount as of December 31, 2011, we would have a decrease in future annual cash flows of approximately \$206,000 over the next twelve month period.

We are also exposed to market risk related to change in foreign currency exchange rates. We contract with contract research organizations and investigational sites globally. We are subject to fluctuations in foreign currency rates in connection with these agreements. We do not hedge our foreign currency exchange rate risk.

**Table of Contents**

**ITEM 8. Financial Statements and Supplementary Data**

**AVEO PHARMACEUTICALS, INC.**

**INDEX TO CONSOLIDATED FINANCIAL STATEMENTS**

<u>Report of Independent Registered Public Accounting Firm</u>	110
<u>Consolidated Balance Sheets as of December 31, 2011 and 2010</u>	111
<u>Consolidated Statements of Operations for the Years Ended December 31, 2011, 2010 and 2009</u>	112
<u>Consolidated Statements of Convertible Preferred Stock and Stockholders' Equity for the Years Ended December 31, 2011, 2010 and 2009</u>	113
<u>Consolidated Statements of Cash Flows for the Years Ended December 31, 2011, 2010 and 2009</u>	114
<u>Notes to Consolidated Financial Statements</u>	115

**Table of Contents**

**REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM**

The Board of Directors and Stockholders of

AVEO Pharmaceuticals, Inc.

We have audited the accompanying consolidated balance sheets of AVEO Pharmaceuticals, Inc. as of December 31, 2011 and 2010, and the related consolidated statements of operations, convertible preferred stock and stockholder's equity (deficit), and cash flows for each of the three years in the period ended December 31, 2011. 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 AVEO Pharmaceuticals, Inc. at December 31, 2011 and 2010, and the consolidated results of its operations and its cash flows for each of the three years in the period ended December 31, 2011 in conformity with U.S. generally accepted accounting principles.

As discussed in Note 2 to the consolidated financial statements, effective January 1, 2011, the Company adopted Financial Accounting Standards Board Accounting Standards Update No. 2009-13, *Multiple-Deliverable Revenue Arrangements*.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), AVEO Pharmaceuticals, Inc.'s internal control over financial reporting as of December 31, 2011, based on criteria established in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission and our report dated March 30, 2012 expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP

Boston, Massachusetts

March 30, 2012

**Table of Contents****AVEO Pharmaceuticals, Inc.****Consolidated Balance Sheets****(in thousands, except par value amounts)**

	<b>2011</b>	<b>2010</b>
<b>Assets</b>		
Current assets:		
Cash and cash equivalents	\$ 43,506	\$ 45,791
Marketable securities	177,622	94,407
Accounts receivable	7,210	391
Prepaid expenses and other current assets	6,057	4,864
<b>Total current assets</b>	<b>234,395</b>	<b>145,453</b>
Marketable securities	54,312	
Property and equipment, net	5,471	4,532
Other assets	121	456
Restricted cash	751	607
<b>Total assets</b>	<b>\$ 295,050</b>	<b>\$ 151,048</b>
<b>Liabilities and stockholders equity</b>		
Current liabilities:		
Accounts payable	\$ 8,904	\$ 9,247
Accrued expenses	14,289	10,121
Loans payable, net of discount	8,551	5,766
Deferred revenue	1,294	16,693
Other liabilities	1,249	
Deferred rent	322	266
<b>Total current liabilities</b>	<b>34,609</b>	<b>42,093</b>
Loans payable, net of current portion and discount	15,619	17,636
Deferred revenue, net of current portion	19,684	16,509
Deferred rent, net of current portion	359	553
Other liabilities	1,238	2,487
Commitments and contingencies (Note 8)		
Stockholders equity:		
Preferred stock, \$.001 par value: 5,000 shares authorized; no shares issued and outstanding at December 31, 2011 and 2010, respectively		
Common stock, \$.001 par value: 100,000 shares authorized at December 31, 2011 and 2010, respectively; 43,254 and 35,604 shares issued and outstanding at December 31, 2011 and 2010, respectively	43	36
Additional paid-in capital	429,531	308,268
Accumulated other comprehensive loss	(167)	(20)
Accumulated deficit	(205,866)	(236,514)
<b>Total stockholders equity</b>	<b>223,541</b>	<b>71,770</b>
<b>Total liabilities and stockholders equity</b>	<b>\$ 295,050</b>	<b>\$ 151,048</b>

See accompanying notes





**Table of Contents****AVEO Pharmaceuticals, Inc.****Consolidated Statements of Operations****(in thousands, except per share amounts)**

	Year Ended December 31,		
	2011	2010	2009
Collaboration revenue	\$ 164,849	\$ 44,682	\$ 20,719
Operating expenses:			
Research and development	101,735	86,345	51,792
General and administrative	29,167	14,763	10,120
	130,902	101,108	61,912
Income (loss) from operations	33,947	(56,426)	(41,193)
Other income and expense:			
Other income (expense), net	10	900	(333)
Interest expense	(3,836)	(3,389)	(2,811)
Interest income	527	126	144
Other expense, net	(3,299)	(2,363)	(3,000)
Net income (loss) before benefit for income taxes	30,648	(58,789)	(44,193)
Benefit for income taxes			100
Net income (loss)	\$ 30,648	\$ (58,789)	\$ (44,093)
Basic net income (loss) per share:			
Net income (loss) per share	\$ 0.77	\$ (2.30)	\$ (27.43)
Weighted average number of common shares outstanding	39,715	25,582	1,607
Diluted net income (loss) per share:			
Net income (loss) per share	\$ 0.74	\$ (2.30)	\$ (27.43)
Weighted average number of common shares and dilutive common share equivalents outstanding	41,473	25,582	1,607

See accompanying notes

**Table of Contents****AVEO Pharmaceuticals, Inc.****Consolidated Statements of Convertible Preferred Stock and Stockholders Equity (Deficit)**

(in thousands)

Transaction	Series A E Convertible Preferred Stock		Common Shares		Additional Paid-in Capital	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Total Stockholders Equity (Deficit)	Comprehensive Loss
	Shares	Amount	Shares	Par Value					
Balance at December 31, 2008	64,639	\$ 123,720	1,587	\$ 2	\$ 4,924	\$ 18	\$ (133,632)	\$ (128,688)	
Issuance of Series E Convertible Preferred Stock, net of offering costs of \$63	11,250	32,925			(63)			(63)	
Exercise of Series A warrants	28	60			25			25	
Exercise of stock options			54		159			159	
Stock-based compensation expense related to stock options granted to employees					2,120			2,120	
Stock-based compensation expense related to stock options granted to nonemployees					267			267	
Change in unrealized gain/loss on investments						(18)		(18)	\$ (18)
Net loss							(44,093)	(44,093)	(44,093)
Comprehensive loss									\$ (44,111)
Balance at December 31, 2009	75,917	\$ 156,705	1,641	\$ 2	\$ 7,432	\$	\$ (177,725)	\$ (170,291)	
Conversion of convertible preferred stock into common stock	(75,917)	(156,705)	18,979	19	156,686			156,705	
Conversion of preferred stock warrants to common stock warrants					745			745	
Exercise of stock options			448		1,235			1,235	
Exercise of warrants			21		120			120	
Stock-based compensation expense related to stock options granted to employees					4,089			4,089	
Reversal of stock-based compensation expense related to stock options granted to nonemployees					(4)			(4)	
Issuance of common stock under employee stock purchase plan			47		276			276	
Issuance of common stock from initial public offering (net of issuance costs of \$3,135)			9,968	10	80,292			80,302	
Issuance of common stock from PIPE financing (net of issuance costs of \$4,129)			4,500	5	56,617			56,622	
Issuance of warrants in connection with loans payable					780			780	
Change in unrealized gain/loss on investments						(20)		(20)	(20)
Net loss							(58,789)	(58,789)	(58,789)
Comprehensive loss									\$ (58,809)
Balance at December 31, 2010		\$	35,604	\$ 36	\$ 308,268	\$ (20)	\$ (236,514)	\$ 71,770	
Exercise of stock options			565	1	2,457			2,458	
Exercise of warrants			168						

Edgar Filing: AVEO PHARMACEUTICALS INC - Form 10-K

Stock-based compensation expense related to stock options and restricted share awards granted to employees				5,903				5,903
Issuance of common stock under employee stock purchase plan	58			779				779
Issuance of common stock from follow-on stock offering (net of issuance costs of \$6,960)	6,352	6		104,202				104,208
Issuance of common stock from license agreement with Centocor (net of issuance costs of \$113)	438			7,922				7,922
Issuance of restricted stock awards	69							
Change in unrealized gain/loss on investments					(147)		(147)	(147)
Net income						30,648	30,648	30,648
Comprehensive income								\$ 30,501
Balance at December 31, 2011	\$	43,254	\$ 43	\$ 429,531	\$	(167)	\$ (205,866)	\$ 223,541

See accompanying notes

**Table of Contents****AVEO Pharmaceuticals, Inc.****Consolidated Statements of Cash Flows**

(in thousands)

	Year Ended December 31,		
	2011	2010	2009
<b>Operating activities</b>			
Net income (loss)	\$ 30,648	\$ (58,789)	\$ (44,093)
Adjustments to reconcile net income (loss) to net cash provided by (used in) operating activities:			
Depreciation and amortization	1,654	1,350	1,289
Stock-based compensation	5,903	4,085	2,387
Non-cash interest expense	788	1,434	686
Deferred rent	(138)	(176)	(141)
Loss on disposal of property and equipment	35	1	
Remeasurement of warrants to purchase convertible preferred stock		(713)	333
Amortization of premium on investments	3,801	404	373
Changes in operating assets and liabilities:			
Accounts receivable	(6,819)	96	1,594
Prepaid expenses and other current assets	(1,213)	(3,595)	(155)
Other noncurrent assets	335	1,490	(1,825)
Restricted cash	(144)		
Accounts payable	(343)	1,756	3,636
Accrued expenses	4,168	2,732	3,981
Deferred revenue	(12,224)	(1,900)	21,962
Net cash provided by (used in) operating activities	26,451	(51,825)	(9,973)
<b>Investing activities</b>			
Purchases of property and equipment	(2,628)	(1,686)	(1,734)
Purchases of marketable securities	(376,270)	(167,706)	(35,927)
Proceeds from maturities and sales of marketable securities	234,795	78,886	41,075
Net cash (used in) provided by investing activities	(144,103)	(90,506)	3,414
<b>Financing activities</b>			
Proceeds from issuance of common stock, net of issuance costs	112,130	136,923	
Proceeds from issuance of convertible preferred stock, net of issuance costs			32,862
Proceeds from exercise of stock options and issuance of common and restricted stock	3,237	1,632	159
Proceeds from issuance of loans payable		7,555	
Principal payments on loans payable		(3,278)	(1,986)
Net cash provided by financing activities	115,367	142,832	31,035
Net (decrease) increase in cash and cash equivalents	(2,285)	501	24,476
Cash and cash equivalents at beginning of period	45,791	45,290	20,814
Cash and cash equivalents at end of period	\$ 43,506	\$ 45,791	\$ 45,290

**Supplemental cash flow and noncash investing and financing activities**

Edgar Filing: AVEO PHARMACEUTICALS INC - Form 10-K

Issuance of warrants	\$	\$ 900	\$
Conversion of convertible preferred stock	\$	\$ 156,856	\$
Conversion of preferred stock warrants	\$	\$ 745	\$
Cash paid for interest	\$ 3,016	\$ 2,453	\$ 2,125
Cash paid for income taxes	\$	\$	\$

See accompanying notes

**Table of Contents****AVEO Pharmaceuticals, Inc.****Notes to Consolidated Financial Statements****December 31, 2010****1. Nature of Business and Organization**

AVEO Pharmaceuticals, Inc. (the Company) is a cancer therapeutics company committed to discovering, developing and commercializing targeted cancer therapies to impact patients' lives. The Company's product candidates are directed against important mechanisms, or targets, known or believed to be involved in cancer. Tivozanib, the Company's lead product candidate currently in phase 3 clinical development, which the Company partnered with Astellas Pharma Inc. and its wholly-owned direct subsidiaries (Astellas), is designed to provide an optimal blockade of the vascular endothelial growth factor, or VEGF, pathway by inhibiting all three VEGF receptors: VEGF receptors 1, 2 and 3. In January 2012, the Company announced top-line data from its global, phase 3 clinical trial comparing the efficacy and safety of tivozanib with Nexavar® (sorafenib), an approved therapy, for first-line treatment in renal cell carcinoma (RCC). Based on preliminary results, the Company expects to file a New Drug Application (NDA) in the third quarter of 2012. The Company also has a pipeline of monoclonal antibodies, including ficlatuzumab, a product candidate that is currently in phase 2 clinical development, derived from its Human Response Platform, a novel method of building preclinical models of human cancer. As used throughout these consolidated financial statements, the terms AVEO, we, us, and our refer to the business of AVEO Pharmaceuticals, Inc. and its wholly-owned subsidiaries, AVEO Pharma Limited and AVEO Securities Corporation.

The Company has generated an accumulated deficit as of December 31, 2011 of approximately \$205.9 million since inception, and will require substantial additional capital for research, product development and the anticipated commercialization of tivozanib. At December 31, 2011, the Company believes that its cash, cash equivalents and marketable securities totaling approximately \$275.4 million are sufficient to fund its operations into the second half of 2013.

**2. Significant Accounting Policies***Revenue Recognition*

The Company's revenues are generated primarily through collaborative research, development and commercialization agreements. The terms of these agreements generally contain multiple elements, or deliverables, which may include (i) licenses, or options to obtain licenses, to the Company's technology, (ii) research and development activities to be performed on behalf of the collaborative partner and (iii) in certain cases, services in connection with the manufacturing of pre-clinical and clinical material. Payments to the Company under these arrangements typically include one or more of the following: non-refundable, up-front license fees; option exercise fees; funding of research and/or development efforts; milestone payments; and royalties on future product sales.

Effective January 1, 2011, the Company adopted Accounting Standards Update (ASU) No. 2009-13, *Multiple-Deliverable Revenue Arrangements* (ASU 2009-13), which amends Accounting Standards Codification (ASC) Topic 605-25, *Revenue Recognition - Multiple Element Arrangements* (ASC 605-25). In addition, effective January 1, 2011, the Company adopted ASU No. 2010-17, *Revenue Recognition - Milestone Method* (ASU 2010-17). Refer to *New Accounting Pronouncements* below for additional discussion of these standards and their impact on the Company's accounting for collaborative research, development and commercialization agreements.

When evaluating multiple element arrangements, the Company considers whether the deliverables under the arrangement represent separate units of accounting. This evaluation requires subjective determinations and requires management to make judgments about the individual deliverables and whether such deliverables are

---

**Table of Contents**

separable from the other aspects of the contractual relationship. In determining the units of accounting, management evaluates certain criteria, including whether the deliverables have standalone value, based on the consideration of the relevant facts and circumstances for each arrangement. The consideration received is allocated among the separate units of accounting using the relative selling price method, and the applicable revenue recognition criteria are applied to each of the separate units.

The Company determines the estimated selling price for deliverables within each agreement using vendor-specific objective evidence ( VSOE ) of selling price, if available, third-party evidence ( TPE ) of selling price if VSOE is not available, or best estimate of selling price if neither VSOE nor TPE is available. Determining the best estimate of selling price for a deliverable requires significant judgment. The Company typically uses best estimate of selling price to estimate the selling price for licenses to the Company's proprietary technology, since the Company often does not have VSOE or TPE of selling price for these deliverables. In those circumstances where the Company utilizes best estimate of selling price to determine the estimated selling price of a license to the Company's proprietary technology, the Company considers market conditions as well as entity-specific factors, including those factors contemplated in negotiating the agreements as well as internally developed models that include assumptions related to the market opportunity, estimated development costs, probability of success and the time needed to commercialize a product candidate pursuant to the license. In validating the Company's best estimate of selling price, the Company evaluates whether changes in the key assumptions used to determine the best estimate of selling price will have a significant effect on the allocation of arrangement consideration between multiple deliverables.

The Company typically receives up-front, non-refundable payments when licensing its intellectual property in conjunction with a research and development agreement. When management believes the license to its intellectual property does not have stand-alone value from the other deliverables to be provided in the arrangement, the Company generally recognizes revenue attributed to the license on a straight-line basis over the Company's contractual or estimated performance period, which is typically the term of the Company's research and development obligations. If management cannot reasonably estimate when the Company's performance obligation ends, then revenue is deferred until management can reasonably estimate when the performance obligation ends. When management believes the license to its intellectual property has stand-alone value, the Company generally recognizes revenue attributed to the license upon delivery. The periods over which revenue should be recognized are subject to estimates by management and may change over the course of the research and development agreement. Such a change could have a material impact on the amount of revenue the Company records in future periods.

Payments or reimbursements resulting from the Company's research and development efforts for those arrangements where such efforts are considered as deliverables are recognized as the services are performed and are presented on a gross basis so long as there is persuasive evidence of an arrangement, the fee is fixed or determinable, and collection of the related receivable is reasonably assured. Amounts received prior to satisfying the above revenue recognition criteria are recorded as deferred revenue in the accompanying balance sheets.

At the inception of each agreement that includes milestone payments, the Company evaluates whether each milestone is substantive and at risk to both parties on the basis of the contingent nature of the milestone. This evaluation includes an assessment of whether (a) the consideration is commensurate with either (1) the entity's performance to achieve the milestone, or (2) the enhancement of the value of the delivered item(s) as a result of a specific outcome resulting from the entity's performance to achieve the milestone, (b) the consideration relates solely to past performance and (c) the consideration is reasonable relative to all of the deliverables and payment terms within the arrangement. The Company evaluates factors such as the scientific, regulatory, commercial and other risks that must be overcome to achieve the respective milestone, the level of effort and investment required to achieve the respective milestone and whether the milestone consideration is reasonable relative to all deliverables and payment terms in the arrangement in making this assessment. The Company aggregates its milestones into four categories: (i) clinical and development milestones, (ii) regulatory milestones, (iii) commercial milestones, and (iv) patent related milestones. The Company has concluded that the clinical and development, regulatory and patent related milestones pursuant to its research and development arrangements are substantive.

## **Table of Contents**

Clinical and development milestones are typically payable when a product candidate advances into a defined phase of clinical research or completes such phase. For example, a milestone may be due upon the initiation of the phase 3 clinical trial in a new indication, the last phase of clinical development, which if the product candidate is proven to be safe and effective, may lead to ultimate marketing approval by the Food and Drug Administration ( FDA ) or other global regulatory authorities. Regulatory milestones are typically payable upon acceptance of the submission for marketing approval of a product candidate or upon approval to market the product candidate by the FDA or other global regulatory authorities. For example, a milestone may be due to the Company upon the FDA's acceptance of an NDA. Commercial milestones are typically payable when an approved pharmaceutical product reaches certain defined levels of net sales by the licensee. For example, when a product first achieves global sales of a specified amount, or when a product first achieves annual sales of a specified amount. Patent related milestones are typically payable when a patent application is filed or issued with respect to certain intellectual property related to the applicable collaboration.

Revenues from clinical and development, regulatory and patent related milestones, if they are nonrefundable and deemed substantive, are recognized upon successful accomplishment of the milestones. Milestones that are not considered substantive are accounted for as license payments and recognized on a straight-line basis over the remaining period of performance. Commercial milestones are accounted for as royalties and are recorded as revenue upon achievement of the milestone, assuming all other revenue recognition criteria are met.

### *Principles of Consolidation*

The Company's consolidated financial statements include the Company's accounts and the accounts of the Company's wholly-owned subsidiaries, AVEO Pharma Limited and AVEO Securities Corporation. All intercompany transactions have been eliminated.

### *Research and Development Expenses*

Research and development expenses are charged to expense as incurred. Research and development expenses comprise costs incurred in performing research and development activities, including personnel-related costs, stock-based compensation, facilities, research-related overhead, clinical trial costs, manufacturing costs and other contracted services, license fees, and other external costs.

Nonrefundable advance payments for goods and services that will be used in future research and development activities are expensed when the activity has been performed or when the goods have been received rather than when the payment is made in accordance with the provisions of ASC 730, *Research and Development* ( ASC 730 ).

### *Cash and Cash Equivalents*

The Company considers highly liquid investments with a maturity of three months or less when purchased to be cash equivalents. Cash equivalents at December 31, 2011 consist of a money market fund and commercial paper. Cash equivalents at December 31, 2010 consist of a money market fund, a U.S. government agency security, and corporate debt securities, including commercial paper.

### *Marketable Securities*

Marketable securities at December 31, 2011 consist of U.S. government agency securities, a foreign government bond, an asset-backed security, and corporate debt securities, including commercial paper, maintained by an investment manager. Marketable securities at December 31, 2010 consist of U.S. government agency securities, a U.S. treasury, a foreign government agency security, and corporate debt securities, including commercial paper, maintained by an investment manager. Credit risk is reduced as a result of the Company's policy to limit the amount invested in any one issue. Marketable securities consist primarily of investments



**Table of Contents**

which have expected average maturity dates in excess of three months, but not longer than 24 months. The Company classifies these investments as available-for-sale. Unrealized gains and losses are included in other comprehensive income (loss) as a component of stockholders' equity until realized. The cost of securities sold is based on the specific identification method. There were no realized gains or losses recognized on the sale or maturity of securities during the years ended December 31, 2011 and 2009. The Company sold one security in 2010 for gross proceeds of \$4.5 million, and recognized a gain of \$1,853.

Available-for-sale securities at December 31, 2011 and 2010 consist of the following:

	Amortized Cost	Unrealized Gains (in thousands)	Unrealized Losses	Fair Value
<b>December 31, 2011:</b>				
Corporate debt securities (Due within 1 year)	\$ 149,754	\$ 73	\$ (227)	\$ 149,600
Government agency securities (Due within 1 year)	24,750		(5)	24,745
Government agency securities (Due after 1 year through 2 years)	52,749	13	(3)	52,759
Foreign government bond (Due within 1 year)	3,285		(8)	3,277
Asset-backed security (Due after 2 years through 3 years)	1,563		(10)	1,553
	\$ 232,101	\$ 86	\$ (253)	\$ 231,934
<b>December 31, 2010:</b>				
Corporate debt securities (Due within 1 year)	\$ 71,615	\$ 19	\$ (27)	\$ 71,607
U.S. treasury (Due within 1 year)	5,178		(1)	5,177
Government agency securities (Due within 1 year)	13,503		(6)	13,497
Foreign government agency security (Due within 1 year)	4,131		(5)	4,126
	\$ 94,427	\$ 19	\$ (39)	\$ 94,407

The aggregate fair value of securities in an unrealized loss position for less than 12 months at December 31, 2011 was \$114.8 million, representing twenty nine securities. There were no securities that were in an unrealized loss position for greater than 12 months at December 31, 2011. The unrealized loss was caused by a temporary change in the market for those securities. There was no change in the credit risk of the securities. To determine whether an other-than-temporary impairment exists, the Company performs an analysis to assess whether it intends to sell, or whether it would more likely than not be required to sell, the security before the expected recovery of the amortized cost basis. Where the Company intends to sell a security, or may be required to do so, the security's decline in fair value is deemed to be other-than-temporary and the full amount of the unrealized loss is recorded in the statement of operations as an other-than-temporary impairment charge. When this is not the case, the Company performs additional analysis on all securities with unrealized losses to evaluate losses associated with the creditworthiness of the security. Credit losses are identified where the Company does not expect to receive cash flows, based on using a single best estimate, sufficient to recover the amortized cost basis of a security and these are recognized in other income (expense), net.

**Table of Contents**

Marketable securities in an unrealized loss position at December 31, 2011 and 2010 consist of the following:

	Aggregate Fair Value	Unrealized Losses
	(in thousands)	
<b>December 31, 2011:</b>		
Corporate debt securities (Due within 1 year)	\$ 87,263	\$ (227)
Government agency securities (Due within 1 year)	18,745	(5)
Government agency security (Due after 1 year through 2 years)	3,997	(3)
Foreign government bond (Due within 1 year)	3,277	(8)
Asset-backed security (Due after 2 years through 3 years)	1,553	(10)
	\$ 114,835	\$ (253)
<b>December 31, 2010:</b>		
Corporate debt securities (Due within 1 year)	\$ 27,536	\$ (27)
U.S. treasury (Due within 1 year)	5,177	(1)
Government agency securities (Due within 1 year)	13,497	(6)
Foreign government agency security (Due within 1 year)	4,126	(5)
	\$ 50,336	\$ (39)

Based on consideration of those factors described in the previous paragraph, the Company does not believe an other-than temporary impairment exists with respect to those securities in an unrealized loss position at December 31, 2011.

*Concentrations of Credit Risk*

Financial instruments that potentially subject the Company to credit risk primarily consist of cash and cash equivalents and available-for-sale marketable securities. The Company maintains deposits in federally insured financial institutions in excess of federally insured limits.

Management believes that the Company is not exposed to significant credit risk due to the financial position of the depository institutions in which those deposits are held.

The Company's credit risk related to marketable securities is reduced as a result of the Company's policy to limit the amount invested in any one issue.

*Fair Value Measurements*

The carrying amounts of the Company's financial instruments not required to be measured at fair value, which include accounts receivable, accounts payable, and loans payable, approximate their fair values at December 31, 2011 and December 31, 2010.

The Company records cash equivalents and marketable securities at fair value. ASC 820, *Fair Value Measurements and Disclosures*, establishes a fair value hierarchy for those instruments measured at fair value that distinguishes between fair value measurements based on market data (observable inputs) and those based on the Company's own assumptions (unobservable inputs). The hierarchy consists of three levels:

Level 1 Quoted market prices in active markets for identical assets or liabilities. Assets utilizing Level 1 inputs include U.S. government securities.

## Edgar Filing: AVEO PHARMACEUTICALS INC - Form 10-K

Level 2 Inputs other than Level 1 inputs that are either directly or indirectly observable, such as quoted market prices, interest rates and yield curves. Assets utilizing Level 2 inputs include government agency securities, including direct issuance bonds, and corporate bonds. These assets are valued using third party pricing sources which generally use interest rates and yield curves observable at commonly quoted intervals of similar assets as observable inputs for pricing.

**Table of Contents**

Level 3 Unobservable inputs developed using estimates and assumptions developed by the Company, which reflect those that a market participant would use. The Company currently has no assets or liabilities valued with Level 3 inputs. The following tables summarize the cash equivalents and marketable securities measured at fair value on a recurring basis in the accompanying consolidated balance sheets as of December 31, 2011 and 2010.

	Fair Value Measurements of Cash Equivalents and Marketable Securities as of December 31, 2011			Total
	Level 1	Level 2 (in thousands)	Level 3	
Cash equivalents	\$ 35,508	\$ 3,000	\$	\$ 38,508
Marketable securities		231,934		231,934
	\$ 35,508	\$ 234,934	\$	\$ 270,442

	Fair Value Measurements of Cash Equivalents and Marketable Securities as of December 31, 2010			Total
	Level 1	Level 2 (in thousands)	Level 3	
Cash equivalents	\$ 28,767	\$ 14,015	\$	\$ 42,782
Marketable securities	5,177	89,230		94,407
	\$ 33,944	\$ 103,245	\$	\$ 137,189

The Company's Level 2 securities include corporate debt securities, which include commercial paper, as well as U.S. government agency securities, a foreign government agency security, a foreign government bond, and an asset-backed security and are valued using third-party pricing sources. These sources generally use interest rates and yield curves observable at commonly quoted intervals of similar assets as observable inputs for pricing.

*Property and Equipment*

Property and equipment are stated at cost and are depreciated using the straight-line method over the estimated useful lives of the respective assets. Maintenance and repair costs are charged to expense as incurred.

*Long-lived Assets*

The Company reviews long-lived assets, including property and equipment, for impairment whenever changes in business circumstances indicate that the carrying amount of the asset may not be fully recoverable. The Company has not recognized any impairment losses through December 31, 2011.

*Stock-Based Compensation*

The Company applies the provisions of ASC 718, *Compensation-Stock Compensation*, to share-based payments. All awards are recognized in the Company's statements of operations on a straight-line basis over their requisite service periods based on their grant date fair values as calculated using the measurement and recognition provisions of ASC 718. During the years ended December 31, 2011, 2010 and 2009, the Company recorded the following stock-based compensation expense:

	Years Ended December 31,		
	2011	2010	2009
Research and development	\$ 2,504	\$ 1,825	\$ 1,245

Edgar Filing: AVEO PHARMACEUTICALS INC - Form 10-K

General and administrative	3,399	2,260	1,142
Total stock-based compensation expense	\$ 5,903	\$ 4,085	\$ 2,387

---

## **Table of Contents**

Allocations to research and development and general and administrative expense are based upon the department to which the associated employee reported. No related tax benefits of the stock-based compensation expense have been recognized. Share-based payments issued to nonemployees are recorded at their fair values, and are periodically revalued as the equity instruments vest and are recognized as expense over the related service period.

### *Income Taxes*

The Company provides for income taxes using the liability method. Under this method, deferred tax assets and liabilities are determined based on differences between financial reporting and tax bases of assets and liabilities, and are measured using the enacted tax rates and laws that will be in effect when the differences are expected to reverse.

The Company accounts for income taxes under ASC 740, *Income Taxes* ( ASC 740 ), which provides a comprehensive model for the financial statement recognition, measurement, presentation and disclosure of uncertain tax positions taken or expected to be taken in income tax returns. Unrecognized tax benefits represent tax positions for which reserves have been established.

### *Segment and Geographic Information*

Operating segments are defined as components of an enterprise engaging in business activities for which discrete financial information is available and regularly reviewed by the chief operating decision maker in deciding how to allocate resources and in assessing performance. The Company views its operations and manages its business in one operating segment and the Company operates in only one geographic segment.

### *Use of Estimates*

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

### *New Accounting Pronouncements*

In December 2011, the Financial Accounting Standards Board (the FASB ) issued ASU 2011-11, *Balance Sheet (Topic 210): Disclosures about Offsetting Assets and Liabilities* ( ASU 2011-11 ). This newly issued accounting standard requires an entity to disclose both gross and net information about instruments and transactions eligible for offset in the statement of financial position as well as instruments and transactions executed under a master netting or similar arrangement and was issued to enable users of financial statements to understand the effects or potential effects of those arrangements on its financial position. This ASU is required to be applied retrospectively and is effective for fiscal years, and interim periods within those years, beginning on or after January 1, 2013. The adoption of this standard is not expected to have an impact on the Company's financial position or results of operations.

In June 2011, the FASB issued ASU 2011-05, *Comprehensive Income (Topic 220): Presentation of Comprehensive Income* ( ASU 2011-05 ). This newly issued accounting standard (1) eliminates the option to present the components of other comprehensive income as part of the statement of changes in stockholders' equity; (2) requires the consecutive presentation of the statement of net income and other comprehensive income; and (3) requires an entity to present reclassification adjustments on the face of the financial statements from other comprehensive income to net income. The amendments in this ASU do not change the items that must be reported in other comprehensive income or when an item of other comprehensive income must be reclassified to net income nor do the amendments affect how earnings per share is calculated or presented. In December 2011, the FASB issued ASU 2011-12, *Deferral of the Effective Date for Amendments to the Presentation of Reclassifications of Items Out of Accumulated Other Comprehensive Income in Accounting Standards Update*

**Table of Contents**

No. 2011-05, which defers the requirement within ASU 2011-05 to present on the face of financial statements the effects of reclassifications out of accumulated other comprehensive income on the components of net income and other comprehensive income for all periods presented. During the deferral, entities should continue to report reclassifications out of accumulated other comprehensive income consistent with the presentation requirements in effect prior to the issuance of ASU 2011-05. These ASUs are required to be applied retrospectively and are effective for fiscal years, and interim periods within those years, beginning after December 15, 2011. The adoption of these standards is not expected to have an impact on the Company's financial position or results of operations.

In May 2011, the FASB issued ASU 2011-04, *Amendments to Achieve Common Fair Value Measurement and Disclosure Requirements in U.S. GAAP and IFRSs* (ASU 2011-04). ASU 2011-04 amends ASC 820, *Fair Value Measurement*, to ensure that fair value has the same meaning in U.S. GAAP and International Financial Reporting Standards (IFRS) and improves the comparability of the fair value measurement and disclosure requirements in U.S. GAAP and IFRS. ASU 2011-04 applies to all entities that measure assets, liabilities or instruments classified in shareholder's equity at fair value, or provide fair value disclosures for items not recorded at fair value. ASU 2011-04 results in common fair value measurement and disclosure requirements in U.S. GAAP and IFRSs. Consequently, ASU 2011-04 changes the wording used to describe many of the requirements in U.S. GAAP for measuring fair value and for disclosing information about fair value measurements. For many of the requirements, ASU 2011-04 will not result in a change in the application of the requirements in ASC 820. Some of the requirements in ASU 2011-04 clarify the FASB's intent about the application of existing fair value measurement requirements. Other requirements change a particular principle or requirement for measuring fair value or for disclosing information about fair value measurements. ASU 2011-04 is effective for public companies for interim and annual periods beginning after December 15, 2011 and should be applied prospectively. Early application is not permitted. The adoption of this standard is not expected to have an impact on the Company's financial position or results of operations.

Effective January 1, 2011, the Company adopted ASU 2009-13, which amended ASC 605-25 to eliminate the residual method of allocation for multiple-deliverable revenue arrangements and required that arrangement consideration be allocated at the inception of an arrangement to all deliverables using the relative selling price method. ASU 2009-13 also established a selling price hierarchy for determining the selling price of a deliverable, which includes: (1) vendor-specific objective evidence (VSOE) if available; (2) third-party evidence (TPE) if VSOE is not available; and (3) estimated selling price if neither VSOE nor TPE is available.

Prior to the adoption of ASU 2009-13, ASC 605-25 required that the fair value of an undelivered item be determined by reference to VSOE or TPE. This was difficult to determine when a deliverable was not individually sold because of its unique features. Prior to the adoption of ASU 2009-13, if the fair value of the undelivered elements in the arrangement was not determinable, then revenue was generally deferred and recognized over the delivery period of the longest deliverable or when fair value was determined for the undelivered elements. The Company prospectively applied the provisions of ASU 2009-13 to all multiple-deliverable revenue arrangements entered into or materially modified after January 1, 2011. The adoption of ASU 2009-13 had a material impact on the Company's financial position and results of operations for the year ended December 31, 2011 as discussed in Note 4, Collaborations and License Agreements.

On January 1, 2011, the Company adopted ASU 2010-17, which codified a method of revenue recognition that has been common practice. This guidance concluded that the milestone method is a valid application of the proportional performance model when applied to research or development arrangements. Accordingly, an entity can make an accounting policy election to recognize a payment that is contingent upon the achievement of a substantive milestone in its entirety in the period in which the milestone is achieved. Because the Company's revenue recognition policy for milestone payments is generally consistent with ASU 2010-17, the adoption of this standard did not have a material effect on the Company's condensed consolidated financial position, results of operations or cash flows for the year ended December 31, 2011. This standard may impact the Company's accounting for any milestone payments received in future periods.

**Table of Contents****3. Earnings (Loss) Per Common Share**

The Company reports earnings (loss) per share in accordance with ASC 260, *Earnings Per Share*, which establishes standards for computing and presenting earnings per share. Basic earnings (loss) per share is computed by dividing net income (loss) available to common shareholders by the weighted average number of common shares outstanding during the period. Preferred shares are not included in the calculation of net income (loss) per share until their conversion to common shares. Diluted earnings per share is computed by dividing net income available to common shareholders by the weighted-average number of common shares and dilutive common share equivalents then outstanding. Potential common share equivalents consist of restricted stock awards and the incremental common shares issuable upon the exercise of stock options and warrants. Under the treasury stock method, unexercised in-the-money stock options are assumed to be exercised at the beginning of the period or at issuance, if later. The assumed proceeds are then used to purchase common shares at the average market price during the period. Share-based payment awards that entitle their holders to receive non-forfeitable dividends before vesting are considered participating securities and are included in the calculation of basic and diluted earnings per share. Common share equivalents have not been included in the net loss per share computation for the years ended December 31, 2010 and 2009 because their effect is anti-dilutive.

Basic and diluted earnings per share for the years ended December 31, 2011, 2010 and 2009 are as follows:

	Years Ended December 31,		
	2011	2010	2009
	(in thousands, except per share amounts)		
<b>Basic earnings per share</b>			
Net income (loss)	\$ 30,648	\$ (58,789)	\$ (44,093)
Income allocated to participating securities	(46)		
Income (loss) available to common stockholders	30,602	(58,789)	(44,093)
Basic weighted average common shares outstanding	39,715	25,582	1,607
Basic earnings (loss) per share	\$ 0.77	\$ (2.30)	\$ (27.43)
<b>Diluted earnings per share</b>			
Net income (loss)	\$ 30,648	\$ (58,789)	\$ (44,093)
Income allocated to participating securities	(45)		
Income (loss) available to common stockholders	30,603	(58,789)	(44,093)
Weighted average common shares outstanding	39,715	25,582	1,607
Diluted potential common shares	1,758		
Diluted weighted average common shares and potential common shares	41,473	25,582	1,607
Diluted earnings (loss) per share	\$ 0.74	\$ (2.30)	\$ (27.43)



**Table of Contents****4. Property and Equipment**

Property and equipment consists of the following:

	Estimated Useful Life	December 31, 2011	December 31, 2010
(in thousands)			
Laboratory equipment	5 years	\$ 8,734	\$ 8,075
Computer equipment and software	3 years	2,631	1,595
Office furniture	5 years	227	189
Leasehold improvements	Shorter of asset's useful life or remaining term of lease	4,498	4,109
Construction in process		444	318
		16,534	14,286
Less accumulated depreciation and amortization		(11,063)	(9,754)
Property and equipment, net		\$ 5,471	\$ 4,532

Depreciation expense for the years ended December 31, 2011, 2010 and 2009 was \$1.7 million, \$1.4 million and \$1.3 million, respectively.

**5. Accrued Expenses**

Accrued expenses consisted of the following:

	December 31, 2011	December 31, 2010
(in thousands)		
Clinical expenses	\$ 6,749	\$ 5,676
Salaries and benefits	5,494	3,696
Accrued collaboration expenses	742	
Professional fees	393	204
Accrued interest	256	256
Other	655	289
	\$ 14,289	\$ 10,121

**6. Loans Payable**

On May 15, 2008, the Company entered into a \$21.0 million financing agreement with Hercules Technology Growth Capital Inc., or Hercules Technology Growth, and Comerica Bank, referred to as the prior loan agreement. On May 28, 2010, the Company entered into a new loan and security agreement with Hercules Technology II, L.P. and Hercules Technology III, L.P., affiliates of Hercules Technology Growth, referred to as the new loan agreement, pursuant to which the Company received a loan in the aggregate principal amount of \$25.0 million and repaid the remaining outstanding principal and interest under the prior loan agreement of \$17.4 million. The Company was initially required to repay the aggregate principal balance of the loan that is outstanding under the new loan agreement in 30 equal monthly installments of principal starting on April 1, 2011. However, the new loan agreement provides that such date will be extended under certain circumstances. During 2011, the Company triggered two of two possible extensions to the date from which principal payments will be made. The Company is now required to repay the aggregate principal balance of the loan that is outstanding under the new loan agreement in 30 equal monthly installments of principal starting on January 1, 2012. The current portion of loans payable as of December 31, 2011 considers these extensions. Per annum interest is payable at the greater of 11.9% and an amount equal to 11.9% plus the prime rate of interest minus 4.75%, provided however, that the per annum interest shall not exceed 15.0%. The Company must make interest



**Table of Contents**

payments on the loan each month following the date of borrowing under the new loan agreement. The unpaid principal balance and all accrued but unpaid interest will be due and payable on June 1, 2014. The loan is secured by a lien on all of the Company's personal property as of, or acquired after, the date of the new loan agreement, except for intellectual property.

The new loan agreement requires a deferred charge of \$1.25 million to be paid in May 2012 related to the termination of the prior loan agreement. This amount is included in current liabilities at December 31, 2011. The new loan also includes an additional deferred charge of \$1.24 million due upon the maturity of the new loan which has been recorded as a loan discount and is being amortized to interest expense over the term of the new loan agreement using the effective interest rate method. The Company recorded a long-term liability for the full amount of the charge since the payment of such amount is not contingent on any future event. The Company incurred approximately \$193,000 in loan issuance costs related to the new loan agreement paid directly to the lenders, which have been offset against the loan proceeds as a loan discount. As part of the new loan agreement, the Company issued warrants to the lenders on June 2, 2010 to purchase up to 156,641 shares of the Company's common stock at an exercise price equal to \$7.98 per share. The Company recorded the relative fair value of the warrants of approximately \$780,000 as equity and as a discount to the related loan outstanding and will amortize the value of the discount to interest expense over the term of the loan using the effective interest method. The relative fair value of the warrant was calculated using the Black-Scholes option-pricing model with the following assumptions: volatility of 64.12%, an expected term equal to the contractual life of the warrant (seven years), a risk-free interest rate of 2.81% and no dividend yield. The resulting effective interest rate including the fair value of the warrant, the new loan issuance costs and the deferred charge approximates 16.1%.

The new loan agreement defines events of default, including the occurrence of an event that results in a material adverse effect upon the Company's business operations, properties, assets or condition (financial or otherwise), its ability to perform its obligations under and in accordance with the terms of the new loan agreement, or upon the ability of the lenders to enforce any of their rights or remedies with respect to such obligations, or upon the collateral under the new loan agreement or upon the liens of the lenders on such collateral or upon the priority of such liens. Hercules Technology Growth also received an option, subject to the Company's written consent, not to be unreasonably withheld, to purchase, either with cash or through conversion of outstanding principal under the loan, up to \$2.0 million of equity of the Company sold in any sale by the Company to third parties of equity securities resulting in at least \$10.0 million in net cash proceeds to the Company, subject to certain exceptions. The Company has evaluated the embedded conversion option, and has concluded that it does not need to be bifurcated and separately accounted for. No amount will be recognized for the conversion feature until such time as the conversion feature is exercised and it can be determined whether a beneficial conversion feature exists. As of December 31, 2011, there have been no events of default under the loan. As of December 31, 2011, the principal balance outstanding was \$25.0 million.

Future minimum payments under the loans payable outstanding as of December 31, 2011 are as follows (amounts in thousands):

<b>Years Ending December 31:</b>	
2012	12,860
2013	11,610
2014	7,118
	31,588
Less amount representing interest	(4,101)
Less discount	(830)
Less deferred charges	(2,487)
Less current portion	(8,551)
Loans payable, net of current portion	\$ 15,619

**Table of Contents****7. Collaboration and License Agreements***(a) Out-License Agreements**Astellas Pharma Inc. (Astellas)*

On February 16, 2011, the Company, together with its wholly-owned subsidiary AVEO Pharma Limited, entered into a Collaboration and License Agreement with Astellas (the "Astellas Agreement"), pursuant to which the Company and Astellas will develop and commercialize tivozanib, AVEO's product candidate currently in phase 3 clinical development, for the treatment of a broad range of cancers, including RCC and breast and colorectal cancers. Under the terms of the Astellas Agreement, AVEO and Astellas will share responsibility for continued development and commercialization of tivozanib in North America and in Europe under a joint development plan and a joint commercialization plan, respectively. Throughout the rest of the world (the "Royalty Territory"), excluding Asia, where Kyowa Hakko Kirin ("KHK") has retained all development and commercialization rights, Astellas has an exclusive, royalty-bearing license to develop and commercialize tivozanib. The terms of the Astellas Agreement are subject to the Company's obligations to KHK under a license agreement entered into with KHK in 2006 pursuant to which AVEO acquired exclusive rights to develop and commercialize tivozanib worldwide outside of Asia.

Assuming successful approvals of tivozanib by applicable regulatory agencies, the Company will have lead responsibility for formulating the commercialization strategy for North America under the joint commercialization plan, with each of the Company and Astellas responsible for conducting fifty percent (50%) of the sales efforts and medical affairs activities in North America. Astellas will have lead responsibility for commercialization activities in Europe under the joint commercialization plan, with each of the Company and Astellas responsible for conducting fifty percent (50%) of the medical affairs activities in the major European countries. All costs associated with each party's conduct of development and commercialization activities (including clinical manufacturing and commercial manufacturing costs, if any) in North America and Europe, and any resulting profits or losses, will be shared equally between the parties.

Under the Astellas Agreement, the Company received an initial cash payment of \$125 million, comprised of a \$75 million license fee and \$50 million in research and development funding. The Company retained net proceeds of approximately \$97.6 million of the initial cash payment from Astellas, after payments to KHK and strategic, legal and financial advisors. The Company is also eligible to receive from Astellas an aggregate of approximately \$1.3 billion in potential milestone payments, comprised of (i) up to \$85 million in substantive milestone payments upon achievement of specified clinical and development milestone events, (ii) up to \$490 million in substantive milestone payments upon achievement of specified regulatory milestone events, including up to \$90 million in milestone payments in connection with specified regulatory filings, and receipt of marketing approvals, for tivozanib to treat RCC in the United States and Europe, and (iii) up to approximately \$780 million in milestone payments upon the achievement of specified commercial sales events. The first anticipated clinical and development milestone is due to the Company upon initiation of its next phase 3 clinical trial. The timing of this milestone is uncertain, as the Company has not finalized plans for its future trials. Significant potential near-term regulatory milestones include acceptance by the FDA of the first filing of an NDA for RCC (monotherapy) (\$15 million) and acceptance by the European Medicines Agency of the first filing of a Marketing Authorization Application (\$15 million). In addition, if tivozanib is successfully developed and launched in the Royalty Territory, Astellas will be required to pay to AVEO tiered, double digit royalties on net sales of tivozanib in the Royalty Territory, if any, subject to offsets under certain circumstances. The Company is required to pay KHK low to mid-teen royalties on its net sales in North America, and 30% of certain amounts the Company may receive from Astellas in connection with Astellas' development and commercialization activities in Europe and the Royalty Territory, including up-front license fees, milestone payments and royalties.

Unless terminated earlier in accordance with its terms, the Astellas Agreement expires (a) with respect to the Royalty Territory, on a country-by-country basis, upon the latest to occur of: (i) the expiration of the last-to-expire valid claim of an AVEO patent or joint patent covering the composition of tivozanib, (ii) the expiration of the last-to-expire valid claim of an AVEO patent or joint patent covering the use of tivozanib, but

**Table of Contents**

only for so long as no generic competition exists in such country, and (iii) twelve years from first commercial sale of tivozanib in such country, and (b) with respect to North America and Europe as a whole, upon the expiration of all payment obligations between the parties related to development and commercialization of tivozanib in North America and Europe. After the second anniversary of the effective date of the Astellas Agreement, Astellas has the right to terminate the Astellas Agreement, in its entirety or solely with respect to the Royalty Territory, at any time upon 180 days prior written notice to the Company. Either party may terminate the Astellas Agreement with respect to a specified territory or country as set forth in the Astellas Agreement, if the other party fails to cure a material breach related to such territory or country, as applicable. The Company may also terminate the Astellas Agreement in its entirety upon a patent-related challenge by Astellas, its affiliates or sublicensees, if such patent-related challenge is not withdrawn within 30 days following the Company's notice to Astellas of such termination. There are no refund provisions in the Astellas Agreement.

The Company is accounting for the joint development and commercialization activities in North America and Europe as a joint risk sharing collaboration in accordance with ASC 808, *Collaborative Arrangements*. In addition, these activities were not deemed to be separate deliverables under the Astellas Agreement.

Payments from Astellas with respect to Astellas' share of tivozanib development and commercialization costs incurred by the Company pursuant to the joint development plan are recorded as a reduction to research and development expense and general and administrative expense in the accompanying consolidated financial statements due to the joint risk sharing nature of the activities in North America and Europe. As a result of the cost-sharing provisions in the Astellas Agreement, the Company reduced research and development expense by \$26.7 million during the year ended December 31, 2011, and general and administrative expense by \$1.2 during the year ended December 31, 2011. The net amount due to the Company from Astellas pursuant to the cost-sharing provisions is \$6.4 million at December 31, 2011.

Activities under the Astellas Agreement outside of the joint development and commercialization activities in North America and Europe, including the co-exclusive license to develop and commercialize tivozanib in North America and Europe that was delivered prior to the initiation of the collaborative activities in North America and Europe, were evaluated under ASC 605-25 (as amended by ASU 2009-13) to determine if they represented a multiple element revenue arrangement. The Astellas Agreement includes the following deliverables: (1) a co-exclusive license to develop and commercialize tivozanib in North America and Europe (the License Deliverable); (2) a combined deliverable comprised of an exclusive royalty-bearing license to develop and commercialize tivozanib in the Royalty Territory and the Company's obligation to provide access to clinical and regulatory information resulting from the activities in North America and Europe to Astellas for its development and commercialization of tivozanib in the Royalty Territory (the Royalty Territory Deliverable); and (3) the Company's obligation to supply clinical material to Astellas for development of tivozanib in the Royalty Territory (the Clinical Material Deliverable). The License Deliverable is not sublicensable. Astellas has the right to sublicense the exclusive royalty-bearing license to develop tivozanib in the Royalty Territory. The Company's obligation to provide access to clinical and regulatory information as part of the Royalty Territory Deliverable includes the obligation to provide access, upon request, to all clinical data, regulatory filings, safety data and manufacturing data to Astellas for use in the development of tivozanib in the Royalty Territory. The Clinical Material Deliverable includes the obligation to supply clinical material to Astellas in accordance with current good manufacturing practices applicable to clinical materials and other relevant regulatory authority requirements, upon request, for the development of tivozanib in the Royalty Territory. All of these deliverables were deemed to have stand-alone value and to meet the criteria to be accounted for as separate units of accounting under ASC 605-25. Factors considered in this determination included, among other things, the subject of the licenses and the research and development and commercial capabilities of Astellas.

The Company allocated the up-front consideration of \$125 million to the deliverables based on management's best estimate of selling price of each deliverable using the relative selling price method as the Company did not have VSOE or TPE of selling price for such deliverables. The Company's best estimate of selling price considered discounted cash flow models, the key assumptions of which included the market

---

**Table of Contents**

opportunity for commercialization of tivozanib in North America and Europe and the Royalty Territory, the probability of successfully developing and commercializing tivozanib, the remaining development costs for tivozanib, and the estimated time to commercialization of tivozanib. The Company's analysis included the following market conditions and entity-specific factors: (a) the specific rights provided under the license to develop and commercialize tivozanib in North America and Europe and the Royalty Territory, (b) the potential indications for tivozanib pursuant to the licenses, (c) the relevant territories for the respective licenses, (d) the stage of development of tivozanib by potential indication and estimated remaining development timelines and costs for each indication, (e) the development risk by indication, (f) the market size by indication, (g) the expected product life of tivozanib assuming commercialization and (h) the competitive environment. More specifically, the Company's discounted cash flow model included an assumption that the Company and Astellas would develop and commercialize tivozanib in North America and Europe as a monotherapy for RCC, and in combination with other known anti-cancer agents for RCC, breast cancer and colorectal cancer. Approximately 70% of the value of tivozanib in the discounted cash flow model was a result of the estimated market opportunity for tivozanib as a monotherapy for RCC. The market opportunity for commercialization of tivozanib in North America and Europe was generated using a patient-based forecasting approach, with key epidemiological, market penetration, dosing, compliance, length of treatment, and pricing assumptions derived from primary and secondary market research. While the RCC monotherapy opportunity represented the majority of the market opportunity, clinical trials for tivozanib in the breast cancer and colorectal cancer indications were in earlier stages of development and therefore had more development risk and were assigned a lower probability of success relative to the RCC indication, with a longer timeline to potential cash inflows. The probability of successfully developing and commercializing tivozanib in the various indications throughout the world (other than Asia) was estimated based on standard industry averages for similar product candidates being developed for oncology indications. The remaining development costs were estimated based upon budgets and estimated costs for ongoing and planned clinical trials in all contemplated indications. The time to commercialization was based on the Company's estimates, which projected the launch of tivozanib for RCC monotherapy in 2013. The market opportunity for the Royalty Territory was estimated based upon a specified percentage of total projected European sales and costs of tivozanib. The Company believes that this method for estimating market opportunity outside of North America, Europe and Asia is common in the pharmaceuticals industry. The Company utilized a discount rate of 15% in its analysis, representing the weighted average cost of capital derived from returns on equity for comparable companies.

The Company concluded that a change in the key assumptions used to determine best estimate of selling price for each license deliverable would not have a significant effect on the allocation of arrangement consideration.

The Company allocated up-front consideration of \$120.2 million to the License Deliverable and up-front consideration of \$4.8 million to the Royalty Territory Deliverable. The relative selling price of the Company's obligation under the Clinical Material Deliverable had *de minimus* value.

The Company recorded the \$120.2 million relative selling price of the License Deliverable as collaboration revenue during the three months ended March 31, 2011 upon delivery of the license, and deferred approximately \$4.8 million of revenue representing the relative selling price of the Royalty Territory Deliverable. The Company is recording the \$4.8 million of revenue attributed to the Royalty Territory Deliverable ratably over the Company's period of performance through April 2022, the remaining patent life of tivozanib. The Company estimated the period of performance considering that the Company and Astellas plan to develop tivozanib in several indications outside of RCC, including in breast cancer and colorectal cancer and potentially in other cancer indications. The clinical development of tivozanib in these indications is in earlier stages of development and, as a result, the clinical development timeline is uncertain and is expected to change as the Company obtains additional clinical data in these indications. As a result, the Company estimated the period of performance as the remaining patent life of tivozanib as it represents the longest period over which development of tivozanib could occur. The Company reassesses the period of performance at each reporting period. The Company recorded

**Table of Contents**

approximately \$376,000 of revenue during the year ended December 31, 2011 associated with the Royalty Territory Deliverable.

The Company believes the clinical and development and regulatory milestones that may be received under the Astellas Agreement are consistent with the definition of a milestone included in ASU 2010-17 and, accordingly, the Company will recognize payments related to the achievement of such milestones, if any, when such milestone is achieved. Factors considered in this determination included scientific and regulatory risks that must be overcome to achieve each milestone, the level of effort and investment required to achieve each milestone, and the monetary value attributed to each milestone. The Company did not recognize any milestone payments under the Astellas arrangement during the year ended December 31, 2011.

The adoption of ASU 2009-13 on January 1, 2011 materially affected the Company's accounting for the Astellas Agreement. Prior to the adoption of ASU 2009-13, the Royalty Territory Deliverable would not have met the criteria to be considered a separate unit of accounting because neither VSOE nor TPE of fair value exists for this deliverable. Accordingly, the entire arrangement consideration of \$125 million would have been deferred at the inception of the arrangement and recognized ratably over the Company's period of performance through April 2022, the remaining patent life of tivozanib. If the Astellas Agreement had been accounted for prior to the adoption of ASU 2009-13, the Company would have recognized revenue of \$9.8 million during the year ended December 31, 2011.

*Centocor Ortho Biotech Inc. (Centocor)*

In May 2011, the Company entered into an exclusive license agreement (the "Centocor License Agreement") with Centocor Ortho Biotech Inc. ("Centocor"), for the worldwide development and commercialization of the Company's internally-discovered antibodies targeting the RON receptor (Recepteur d'Origine Nantais), including the grant to Centocor of an exclusive, worldwide license to the Company's proprietary RON-driven tumor models. The Company also granted Centocor a nonexclusive, non-sublicensable, worldwide license to the Company's proprietary list of human genes intended to predict correlation of response to RON-targeted antibodies, (the "RON index"). Centocor is responsible for all clinical development, manufacturing and commercialization activities and costs. Subject to an agreed-upon research plan and budget, Centocor will also fund certain research for a three-year term to be conducted by the Company, including translational research studies using the Company's proprietary Human Response Platform to identify biomarkers for patients most likely to benefit from treatment with RON targeted antibodies.

In connection with the Centocor License Agreement, the Company received a one-time cash payment in the amount of \$7.5 million and a separate equity investment in the amount of approximately \$7.5 million through the purchase by Johnson & Johnson Development Corporation, an affiliate of Centocor, of 438,340 newly issued shares of the Company's common stock at a purchase price of \$17.11 per share. Milestone payments for the successful development and commercialization of a RON-targeted antibody, if all approvals in multiple indications and all sales milestones are achieved, could total, in the aggregate, \$540 million, comprised of (i) up to \$40 million in substantive milestone payments upon achievement of specified clinical and development milestone events, (ii) up to \$165 million in substantive milestone payments upon achievement of specified regulatory milestone events in connection with specified regulatory filings, and receipt of marketing approvals, and (iii) up to \$335 million in milestone payments upon the achievement of specified sales events. The Company could earn the first clinical and development milestone of \$2 million under the Centocor License Agreement upon the selection of a lead antibody for entry into pre-clinical studies, with respect to the first licensed product under the agreement. The Company expects to achieve this milestone during the year ending December 31, 2012. Upon commercialization, the Company is eligible to receive tiered double-digit royalty payments on Centocor's net sales of any RON-targeted antibody, as a percentage of net sales. Centocor's royalty obligations in a particular country begin on the date of first commercial sale of a product in that country, and end on the later of 10 years after the date of first commercial sale of the product in that country or the date of the last to expire of the issued patents covering the product in that country. All milestone payments and royalties will be reduced by a

**Table of Contents**

certain percentage if Centocor develops or commercializes a RON-targeted antibody which has incorporated significant, meaningful improvements made after a specified period by Centocor to the antibodies delivered by the Company. The royalties will also be reduced by a certain percentage on a country-by-country basis upon the entry of a generic competitor.

The Centocor License Agreement will remain in effect until the expiration of all of Centocor's royalty obligations to the Company, determined on a product-by-product and country-by-country basis. Prior to the filing of an investigational new drug application with the FDA or a similar application filed with another regulatory authority outside of the United States (IND Submission), Centocor has the right to terminate the Centocor License Agreement at will upon 90 days written notice to the Company. After IND Submission, Centocor may terminate the Centocor License Agreement at will upon 180 days written notice to the Company. Either party has the right to terminate the Centocor License Agreement in connection with an insolvency event involving the other party or a material breach of the Centocor License Agreement by the other party that remains uncured for a specified cure period. In the event that Centocor terminates the Centocor License Agreement at will, or if the Company terminates the Centocor License Agreement due to Centocor's material breach or insolvency, worldwide rights to the development, manufacture, and commercialization of RON-targeted antibodies revert back to the Company. There are no refund provisions in the Centocor License Agreement.

As noted above, Johnson & Johnson Development Corporation paid \$7.5 million for 438,340 shares of the Company's common stock at a purchase price of \$17.11 per share, which reflected the average of the daily volume weighted average prices for the Company's common stock for the 30 consecutive trading days ending on May 26, 2011. This weighted average sales price of \$17.11 per share resulted in a \$1.22 per share discount from the May 31, 2011 closing price of \$18.33 per share, or a discount of \$534,775 from the fair market value of the common stock on the effective date of the Centocor License Agreement. The Company determined this transaction was not within the scope of ASC 605-25 and, accordingly, the Company recorded the sale of common stock to Johnson & Johnson Development Corporation at fair value based on the closing price of the Company's stock on May 31, 2011 of \$18.33 per share.

The remaining activities under the Centocor License Agreement were evaluated under ASC 605-25 (as amended by ASU 2009-13) to determine if they represented a multiple element revenue arrangement. The Company determined that the Centocor License Agreement included the following deliverables:

Exclusive, sublicensable commercialization and development license related to RON antibodies (the RON license);

Non-exclusive license to use the Company's RON index (the RON Index license); and

The Company's obligation to provide research services.

The Company determined that each deliverable had stand-alone value upon delivery and therefore represents a separate unit of accounting. Factors considered in this determination included, among other things, the subject of the licenses and the research and development and commercial capabilities of Centocor.

The Company excluded the fair value of the common stock purchased by Johnson & Johnson Development Corporation from the arrangement consideration to be allocated to the identified deliverables and allocated the remaining \$7.0 million of up-front consideration attributable to the deliverables based on the relative selling price method. The Company determined the estimated selling price for the RON license and the RON Index license based on management's best estimate of selling price as the Company did not have VSOE or TPE of selling price for those deliverables. In determining its best estimate of selling price for the RON license and the RON Index license, the Company considered market conditions as well as entity-specific factors, including those factors contemplated in negotiating the Centocor License Agreement and internally developed revenue models. The Company's best estimate of selling price for the RON license and RON Index license considered discounted cash flow models, the key assumptions of which included the market opportunity for commercialization of a potential



## **Table of Contents**

product candidate using the RON receptor worldwide, an estimate of costs related to phase 1, 2 and 3 clinical studies with certain multiplication factors related to the probability of success, and the time to commercialization of a potential product candidate. This analysis used various assumptions that are typical for similarly staged monoclonal antibodies and other reasonable cost assumptions in determining research and development, and sales, general and administrative costs. More specifically, the Company's estimate of peak revenues was consistent with what might be expected from an approved antibody product. Other key assumptions included: cost of goods sold, which was assumed to be a specified percentage of revenues based on estimated cost of goods sold of a typical oncology antibody product; clinical trial costs, which were based on estimated clinical costs for a single phase 1 safety study, followed by phase 2 and 3 studies for a single oncology indication; and sales and marketing costs, which were based on the costs required to field an oncology sales force and marketing group, including external costs required to promote an oncology product. The factors used to estimate the probability of success and the time to commercialization of a product candidate were based on standard industry averages for antibodies being developed for oncology indications. The results of the Company's analysis indicated an estimated selling price for the licenses of approximately \$39 million. The analysis used a weighted average cost of capital of 15% derived from returns on equity for comparable companies.

With respect to the research services, the Company considered the nature of the research services to be provided (basic translational research related to a pre-clinical, antibody-based technology) and the fact that other vendors could provide the research services. As a result, the Company concluded that TPE of selling price exists for the research services deliverable. In supporting TPE of selling price, the Company considered the nature of the research services, the rates charged by vendors in the marketplace for similar services and rates charged by the Company for other non-complex, pre-clinical research services in its other license and development agreements.

As the relative selling price of the RON license and RON Index license (the delivered items) exceeds the up-front consideration attributable to the deliverables of \$7.0 million, the entire up-front payment was recognized as revenue upon delivery of the licenses during the three months ended June 30, 2011. The Company concluded that a change in the assumptions used to determine estimated selling price for the units of accounting would not have a significant effect on the allocation of arrangement consideration.

The Company will record revenue related to research and development services as the services are delivered at the contractual rate, which approximates fair value for those services.

The Company may be entitled to receive future milestone payments totaling \$540 million. The Company's accounting policy is to recognize all milestone payments as revenue once the milestones have been triggered if the milestone is deemed to be substantive. The Company believes the clinical and development and regulatory that may be received under the Centocor License Agreement are consistent with the definition of a milestone included in ASU 2010-17 and, accordingly, the Company will recognize payments related to the achievement of such milestones, if any, when such milestone is achieved. Factors considered in this determination included scientific and regulatory risks that must be overcome to achieve each milestone, the level of effort and investment required to achieve each milestone, and the monetary value attributed to each milestone. The Company did not recognize any milestone payments under this arrangement during the year ended December 31, 2011.

Under the agreement, the Company received cash payments related to upfront license fees, reimbursable payments, and equity of \$16.3 million for the year ended December 31, 2011, and recorded revenue of \$8.8 million for the year ended December 31, 2011.

The adoption of ASU 2009-13 did not materially affect the Company's accounting for the Centocor License Agreement.

---

**Table of Contents***Merck (Formerly Schering-Plough Corporation)*

In March 2007, the Company entered into an agreement with Schering-Plough Corporation, or Schering-Plough (now Merck & Co., Inc., or Merck), through its subsidiary Schering Corporation, acting through its Schering-Plough Research Institute division, under which the Company granted Merck exclusive, worldwide rights to develop and commercialize all of the Company's monoclonal antibody antagonists of hepatocyte growth factor, or HGF, including ficlatuzumab, for therapeutic and prophylactic use in humans and for veterinary use. The Company also granted Merck an exclusive, worldwide license to related biomarkers for diagnostic use. The Company also conducted translational research using its Human Response Platform to guide the clinical development of ficlatuzumab. Merck was responsible for all costs related to the clinical development of ficlatuzumab and clinical and commercial manufacturing. On September 28, 2010, the Company received notice from Merck of termination of the collaboration agreement effective as of December 27, 2010, at which point the Company became responsible for the performance and funding of all future research, development, manufacturing and commercialization activities for ficlatuzumab.

Under the agreement, Merck paid the Company an up-front payment of \$7.5 million in May 2007, which was being amortized over the Company's period of substantial involvement, which was initially estimated to be through completion of the first phase 2 proof-of-concept trial for ficlatuzumab (which was expected to be the first half of 2012), but was adjusted to reflect the termination of the agreement effective on December 27, 2010. In addition, Merck purchased 4,000,000 shares of the Company's series D convertible preferred stock, at a per share price of \$2.50, resulting in gross proceeds to the Company of \$10.0 million. The amount paid for the series D convertible preferred stock represented fair value as it was the same as the amounts paid by unrelated investors in March and April 2007. In connection with the initial public offering which the Company consummated in March 2010, and the related 1:4 reverse stock split of the Company's common stock, each four shares of outstanding series D convertible preferred stock were converted into one share of common stock.

In June 2010, the Company earned and received an \$8.5 million milestone payment in connection with the enrollment of patients in the Company's phase 2 clinical trial of ficlatuzumab under the agreement. Since the \$8.5 million milestone payment earned in June 2010 and was considered substantive, it was included in revenue for the year ended December 31, 2010.

In March 2011, in connection with the transition of responsibility for the ficlatuzumab program from Merck back to the Company, the Company made a \$10.2 million payment to Merck for the purchase of a supply of ficlatuzumab to support ongoing clinical studies. The Company had taken title to a portion of this material as of March 31, 2011 and the remainder of this material as of June 30, 2011 and, pursuant to the provisions of ASC 730, recognized \$10.2 million as research and development expense during year ended December 31, 2011, when title passed to the Company.

Under the agreement, the Company received cash payments related to upfront license fees, milestone payments, research and development funding, and equity of \$19.8 million, and \$10.6 million, and recorded revenue of \$22.5 million, and \$10.9 million, for the years ended December 31, 2010 and 2009, respectively. The Company did not receive and cash or record any revenue under the agreement during the year ended December 31, 2011. As a result of adjusting the period of substantial involvement to reflect the termination of the agreement effective on December 27, 2010, the Company recognized revenue of \$1.9 million for the year ended December 31, 2010 that would have been recognized in future periods had Merck not terminated the agreement.

*OSI Pharmaceuticals Inc. (OSI)*

In September 2007, the Company entered into a collaboration and license agreement with OSI Pharmaceuticals, Inc., (a wholly-owned subsidiary of Astellas US Holding Inc., a holding company owned by Astellas Pharma Inc.) or OSI, which provided for the use of the Company's proprietary *in vivo* models by the Company's scientists at its facilities, use of the Company's bioinformatics tools and other target validation and

---

**Table of Contents**

biomarker research to further develop and advance OSI's small molecule drug discovery and translational research related to cancer and other diseases. In July 2009, the Company and OSI expanded the strategic partnership, and the Company granted OSI a non-exclusive license to use the Company's proprietary bioinformatics platform, and non-exclusive perpetual licenses to use bioinformatics data and the Company's proprietary gene index related to a specific target pathway. Further, as part of the expanded strategic partnership, the Company granted OSI an option, exercisable upon payment of an option fee, to receive non-exclusive perpetual rights to certain elements of the Company's Human Response Platform and to use the Company's bioinformatics platform, and the Company granted OSI the right to obtain certain of its tumor models and tumor archives.

The Company accounts for the OSI arrangement pursuant to ASC 605-25. The deliverables under the arrangement include use of the Company's proprietary *in vivo* models, research and development services provided using the Company's proprietary *in vivo* models by the Company's scientists at its facilities, use of the Company's bioinformatics tools and other target validation and biomarker research to further develop and advance OSI's small molecule drug discovery, translational research related to cancer and other diseases and a non-exclusive license to use the Company's proprietary bioinformatics platform, and non-exclusive perpetual licenses to use bioinformatics data and a Company proprietary gene index related to a specific target pathway. Since these services were provided using the Company's proprietary technology, management concluded the arrangement should be accounted for as a single unit of accounting.

Under the agreement, OSI paid the Company an up-front payment of \$7.5 million, which was recorded in deferred revenue and was amortized over the Company's period of substantial involvement, which ended in July 2011 (the date the Company satisfied its performance obligations under the OSI arrangement). OSI also paid the Company \$2.5 million for the first year of research program funding, which was recorded in deferred revenue and was recognized as revenue over the performance period and, thereafter, OSI made research payments of \$625,000 per quarter through July 2009. In addition, OSI purchased 1,833,334 shares of Series C Convertible Preferred Stock, at a per share price of \$3.00, resulting in gross proceeds to the Company of \$5.5 million. The Company determined that the price paid of \$3.00 per share by OSI included a premium of \$0.50 over the price per share of the Company's Series D Convertible Preferred Stock sold in April 2007; accordingly, the Company recognized the premium of \$917,000 as additional license revenue on a straight-line basis over the period of substantial involvement. In connection with the initial public offering consummated by the Company in March 2010 and the related 1:4 reverse stock split of the common stock, each four shares of outstanding Series C Convertible Preferred Stock were converted into one share of common stock.

In consideration for the additional rights provided for pursuant to the July 2009 expanded agreement, OSI paid the Company an up-front payment of \$5.0 million, which was recorded in deferred revenue and was amortized over the Company's remaining period of substantial involvement, which ended in July 2011. OSI also agreed to fund research costs through June 30, 2011. In addition, OSI purchased 3,750,000 shares of Series E Convertible Preferred Stock, at a per share price of \$4.00, resulting in gross proceeds to the Company of \$15.0 million. In connection with the initial public offering consummated by the Company in March 2010 and the related 1:4 reverse stock split of the common stock, each four shares of outstanding Series E Convertible Preferred Stock were converted into one share of common stock. The Company determined that the price of \$4.00 per share paid by OSI included a premium of \$1.04 per share over the fair value of the Series E Convertible Preferred Stock of \$2.96 as calculated by the Company in its retrospective stock valuation. Accordingly, the Company recognized the premium of \$3,900,000 as additional license revenue on a straight-line basis over the period of substantial involvement, which ended in July 2011.

Under the July 2009 expanded agreement, if all applicable milestones are achieved, payments for the successful achievement of discovery, development and commercialization milestones could total, in the aggregate, over \$94.0 million for each target and its associated products, comprised of (i) up to \$17.6 million in substantive milestone payments upon achievement of specified clinical and development milestone events, (ii) up to \$41.3 million in substantive milestone payments upon achievement of specified regulatory milestone events,

---

**Table of Contents**

(iii) up to \$35.0 million in milestone payments upon the achievement of specified sales events, and (iv) up to \$250,000 in patent related milestones. The first milestone that the Company may receive pursuant to this agreement is either a patent related milestone of \$250,000 upon filing of a patent application, or a clinical and development milestone of \$750,000 for commencement of GLP toxicology studies. The timing of these milestones is uncertain.

In addition, the Company is eligible to receive up to \$24.0 million in biomarker related milestones. In March 2011, the Company earned \$1.5 million related to achieving certain of these research milestones under the agreement. These research milestones were not considered to be substantive, therefore, the \$1.5 million in payments was deferred and was recognized on a straight-line basis over the remaining estimated period of substantial involvement, which ended in July 2011. The next regulatory milestone the Company may receive pursuant to this agreement is \$7.0 million to be achieved for the filing of the NDA with the FDA. The Company does not expect to achieve this milestone in the year ending December 31, 2012. Upon commercialization of products under the agreement, the Company is eligible to receive tiered royalty payments on sales of products by OSI, its affiliates and sublicensees. All milestones earned to date are for selection of targets, delivery of models, delivery of tumor archives or delivery of cell lines.

The Company did not recognize any substantive milestone payments under this arrangement during the years ended December 31, 2011 or 2010.

In November 2010, OSI exercised its option under the July 2009 expanded agreement providing the right for OSI to license certain elements of the Company's proprietary technology platform, including components of the Human Response Platform for the identification/characterization of novel epithelial-mesenchymal transition agents and proprietary patient selection biomarkers, in support of OSI's clinical development programs. The Company did not consider the option granted to OSI in July 2009 as a deliverable as there was significant uncertainty that this option would ultimately be exercised. The Company received \$12.5 million upon delivery of the notice of option exercise, and completed the transfer of the relevant technology to OSI in July 2011. The remaining \$12.5 million was paid in July 2011 following the successful transfer of the applicable technology. The Company deferred the initial \$12.5 million payment, and recognized the full \$25.0 million relating to the option exercise by OSI over the technology transfer period, which was completed in July 2011.

The Company believes the application of the provisions of ASU 2009-13 to this arrangement would not change the units of accounting under the arrangement or the manner in which the Company recognizes revenue for the arrangement.

Under these agreements, the Company received cash payments related to upfront license fees, milestone payments, research and development funding, and equity of \$16.5 million, \$17.9 million and \$26.5 million, and recorded revenue of \$29.6 million, \$16.2 million and \$9.8 million, for the years ended December 31, 2011, 2010 and 2009, respectively.

*Biogen Idec International GmbH (Biogen Idec)*

In March 2009, the Company entered into an exclusive option and license agreement with Biogen Idec International GmbH, a subsidiary of Biogen Idec Inc., collectively referred to herein as "Biogen Idec", regarding the development and commercialization of the Company's discovery-stage ErbB3-targeted antibodies for the potential treatment and diagnosis of cancer and other diseases outside of the United States, Canada and Mexico.

The Company accounts for the Biogen Idec arrangement pursuant to ASC 605-25. The deliverables under the arrangement include an option for a co-exclusive, world-wide license to develop and manufacture ErbB3 antibody products and an option for an exclusive license to commercialize ErbB3 antibody products in all countries in the world other than the United States, Canada and Mexico. The Company determined that these deliverables did not have standalone value due to the fact that the program was still in preclinical development

**Table of Contents**

and required the Company's experience to advance development of the product. As such, the Company determined that the agreement should be accounted for as one unit of accounting.

Under the terms of the agreement, Biogen Idec paid the Company an upfront cash payment of \$5.0 million in March 2009, which is being amortized over the Company's period of substantial involvement, defined as the patent life of the development candidate. In addition, Biogen Idec purchased 7,500,000 shares of Series E Convertible Preferred Stock at a per share price of \$4.00, resulting in gross proceeds to the Company of \$30.0 million. In connection with the initial public offering consummated by the Company in March 2010 and the related 1:4 reverse stock split of the common stock, each four shares of outstanding Series E Convertible Preferred Stock were converted into one share of common stock. The Company determined that the price of \$4.00 paid by Biogen Idec included a premium of \$1.09 per share over the fair value of the Series E Convertible Preferred Stock of \$2.91 as calculated by the Company in its retrospective stock valuation. Accordingly, the Company is recognizing the premium of \$8,175,000 as revenue on a straight-line basis over the period of substantial involvement. The Company received a \$5.0 million milestone payment for achievement of the first pre-clinical discovery milestone under the agreement in June 2009 which was not considered at risk and was therefore deferred and is being recognized over the period of substantial involvement. The Company earned a second \$5.0 million milestone payment upon selection of a development candidate in March 2010. This milestone was considered substantive and was included in revenue for the quarter ended March 31, 2010. The Company earned a third \$5.0 million milestone payment based on achieving the GLP toxicology initiation milestone in June 2011. This milestone was considered substantive and was included in revenue for the quarter ended June 30, 2011. The Company could also receive an option exercise fee and regulatory milestone payments of up to \$45.0 million in the aggregate if Biogen Idec exercises its option to obtain exclusive rights to commercialize ErbB3 antibody products in its territory. The first regulatory milestone the Company may receive pursuant to this agreement of \$25.0 million is due upon the receipt of the first regulatory approval of a licensed product from the EMA. The Company does not expect to achieve this milestone in the year ending December 31, 2012.

The Company recognized milestone payments under this arrangement of \$5.0 million during the year ended December 31, 2011.

If Biogen Idec exercises its exclusive option under the agreement, Biogen Idec will pay the Company royalties on Biogen Idec's sales of ErbB3 antibody products in its territory, and the Company will pay Biogen Idec royalties on the Company's sale of ErbB3 antibody products in the United States, Canada and Mexico.

The Company believes the application of the provisions of ASU 2009-13 would not change the units of accounting under the arrangement or the manner in which the Company recognizes revenue for the arrangement.

Under the agreement, the Company received cash payments related to upfront license fees, milestone payments, and equity of \$5.0 million, \$5.0 million and \$40.0 million for the years ended December 31, 2011, 2010 and 2009, respectively, and recorded revenue of \$5.9 million and \$5.8 million for the years ended December 31, 2011, and 2010, respectively.

*(b) In-license Agreements**Kirin Brewery Co. Ltd. (KHK)*

In December 2006, the Company entered into an exclusive license agreement, with the right to grant sublicenses, subject to certain restrictions, with Kirin Brewery Co. Ltd. (now Kyowa Hakko Kirin) ( KHK ) to research, develop, manufacture and commercialize tivozanib (f/k/a KRN951), pharmaceutical compositions thereof and associated biomarkers in all territories in the world except for Asia (the KHK Agreement ). Upon entering into the KHK Agreement, the Company made a cash payment in the amount of \$5.0 million.

**Table of Contents**

Under the KHK Agreement, the Company may be required to (i) make up to an aggregate of \$50.0 million in future milestone payments upon the achievement of specified regulatory milestones, (ii) pay tiered royalty payments on net sales it makes of tivozanib in its territory ranging from the low to mid-teens as a percentage of the Company's net sales of tivozanib, and (iii) pay 30% of certain amounts the Company receives under the Astellas Agreement in connection with Astellas' development and commercialization activities in Europe and the Royalty Territory, including up-front license fees, milestone payments and royalties the Company may receive from Astellas. The Company is not obligated to make any payments to KHK in respect of research and development funding or equity investments, subject to certain limitations.

In March 2010, the Company made a \$10.0 million milestone payment to KHK in connection with the dosing of the first patient in the Company's phase 3 clinical trial of tivozanib.

The Company also recorded \$22.5 million of research and development expense in the year ended December 31, 2011 associated with the payment made to KHK related to the up-front license payment received under the Astellas Agreement.

*Other License Agreements*

The Company has entered into various cancelable license agreements for patented technology and other technology related to research projects, including technology to humanize ficlatuzumab, AV-203 and other antibody product candidates. The Company is obligated to pay annual maintenance payments of \$475,000, which are recognized as research and development expense over the maintenance period. Under one of these agreements, if the parties agree to the use of the licensed technology in development of a product, the Company will be required to make a \$1.0 million license payment per product. These agreements also include development and sales-based milestones of up to \$22.5 million, \$6.3 million and \$4.2 million per product, and single digit royalties as a percentage of sales.

Certain other research agreements require the Company to remit royalties in amounts ranging from 0.5% to 1.5% based on net sales of products utilizing the licensed technology. Total license expense incurred under these other license agreements amounted to \$0.52 million, \$0.40 million, and \$0.44 million for the years ended December 31, 2011, 2010 and 2009, respectively. The Company has not paid any royalties to date.

**8. Commitments and Contingencies***Operating Leases*

The Company leases office and lab space and equipment under various operating lease agreements. Rent expense under the operating leases amounted to \$2.7 million, \$2.2 million and \$2.2 million for the years ended December 31, 2011, 2010 and 2009, respectively.

In July 2004, the Company entered into a sublease agreement with Millennium Pharmaceuticals, Inc., to sublease 55,200 square feet of office and lab space located at 75 Sidney Street in Cambridge, MA. The sublease will expire on February 28, 2014. In conjunction with the signing of this lease, the Company entered into a standby letter of credit in the amount of \$552,000 to expire on July 12, 2005, subject to automatic extensions for periods of one year as a security deposit on said lease. The letter of credit has been collateralized by a money market account held by the bank which issued the letter of credit and has been automatically extended through July 12, 2012. The Company has classified this money market account within restricted cash on its balance sheets at December 31, 2011 and 2010. The Company received six free months of rent under this arrangement and has recorded rent on a straight-line basis over the lease term resulting in deferred rent of approximately \$547,000, and \$799,000 at December 31, 2011 and 2010, respectively.

In September 2008, the Company entered into a sublease agreement with Alkermes, Inc., to sublease 7,407 square feet of office space located at 64 Sidney Street in Cambridge, MA. The sublease will expire on April 30,

**Table of Contents**

2012. Additionally, in September 2011, the Company entered into a lease agreement with UP 64 Sidney, LLC, to lease the same 7,407 square feet of office space located at 64 Sidney Street in Cambridge, MA. This lease commences on the earlier of the termination of the Company's sublease with Alkermes, Inc. on May 1, 2012 or the termination of the master lease between Alkermes, Inc. and the landlord, and will expire on February 28, 2014. In conjunction with the lease, the Company entered into a standby letter of credit in the amount of \$42,590, and will expire on March 30, 2013, subject to an automatic extension period of one year related to the term of the sublease. The letter of credit has been collateralized by a money market account held by the bank which issued the letters of credit. The Company has classified these money market accounts within restricted cash on its balance sheets at December 31, 2011 and 2010. The Company received six free weeks of rent under the sublease with Alkermes and has recorded rent on a straight-line basis over the lease term resulting in deferred rent of approximately \$15,700 and \$20,200 at December 31, 2011 and 2010, respectively.

On February 28, 2011, the Company entered into a sublease agreement with Acceleron Pharma, Inc. to sublease 14,214 square feet of office space located at 12 Emily Street in Cambridge, MA. The sublease will expire on May 30, 2015. In conjunction with the lease, the Company entered into a standby letter of credit in the amount of \$97,129 which will expire on May 31, 2012 subject to automatic extensions for periods of one year related to the term of the sublease. The letter of credit has been collateralized by a money market account held by the bank which issued the letter of credit. The Company has classified the money market account within restricted cash on its balance sheet at December 31, 2011. This sublease has scheduled increases over the period of the lease and the Company has recorded rent on a straight-line basis over the lease term resulting in deferred rent of approximately \$34,100 at December 31, 2011.

On November 4, 2011, the Company entered into a lease agreement with the Massachusetts Institute of Technology, to lease an additional 11,500 square feet of office space located at 12 Emily Street in Cambridge, MA. The lease commenced on December 15, 2011 and will expire on February 28, 2014. Subject to the terms of the lease, the Company may extend the term until May 31, 2015. In conjunction with the lease, the Company entered into a standby letter of credit in the amount of \$46,000 which will expire on April 29, 2013, subject to an automatic extension period of one year related to the term of the sublease. The letter of credit has been collateralized by a money market account held by the bank which issued the letter of credit. The Company has classified the money market account within restricted cash on its balance sheet at December 31, 2011. As part of this lease, the Company obtained a tenant improvement allowance in the amount of \$115,000 to be used for costs incurred by the tenant for the tenant's work. The Company used approximately \$60,000 of this allowance as of December 31, 2011. The Company also received six free weeks of rent under this arrangement and has recorded rent on a straight-line basis over the lease term, as well as the portion of the tenant improvement allowance used as of December 31, 2011, resulting in deferred rent of approximately \$83,713 at December 31, 2011.

Future annual minimum lease payments under all noncancelable operating leases at December 31, 2011 are as follows (amounts in thousands):

<b>Years Ending December 31:</b>	
2012	\$ 3,306
2013	3,339
2014	1,044
2015	241
	<b>\$ 7,930</b>

*Employment Agreements*

Certain key executives are covered by severance and change in control agreements. Under these agreements, if the executive is terminated without cause or if the executive terminates his employment for good reason, such executive will be entitled to receive severance equal to his base salary, benefits and prorated bonuses for a period

**Table of Contents**

of time equal to either 12 months or 18 months, depending on the terms of such executive's individual agreement. In addition, in December 2007, the Company approved a key employee change in control severance benefits plan, which was amended in November 2009, and which provides for severance and other benefits under certain qualifying termination events upon a change in control for a period of time ranging from 6 months to 18 months, depending on the position of the key employee.

**9. Income Taxes**

The Company accounts for income taxes under the provisions of ASC 740. For the year ended December 31, 2011, the Company did not have any federal or state income tax expense as it was able to utilize net operating loss carryforwards (NOLs) to fully offset taxable income in all filing jurisdictions. For the tax year ended December 31, 2010, the Company did not have any federal or state tax expense given its continued net operating loss position. The Company recorded a tax benefit for the year ended December 31, 2009 in the amount of \$100,056 representing a current benefit for federal income taxes related to certain refundable credits.

A reconciliation of the expected income tax benefit computed using the federal statutory income tax rate to the Company's effective income tax rate is as follows for the years ended December 31, 2011, 2010 and 2009:

	December 31, 2011	December 31, 2010	December 31, 2009
Income tax computed at federal statutory tax rate	34.0%	34.0%	34.0%
State taxes, net of federal benefit	5.3%	5.3%	6.3%
Research and development credits	(5.1)%	2.5%	2.5%
Permanent differences	2.8%	(0.3)%	(1.0)%
Other	0.3%	(3.5)%	%
Change in valuation allowance	(37.3)%	(38.0)%	(41.6)%
<b>Total</b>	<b>0.0%</b>	<b>0.0%</b>	<b>0.2%</b>

Prior to 2011, the Company had incurred net operating losses from inception. At December 31, 2011, the Company had domestic federal and state net operating loss carryforwards of approximately \$164.4 million and \$112.8 million, respectively, available to reduce future taxable income, which expire at various dates. The federal net operating loss carryforwards expire beginning in 2022 through 2030 and the state loss carryforwards begin to expire in 2012 and continue through 2030. The Company also had federal and state research and development tax credit carryforwards of approximately \$5.8 million and \$3.1 million, respectively, available to reduce future tax liabilities and which expire at various dates. The federal credits expire beginning in 2022 through 2031 and the state credits begin to expire in 2014. The net operating loss and research and development carryforwards are subject to review and possible adjustment by the Internal Revenue Service and may be limited in the event of certain changes in the ownership interest of significant stockholders.

The Company's net deferred tax assets as of December 31, 2011 and 2010 are as follows:

	2011	2010
	(in thousands)	
NOL carryforwards	\$ 61,854	\$ 70,880
Research and development credits	7,892	6,321
Deferred revenue	8,240	13,042
Other temporary differences	4,704	3,898
Valuation allowance	(82,690)	(94,141)
	\$	\$

A full valuation allowance has been recorded in the accompanying consolidated financial statements to offset these deferred tax assets because the future realizability of such assets is uncertain. This determination is





**Table of Contents**

based primarily on historical losses without considering the impact of any potential upturn in the Company's business. Accordingly, future favorable adjustments to the valuation allowance may be required, if and when circumstances change. The valuation allowance decreased by \$11.5 million during 2011, primarily due to utilization of net operating loss carryforwards.

As of December 31, 2011, the Company had federal and state net operating losses of approximately \$3.7 million related to excess tax deductions that have been excluded from the above table. The benefit of these net operating losses will be recognized as an increase in additional paid in capital when it results in a reduction in taxable income.

In June 2006, FASB issued Interpretation No. 48, *Accounting for Uncertainty in Income Taxes, an interpretation of FAS 109* (codified within ASC 740, *Income Taxes*), which provides a comprehensive model for the financial statement recognition, measurement, presentation and disclosure of uncertain tax positions taken or expected to be taken in income tax returns. Unrecognized tax benefits represent tax positions for which reserves have been established. The Company adopted this new accounting guidance on January 1, 2009. At the adoption date of January 1, 2009, the Company had \$1.2 million of unrecognized tax benefits. A full valuation allowance has been provided against the Company's deferred tax assets, so that the effect of the unrecognized tax benefits is to reduce the gross amount of the deferred tax asset and the corresponding valuation allowance. Therefore, there is no effect of adopting this guidance. Since the Company has incurred net operating losses since inception, it has never been subject to a revenue agent review. As a result, all periods since inception remain subject to examination by U.S. federal and Massachusetts tax jurisdictions.

The Company may from time to time be assessed interest or penalties by major tax jurisdictions. The Company recognizes interest and penalties related to uncertain tax positions in income tax expense. No interest and penalties have been recognized by the Company to date.

The Company anticipates that the amount of unrecognized tax benefits recorded will not change in the next twelve months.

The following is a reconciliation of the Company's gross uncertain tax positions at December 31, 2011 and 2010:

	Year ended December 31, 2011	Year ended December 31, 2010
	(in thousands)	
Amount established upon adoption	\$ 1,200	\$ 1,200
Additions for current year tax positions		
Additions for prior year tax positions		
Reductions of prior year tax positions		
Balance as of end of year	\$ 1,200	\$ 1,200

*Qualifying Therapeutic Discovery Project Grants*

On October 29, 2010, the Company received notification from the Internal Revenue Service that it had been awarded three separate grants in the aggregate amount of \$733,438 pursuant to the qualifying therapeutic discovery grant program established by the Internal Revenue Service and the Secretary of Health and Human Services under the Patient Protection and Affordable Care Act of 2010. The grants were made with respect to certain of the Company's qualifying research and development programs. The Company received the full amount related to these grants during the fourth quarter of 2010, and this amount was recorded as other income in the statement of operations for the year ended December 31, 2010.

**Table of Contents****10. Warrants and Common Stock**

As of December 31, 2011, the Company had 100,000,000 authorized shares of common stock, \$0.001 par value, of which 43,253,961 shares were issued and outstanding.

As of December 31, 2011, the Company had the following warrants outstanding:

	Number of Shares	Exercise Price	Expiration Date
Common Stock	10,000	\$ 6.50	2013
	10,000		

*Reverse Stock Split*

On February 2, 2010, the Company's Board of Directors, and on February 11, 2010, the Company's stockholders, approved a 1-for-4 reverse stock split of the Company's common stock. The reverse stock split was effected on February 18, 2010. All share and per share amounts in the condensed consolidated financial statements have been retroactively adjusted for all periods presented to give effect to the reverse stock split, including reclassifying an amount equal to the reduction in par value to additional paid-in capital.

*Initial Public Offering*

In March 2010, the Company raised \$81.0 million in gross proceeds from the sale of 9,000,000 shares of its common stock in an initial public offering at \$9.00 per share. The net offering proceeds after deducting approximately \$3.1 million in offering related expenses and underwriters discounts were approximately \$72.2 million. In March 2010, the underwriters of the initial public offering exercised their option to purchase, and in April 2010, the Company closed the sale to such underwriters of an additional 968,539 shares of common stock at \$9.00 per share resulting in additional net proceeds to the Company of approximately \$8.1 million. All outstanding shares of the Company's convertible preferred stock were converted into 18,979,155 shares of common stock upon the completion of the initial public offering.

*Private Placement*

On October 28, 2010, the Company entered into a definitive agreement with respect to the private placement of 4.5 million shares of its unregistered common stock at \$13.50 per share to a group of institutional and accredited investors. The Company completed the private placement on November 3, 2010, resulting in approximately \$56.6 million in net proceeds to the Company.

On May 31, 2011, the Company entered into a definitive agreement with respect to the sale of 438,340 shares of its unregistered common stock at \$17.11 per share to Johnson & Johnson Development Corporation in connection with the Centocor license agreement. The Company completed the private placement on May 31, 2011, resulting in approximately \$7.5 million in proceeds to the Company.

*Follow-on Offering*

In June 2011, the Company raised \$100.6 million in gross proceeds from the sale of 5,750,000 shares of its common stock in a follow-on public offering at \$17.50 per share. In June 2011, the underwriters of the public offering exercised their option to purchase an additional 602,119 shares of common stock at \$17.50 per share resulting in additional gross proceeds to the Company of approximately \$10.5 million. The combined net offering proceeds after deducting approximately \$7.0 million in offering related expenses and underwriters' discounts and commissions were approximately \$104.2 million.

**Table of Contents****11. Employee Stock Purchase Plan**

On February 2, 2010, the Board of Directors adopted the 2010 Employee Stock Purchase Plan (the "ESPP") pursuant to which the Company may sell up to an aggregate of 250,000 shares of Common Stock. The ESPP was approved by the Company's stockholders on February 11, 2010. The ESPP allows eligible employees to purchase common stock at a price per share equal to 85% of the lower of the fair market value of the common stock at the beginning or end of each six month period during the term of the ESPP. The first offering period began on July 1, 2010. Pursuant to the ESPP, the Company sold a total of 57,187 shares of common stock during the year ended December 31, 2011 at purchase prices of \$12.64 and \$14.62, respectively, which represent 85% of the closing price of the Company's stock on January 3, 2011 and December 30, 2011, respectively. Pursuant to the ESPP, the Company sold a total of 46,565 shares of common stock during the year ended December 31, 2010 at a purchase price of \$5.92, which represents 85% of the closing price of the Company's stock on July 1, 2010. The total stock-based compensation expense recorded as a result of the ESPP was approximately \$292,000 and \$99,000 during the years ended December 31, 2011 and 2010, respectively.

**12. Stock-Based Compensation**

The Company maintains the 2010 Stock Incentive Plan (the "Plan") for employees, consultants, advisors, and directors. The Plan provides for the grant of incentive and nonqualified stock options and restricted stock grants. The Plan also provides for the issuance of shares of common stock as determined by the Board.

On February 15, 2011, the Company's Board of Directors adopted amendment no. 1 to the Plan that became effective upon its approval by the Board to increase the size of options granted to newly elected Board members. Also on February 15, 2011, the Company's Board of Directors adopted amendment no. 2 to the Plan to increase the number of shares of common stock reserved for issuance under the Plan by 3,000,000 which amendment was approved by the Company's stockholders on June 1, 2011. Pursuant to amendment no. 2, the number of shares of the Company's common stock reserved for issuance under the Plan is the sum of (i) 4,875,000 and (ii) the number of shares of common stock subject to awards granted under the Company's 2002 Stock Incentive Plan which expire, terminate or are otherwise surrendered, cancelled, forfeited or repurchased by the Company at their original issuance price pursuant to a contractual repurchase right, up to a maximum of 5,500,000 shares.

On April 12, 2011, the Company's Board of Directors approved an amendment no. 3 to the Plan that became effective upon its approval by the Board, to include the following provisions:

restrictions on repricing, within the meaning of the rules of the NASDAQ Stock Market, any stock option or stock appreciation rights, or SARs, award unless such action is approved by the Company's stockholders;

minimum vesting provisions with respect to certain awards granted under the Plan;

a maximum limit on the aggregate number of shares that may be granted as awards other than options; and

revised share counting rules that prohibit the recycling of shares that are tendered or withheld to pay the exercise price of an award or to satisfy tax withholding obligations.

The Company has reserved 5,039,003 shares of common stock under the Plan, and at December 31, 2011, the Company has 3,469,908 shares available for future issuance under the Plan. Shares issued upon exercise of options are generally issued from new shares of the Company. The Plan provides that the exercise price of incentive stock options cannot be less than 100% of the fair market value of the common stock on the date of the award for participants who own less than 10% of the total combined voting power of stock of the Company and not less than 110% for participants who own more than 10% of the total combined voting power of the stock of the Company. Options and restricted stock granted under the Plan vest over periods as determined by the Board, which generally are equal to four years. Options generally expire ten years from the date of grant.

**Table of Contents**

The fair value of each stock option granted is estimated on the date of grant using the Black-Scholes option-pricing model using the assumptions noted in the following table:

	Years Ended December 31,		
	2011	2010	2009
Volatility	64.37%-65.56%	63.92%-66.81%	70.35%-72.04%
Expected Term (in years)	5.50-6.25	5.50-6.25	5.50-6.25
Risk-Free Interest Rates	1.09%-2.57%	1.59%-2.92%	1.98%-3.04%
Dividend Yield			

The risk-free interest rate is determined based upon the United States Treasury rates for U.S. Treasury zero-coupon bonds with maturities similar to those of the expected term of the options being valued. The Company does not expect to pay dividends in the foreseeable future.

Since the Company completed its initial public offering in March 2010, it has not had sufficient historical data to support a calculation of expected term and volatility. As such, the Company has used a weighted-average volatility considering the Company's own volatility since March 2010, and the volatilities of several peer companies. For purposes of identifying similar entities, the Company considered characteristics such as industry, length of trading history, similar vesting terms and in-the-money option status. For 2009, 2010 and 2011 due to lack of available quarterly data, the Company elected to use the simplified method for plain vanilla options to estimate the expected term of the stock option grants. Under this approach, the weighted-average expected life is presumed to be the average of the vesting term and the contractual term of the option. Additionally, under the provisions of ASC 718, the Company is required to include an estimate of the value of the awards that will be forfeited in calculating compensation costs, which the Company estimates based upon actual historical forfeitures. The forfeiture estimates are recognized over the requisite service period of the awards on a straight-line basis. Based upon these assumptions, the weighted-average grant date fair value of stock options granted during the years ended December 31, 2011, 2010, and 2009 was \$9.55, \$7.17 and \$6.48 per share, respectively.

As of December 31, 2011, there was \$9.6 million of total unrecognized stock-based compensation expense related to stock options granted under the Company's 2002 Stock Incentive Plan and 2010 Stock Incentive Plan (the Plans). The expense is expected to be recognized over a weighted-average period of 2.7 years. The intrinsic value of options exercised was \$6.5 million, \$3.4 million and \$0.3 million for the years ended December 31, 2011, 2010 and 2009, respectively.

The following table summarizes the activity of the Plans for the year ended December 31, 2011:

	Number of Options	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Life (in years)	Aggregate Intrinsic Value
Outstanding at December 31, 2010	3,605,718	\$ 6.44		
Granted	1,034,591	\$ 15.81		
Exercised	(565,339)	\$ 4.35		
Forfeited	(80,642)	\$ 10.34		
Outstanding at December 31, 2011	3,994,328	\$ 9.08	6.86	\$ 33,021,336
Exercisable at December 31, 2011	2,636,521	\$ 6.41	5.80	\$ 28,517,914
Vested or expected to vest at December 31, 2011	3,833,683	\$ 8.83	6.76	\$ 32,620,697

**Table of Contents***Stock Option Grants to Nonemployees*

During 2008, the Company granted 50,625 shares of nonqualified common stock options to nonemployee consultants, with an average exercise price of \$6.84 per share. There were no stock options granted to nonemployee consultants during 2011, 2010 or 2009. The Company valued these options using the Black-Scholes option-pricing model and recognizes expense related to these awards using the graded-vesting method. The unvested shares held by consultants have been and will be revalued using the Company's estimate of fair value at each reporting period through the remaining vesting period. The reassessment may result in additional charges to expense in the future. Stock-based compensation expense recorded for the years ended December 31, 2011 and 2010 was not material to the financial statements. Stock-based compensation expense of approximately \$266,600 was recorded during the year ended December 31, 2009 relating to nonemployee stock option awards.

*Restricted Stock*

In February 2011, the Company granted to certain executive officers awards of milestone-based restricted common stock. These restricted stock awards were granted with a term of 10 years (subject to continued employment with our company) and a grant price of \$14.16 per share, which was the closing price of the Company's common stock on the date of grant.

The restricted stock activity for the year ended December 31, 2011 is as follows:

	Number of Shares	Weighted-Average Exercise Price
Unvested at December 31, 2010		
Granted	69,000	\$ 14.16
Cancelled		
Expired		
Vested/Released		
Unvested at December 31, 2011	69,000	\$ 14.16

As of December 31, 2011, there was \$0.3 million of total unrecognized stock-based compensation expense related to restricted stock awards granted under the Plan. The expense is expected to be recognized over a weighted-average period of 0.6 years.

**13. Employee Benefit Plan**

In 2002, the Company established the AVEO Pharmaceuticals, Inc. 401(k) Plan (the "401(k) Plan") for its employees, which is designed to be qualified under Section 401(k) of the Internal Revenue Code. Eligible employees are permitted to contribute to the 401(k) Plan within statutory and 401(k) Plan limits. The Company makes matching contributions of 50% of the first 5% of employee contributions. The Company made matching contributions of \$396,000, \$304,000, and \$301,000 for the years ended December 31, 2011, 2010, and 2009, respectively.

**Table of Contents****14. Quarterly Results (Unaudited)**

	March 31, 2011	Three Months Ended		December 31, 2011
		June 30, 2011	September 30, 2011	
		(in thousands, except per share data) (unaudited)		
Collaboration revenue	\$ 133,614	\$ 26,554	\$ 3,585	\$ 1,096
Operating expenses	47,245	31,449	26,680	25,528
Income (loss) from operations	86,369	(4,895)	(23,095)	(24,432)
Other expense, net	(1,003)	(836)	(723)	(737)
Net income (loss)	\$ 85,366	\$ (5,731)	\$ (23,818)	\$ (25,169)
Net income (loss) per share basic	\$ 2.38	\$ (0.16)	\$ (0.55)	\$ (0.58)
Net income (loss) per share diluted	\$ 2.28	\$ (0.16)	\$ (0.55)	\$ (0.58)

	March 31, 2010	Three Months Ended		December 31, 2010
		June 30, 2010	September 30, 2010	
		(in thousands, except per share data) (unaudited)		
Collaboration revenue	\$ 10,881	\$ 15,622	\$ 6,222	\$ 11,957
Operating expenses	25,371	29,832	23,863	22,042
Loss from operations	(14,490)	(14,210)	(17,641)	(10,085)
Other income (expense), net	112	(1,279)	(967)	(229)
Net loss	\$ (14,378)	\$ (15,489)	\$ (18,608)	\$ (10,314)
Net loss per share basic and diluted	\$ (2.27)	\$ (0.50)	\$ (0.60)	\$ (0.30)

**15. Subsequent Events***Top-Line Data*

On January 2, 2012, the Company announced that its investigational drug tivozanib demonstrated superiority over Nexavar in the primary endpoint of progression-free survival (PFS) in TIVO-1, a global, randomized Phase 3 clinical trial evaluating the efficacy and safety of tivozanib compared to Nexavar in 517 patients with advanced RCC. Based on these data, the Company, together with its collaborative partner, Astellas, currently plan to submit filings seeking marketing approval for tivozanib to treat advanced RCC in the United States and Europe in 2012.

*Massachusetts Life Sciences Center Grant*

In February 2012, the Company was notified that it was granted a \$2.3 million tax incentive associated with the Life Sciences Tax Incentive Program from the Massachusetts Life Sciences Center. This program was established in 2008 in order to incentivize life sciences companies to create new sustained jobs in Massachusetts. Jobs must be maintained for at least five years, during which time the grant proceeds can be recovered by the Department of Revenue if the Company does not meet and maintain its job creation commitments.

---

**Table of Contents**

**ITEM 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure**

None.

**ITEM 9A. Controls and Procedures  
Evaluation of Disclosure Controls and Procedures**

Our management, with the participation of our Chief Executive Officer and Chief Financial Officer, evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2011. In designing and evaluating our disclosure controls and procedures, management recognized that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and our management necessarily applied its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Based on this evaluation, our Chief Executive Officer and Chief Financial Officer concluded that as of December 31, 2011, our disclosure controls and procedures were (1) designed to ensure that material information relating to us is made known to our management including our principal executive officer and principal financial officer by others, particularly during the period in which this report was prepared and (2) effective, in that they provide reasonable assurance that information required to be disclosed by us in the reports we file or submit under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms.

Management's report on the Company's internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) appears below.

**Internal Control Over Financial Reporting**

***(a) Management's Report on Internal Control Over Financial Reporting***

Our management is responsible for establishing and maintaining adequate internal control over financial reporting. Internal control over financial reporting is defined in Rules 13a-15(f) and 15d-15(f) promulgated under the Exchange Act as a process designed by, or under the supervision of, the company's principal executive and principal financial officers and effected by the company's board of directors, management and other personnel, 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 and includes those policies and procedures that:

Pertain to the maintenance of records that in reasonable detail accurately and fairly reflect the transactions and dispositions of the assets of the company;

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

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. Therefore, even those systems determined to be effective can provide only reasonable assurance with respect to financial statement preparation and presentation. 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.

Our management assessed the effectiveness of our internal control over financial reporting as of December 31, 2011. In making this assessment, management used the criteria set forth by the Committee of



---

**Table of Contents**

Sponsoring Organizations of the Treadway Commission (COSO) in *Internal Control Integrated Framework*. Based on its assessment, management believes that, as of December 31, 2011, our internal control over financial reporting is effective based on those criteria.

Our independent registered public accounting firm has issued an attestation report of our internal control over financial reporting. This report appears below.

***(b) Report of Independent Registered Public Accounting Firm on Internal Control over Financial Reporting***

**REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM**

The Board of Directors and Stockholders of

AVEO Pharmaceuticals, Inc.

We have audited AVEO Pharmaceuticals, Inc.'s internal control over financial reporting as of December 31, 2011, based on criteria established in *Internal Control Integrated Framework* issued by the Committee of Sponsoring Organizations of the Treadway Commission (the COSO criteria). AVEO 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, AVEO Pharmaceuticals, Inc. maintained, in all material respects, effective internal control over financial reporting as of December 31, 2011, 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 as of December 31, 2011 and 2010, and the related consolidated

**Table of Contents**

statements of operations, convertible preferred stock and stockholders' equity (deficit), and cash flows for each of the three years in the period ended December 31, 2011 of AVEO Pharmaceuticals, Inc. and our report dated March 30, 2012 expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP

Boston, Massachusetts

March 30, 2012

**Changes in Internal Control Over Financial Reporting**

There were no changes in our internal control over financial reporting that occurred during the quarter ended December 31, 2011 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

**ITEM 9B. Other Information**

None.

**Table of Contents**

**PART III**

**ITEM 10. Directors, Executive Officers and Corporate Governance**

The information required by this Item 10 will be contained in the sections entitled Election of Directors and Section 16(a) Beneficial Ownership Reporting Compliance appearing in the definitive proxy statement we will file in connection with our 2012 Annual Meeting of Stockholders and is incorporated by reference herein. The information required by this item relating to executive officers may be found in Part I, Item 1 of this report under the heading Business Executive Officers and is incorporated herein by reference.

**ITEM 11. Executive Compensation**

The information required by this Item 11 will be contained in the sections entitled Executive and Director Compensation, Compensation Committee Interlocks and Insider Participation and Compensation Committee Report appearing in the definitive proxy statement we will file in connection with our 2012 Annual Meeting of Stockholders and is incorporated by reference herein.

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

The information required by this Item 12 will be contained in the sections entitled Ownership of Our Common Stock and Executive and Director Compensation Equity Compensation Plan Information appearing in the definitive proxy statement we will file in connection with our 2012 Annual Meeting of Stockholders and is incorporated by reference herein.

**ITEM 13. Certain Relationships and Related Person Transactions, and Director Independence**

The information required by this Item 13 will be contained in the sections entitled Management and Certain Relationships and Related Person Transactions appearing in the definitive proxy statement we will file in connection with our 2012 Annual Meeting of Stockholders and is incorporated by reference herein.

**ITEM 14. Principal Accounting Fees and Services**

The information required by this Item 14 will be contained in the section entitled Corporate Governance Principal Accountant Fees and Services appearing in the definitive proxy statement we will file in connection with our 2012 Annual Meeting of Stockholders and is incorporated by reference herein.

**Table of Contents**

**PART IV**

**ITEM 15. Exhibits and Financial Statement Schedules**

(a) Documents filed as part of Form 10-K.

(1) Financial Statements

Report of Independent Registered Public Accounting Firm  
Consolidated Balance Sheets  
Consolidated Statements of Operations  
Consolidated Statements of Stockholder's Equity (Deficit)  
Consolidated Statements of Cash Flows  
Notes to Consolidated Financial Statements

(2) Schedules

Schedules have been omitted as all required information has been disclosed in the financial statements and related footnotes.

(3) Exhibits

The Exhibits listed in the Exhibit Index are filed as a part of this Form 10-K.

**Table of Contents****SIGNATURES**

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

**AVEO PHARMACEUTICALS, INC.**

Date: March 30, 2012

By: /s/ TUAN HA-NGOC  
**Tuan Ha-Ngoc**

*President & Chief Executive Officer*  
*(Principal Executive Officer)*

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated.

Signature	Title	Date
/s/ TUAN HA-NGOC  <b>Tuan Ha-Ngoc</b>	President, Chief Executive Officer and Director  <i>(Principal Executive Officer)</i>	March 30, 2012
/s/ DAVID B. JOHNSTON  <b>David B. Johnston</b>	Chief Financial Officer  <i>(Principal Financial and Accounting Officer)</i>	March 30, 2012
/s/ KENNETH M. BATE  <b>Kenneth M. Bate</b>	Director	March 30, 2012
/s/ RONALD A. DEPINHO  <b>Ronald A. DePinho</b>	Director	March 29, 2012
/s/ ANTHONY B. EVNIN  <b>Anthony B. Evnin</b>	Director	March 30, 2012
/s/ NICHOLAS GALAKATOS  <b>Nicholas Galakatos</b>	Director	March 30, 2012
/s/ RAJU KUCHERLAPATI  <b>Raju Kucherlapati</b>	Director	March 30, 2012
/s/ HENRI TERMEER  <b>Henri Termeer</b>	Director	March 30, 2012
/s/ KENNETH E. WEG  <b>Kenneth E. Weg</b>	Director	March 30, 2012

Edgar Filing: AVEO PHARMACEUTICALS INC - Form 10-K

**Kenneth E. Weg**

/s/ ROBERT C. YOUNG

Director

March 30, 2012

**Robert C. Young**

150

**Table of Contents****Exhibit Index**

Exhibit Number	Description of Exhibit	Form	Incorporated by Reference		Exhibit Number	Filed Herewith
			File Number	Date of Filing		
<i>Articles of Incorporation and Bylaws</i>						
3.1	Restated Certificate of Incorporation of the Registrant	8-K	001-34655	03/18/2010	3.1	
3.2	Second Amended and Restated Bylaws of the Registrant	S-1/A	333-163778	02/08/2010	3.5	
<i>Instruments Defining the Rights of Security Holders, Including Indentures</i>						
4.1	Specimen Stock Certificate evidencing the shares of common stock	S-1/A	333-163778	03/09/2010	4.1	
<i>Material Contracts Management Contracts and Compensatory Plans</i>						
10.1	2002 Stock Incentive Plan, as amended	S-1/A	333-163778	02/23/2010	10.1	
10.2	Form of Incentive Stock Option Agreement under 2002 Stock Incentive Plan	S-1	333-163778	12/16/2009	10.2	
10.3	Form of Nonstatutory Stock Option Agreement under 2002 Stock Incentive Plan	S-1	333-163778	12/16/2009	10.3	
10.4	Form of Restricted Stock Agreement under 2002 Stock Incentive Plan	S-1	333-163778	12/16/2009	10.4	
10.5	2010 Stock Incentive Plan	8-K	001-34655	06/07/2011	99.1	
10.6	Form of Incentive Stock Option Agreement under 2010 Stock Incentive Plan	S-1/A	333-163778	02/08/2010	10.6	
10.7	Form of Nonqualified Stock Option Agreement under 2010 Stock Incentive Plan	S-1/A	333-163778	02/08/2010	10.7	
10.8	Form of Restricted Stock Agreement under 2010 Stock Incentive Plan					X
10.9	Key Employee Change in Control Severance Benefits Plan	S-1	333-163778	12/16/2009	10.8	
10.10	Amended and Restated Employment Agreement, dated as of December 19, 2008, by and between the Registrant and Tuan Ha-Ngoc	S-1	333-163778	12/16/2009	10.9	
10.11	Severance and Change in Control Agreement, dated as of December 11, 2009, by and between the Registrant and Tuan Ha-Ngoc	S-1	333-163778	12/16/2009	10.10	
10.12	Severance and Change in Control Agreement, dated as of December 11, 2009, by and between the Registrant and Elan Z. Ezickson	S-1	333-163778	12/16/2009	10.11	

**Table of Contents**

Exhibit Number	Description of Exhibit	Form	Incorporated by Reference		Exhibit Number	Filed Herewith
			File Number	Date of Filing		
10.13	Severance and Change in Control Agreement, dated as of December 11, 2009, by and between the Registrant and Jenó Gyuris	S-1	333-163778	12/16/2009	10.12	
10.14	Severance and Change in Control Agreement, dated as of December 11, 2009, by and between the Registrant and David B. Johnston	S-1	333-163778	12/16/2009	10.13	
10.15	Severance and Change in Control Agreement, dated as of December 11, 2009, by and between the Registrant and William Slichenmyer	S-1	333-163778	12/16/2009	10.14	
10.16	2010 Employee Stock Purchase Plan, as amended	S-1/A	333-163778	02/23/2010	10.17	
10.17	Severance Agreement, dated September 13, 2010, by and between the Registrant and Michael Bailey	10-Q	001-34655	11/05/2010	10.1	
10.18	Consulting Agreement, executed November 4, 2010 and effective as of January 1, 2010, by and between the Registrant and Ronald DePinho	10-Q	001-34655	11/05/2010	10.2	
10.19	Extension Letter Amendment, dated March 30, 2011 and effective as of January 1, 2011, to the Consulting Agreement, executed November 4, 2010 and effective as of January 1, 2010, by and between the Company and Ron DePinho	10-Q	001-34655	05/12/2011	10.1	
10.20	Consultation and Scientific Advisory Board Agreement, effective as of January 1, 2010, by and between the Registrant and Lynda Chin	10-K	001-34655	03/11/2011	10.19	
10.21	Extension Letter Amendment, dated March 30, 2011 and effective as of January 1, 2011 to the Consulting Agreement, effective as of January 1, 2010, by and between the Company and Lynda Chin	10-Q	001-34655	05/12/2011	10.2	
10.22	Consulting Agreement, effective as of January 1, 2010, by and between the Company and Raju Kucherlapti	10-Q	001-34655	05/12/2011	10.3	
10.23	Extension Letter Amendment, dated October 31, 2011, to the Consulting Agreement, effective as of January 1, 2010, by and between the Company and Raju Kucherlapti					X



**Table of Contents**

Exhibit Number	Description of Exhibit	Incorporated by Reference			Exhibit Number	Filed Herewith
		Form	File Number	Date of Filing		
<i>Material Contracts Financing Agreements</i>						
10.24	Loan and Security Agreement dated May 28, 2010 by and among the Registrant, Hercules Technology II, L.P. and Hercules Technology III, L.P.	8-K	001-34655	06/04/2010	10.1	
10.25	Amendment No. 1 to Loan and Security Agreement, dated December 21, 2011, by and among the Registrant, Hercules Technology II, L.P. and Hercules Technology III, L.P.					X
<i>Material Contracts Leases</i>						
10.26	Sublease, dated as of July 2004, by and between the Registrant and Millennium Pharmaceuticals, Inc.	S-1	333-163778	12/16/2009	10.19	
10.27	Sublease, dated as of September 2, 2008, by and between the Registrant and Alkermes, Inc.	S-1	333-163778	12/16/2009	10.20	
10.28	Sublease, dated February 28, 2011, by and between the Company and Acceleron Pharma, Inc.	10-Q	001-34655	05/12/2011	10.4	
10.29	First Amendment to Sublease, dated September 1, 2011, by and between the Company and Acceleron Pharma, Inc.					X
<i>Material Contracts License and Strategic Partnership Agreements</i>						
10.30	Exclusive License Agreement, dated as of March 19, 2002, by and between the Registrant and Dana-Farber Cancer Institute, Inc., as amended on January 1, 2003 and July 22, 2003	S-1	333-163778	12/16/2009	10.21	
10.31	License Agreement, dated as of December 21, 2006, by and between the Registrant and Kirin Brewery Co. Ltd.	S-1	333-163778	12/16/2009	10.22	

**Table of Contents**

Exhibit Number	Description of Exhibit	Form	Incorporated by Reference		Exhibit Number	Filed Herewith
			File Number	Date of Filing		
10.32	Option and License Agreement, dated as of March 18, 2009, by and between the Registrant and Biogen Idec International GmbH	S-1	333-163778	12/16/2009	10.26	
10.33	Amended and Restated Collaboration and License Agreement, dated as of July 16, 2009, by and between the Registrant and OSI Pharmaceuticals, Inc., as amended by the First Amendment, dated as of February 23, 2010	S-1/A 10-Q	001-34655	03/09/2010 08/06/2010	10.28 10.1	
10.34	Collaboration and License Agreement, dated February 16, 2011, by and among the Registrant, AVEO Pharma Limited, Astellas Pharma Inc., Astellas US LLC and Astellas Pharma Europe Limited	10-K	001-34655	03/11/2011	10.30	
10.35	Research and License Agreement, dated May 31, 2011, by and between the Company and Centocor Ortho Biotech Inc.	10-Q/A	001-34655	11/29/2011	10.1	
<b><i>Additional Exhibits</i></b>						
21.1	Subsidiaries of the Registrant					X
23.1	Consent of Ernst & Young LLP					X
31.1	Certification of principal executive officer pursuant to Rule 13a-14(a)/15d-14(a) of the Securities Exchange Act of 1934, as amended.					X
31.2	Certification of principal financial officer pursuant to Rule 13a-14(a)/15d-14(a) of the Securities Exchange Act of 1934, as amended.					X
32.1	Certification of principal executive officer pursuant to 18 U.S.C. §1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.					X
32.2	Certification of principal financial officer pursuant to 18 U.S.C. §1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.					X

**Table of Contents**

<b>Exhibit Number</b>	<b>Description of Exhibit</b>	<b>Incorporated by Reference</b>			<b>Filed Herewith</b>
		<b>Form</b>	<b>File Number</b>	<b>Date of Filing</b>	
101.INS	XBRL Instance Document.				X
101.SCH	XBRL Taxonomy Extension Schema Document.				X
101.CAL	XBRL Taxonomy Calculation Linkbase Document.				X
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document.				X
101.LAB	XBRL Taxonomy Label Linkbase Document.				X
101.PRE	XBRL Taxonomy Presentation Linkbase Document.				X

Confidential treatment has been requested as to certain portions, which portions have been omitted and separately filed with the Securities and Exchange Commission.