

AVEO PHARMACEUTICALS INC

Form 10-K

March 11, 2011

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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, 2010

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.

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(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
Common Stock, \$.001 par value

Name of each exchange on which registered
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

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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, 2010, was \$161,865,077. 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 28, 2011: 35,788,858

Documents incorporated by reference:

Portions of our definitive proxy statement for our 2011 annual meeting of stockholders are incorporated by reference into Part III of this Annual Report on Form 10-K.

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Throughout this Form 10-K, the words we, us, our and AVEO refer to AVEO Pharmaceuticals, Inc. and its consolidated subsidiary, 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, and other 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. Tivozanib, our lead product candidate, which we recently partnered with Astellas Pharma Inc., or 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. Our clinical trials of tivozanib to date have demonstrated a favorable safety and efficacy profile for tivozanib. We have completed a successful 272-patient phase 2 clinical trial of tivozanib in patients with advanced renal cell cancer, or RCC. In this trial, we measured, among other things, each patient's progression-free survival, 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. Final data from the trial show the overall median progression-free survival of patients in the phase 2 clinical trial was 11.7 months. In a retrospective analysis of the subset of 176 patients in our phase 2 clinical trial who had the clear cell type of RCC and who had undergone prior removal of their affected kidney, referred to as a nephrectomy, both of which are inclusion criteria for our phase 3 clinical trial of tivozanib, the median progression-free survival was 14.8 months. 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, which are commonly associated with other VEGF receptor inhibitors, such as diarrhea, rash, mucositis, stomatitis, fatigue, and hand-foot syndrome, was notably low in comparison to clinical trial results of other VEGF receptor inhibitors. Severe (grade 3/4) incidences of these side effects that were considered by the investigator to be possibly related to tivozanib occurred in fewer than two percent of patients. In February 2010, we initiated enrollment in our global, phase 3 clinical trial comparing the efficacy and safety of tivozanib with Nexavar® (sorafenib), 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

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nephrectomy and who have not received any prior VEGF-targeted therapy. In August 2010, we completed enrollment in the TIVO-1 study with 517 patients. We anticipate receiving top-line data from the TIVO-1 study in mid-2011. Nexavar is an oral VEGF receptor inhibitor approved for the treatment of RCC. In its phase 3 clinical trial in patients with advanced clear cell RCC, 94% of whom had undergone a prior nephrectomy, Nexavar demonstrated a median progression-free survival of 5.5 months. Progression-free survival is the primary endpoint in the TIVO-1 study. The TIVO-1 study is designed so that a difference in progression-free survival of three months or more between the treatment arms would be statistically significant.

In addition to the TIVO-1 study, we are evaluating tivozanib in multiple clinical trials including: a completed phase 1b clinical trial in combination with Torisel[®] (temsirolimus), an approved inhibitor of the receptor known as mammalian target of rapamycin, or mTOR, in patients with advanced RCC; a phase 1b clinical trial in combination with the FOLFOX6 chemotherapy regimen in patients with advanced gastrointestinal cancers, including colorectal cancer; a recently completed phase 1b clinical trial in combination with Taxol[®] (paclitaxel) in patients with metastatic breast cancers; a phase 1b clinical trial in combination with Xeloda[®] (capecitabine), an oral chemotherapeutic agent, in patients with breast and colorectal cancers; a completed phase 1b clinical trial as a monotherapy in patients with non-small cell lung cancer; and a phase 2 clinical trial designed to evaluate biomarkers of tivozanib in patients with RCC. In addition, a phase 1 investigator sponsored clinical trial was recently completed in which tivozanib was combined with Afinitor[®] (everolimus), an approved inhibitor of the mTOR receptor, in patients with advanced colorectal cancer. The phase 2 portion of this investigator sponsored trial combining tivozanib with Afinitor was recently initiated in February 2011 and will enroll patients with refractory metastatic colorectal cancer. We expect that the results of these 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 **Recent Developments**, we recently 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, a novel method of building preclinical models of human cancer, which are intended to more accurately represent cancer biology in patients. Ficlatusumab (AV-299), our next most advanced product candidate, is an antibody which binds to hepatocyte growth factor, or HGF, thereby blocking its function. Through the use of our Human Response Platform, our scientists have observed that the HGF/c-Met pathway is a significant driver of tumor growth. We have completed a phase 1 clinical trial of ficlatusumab and initiated a phase 2 clinical trial in patients with non-small cell lung cancer in May 2010. In 2007, we entered into an agreement with Merck and Co., Inc., or Merck (through its subsidiary Schering Corporation), under which we granted Merck exclusive worldwide rights to develop and commercialize ficlatusumab. Pursuant to the agreement, Merck funded all research, development and manufacturing expenses, subject to an agreed-upon budget, and under which Merck was obligated to pay development milestones to us, and, as applicable, royalties on product sales. On September 28, 2010, we received notice from Merck of termination of the collaboration agreement effective as of December 27, 2010, at which point we became responsible for the performance and funding of all future research, development, manufacturing and commercialization activities for ficlatusumab.

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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 antibody discovery programs underway focusing 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, the Notch receptors and the Fibroblast Growth Factor receptors.

Our 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.

Recent Developments

On February 16, 2011, we entered into a collaboration and license agreement with Astellas 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 with Astellas, we will share responsibility with Astellas for continued development and commercialization of tivozanib in North America and in Europe. Throughout the rest of the world (other than North America and Europe, and excluding Asia where KHK has retained all development and commercialization rights), which we refer to as the royalty territory, Astellas has an exclusive, royalty-bearing license to develop and commercialize tivozanib. The terms of the collaboration agreement with Astellas are subject to our obligations to KHK under the license agreement entered into with KHK in 2006.

We 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 in North America and Europe, and any resulting profits or losses, will be shared equally between the parties.

Under the collaboration 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. We expect to retain net proceeds of approximately \$96 million of the initial cash payment from Astellas, after payments to KHK and strategic, legal and financial advisors. We are also eligible to receive from Astellas an aggregate of approximately \$1.3 billion in potential milestone payments relating to development and commercialization milestones for tivozanib. 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' development and commercialization activities in Europe and the royalty territory.

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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.

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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, VEGFR1, 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 blockade 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 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 \$10 billion worldwide in 2010, based on quarterly and annual reports made publicly available by companies marketing such drugs. According to EvaluatePharma[®] 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[®] (bevacizumab), an antibody that blocks only one of the ligands for the VEGF receptors, and Nexavar[®] (sorafenib), Sutent[®] (sunitinib) and Votrient[®] (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

The potential advantages of tivozanib include a high potency and selectivity profile, which we believe is the basis for the favorable efficacy and safety profile observed in the clinical trials of tivozanib to date. We believe

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that this favorable efficacy and safety profile may allow tivozanib to be successfully used as a monotherapy and to be more readily combined with other anti-cancer agents. Coupled with a convenient dosing regimen, we believe these advantages 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.

Potency. Based on published preclinical data to date of marketed products or compounds in clinical development that target the VEGF receptors, we believe that tivozanib is the most potent inhibitor of all three VEGF receptors and that tivozanib provides the most comprehensive blockade of the VEGF pathway. Tivozanib is administered at a dose of 1.5 mg per day. In contrast, the daily dose of the other approved VEGF receptor inhibitors ranges from 50 mg per day to 800 mg per day. Because tivozanib's high potency allows it to be administered at a low dose, patients who take tivozanib have less drug circulating in their body.

Selectivity. Tivozanib more selectively inhibits all three VEGF receptors than it does any other target in the body. This selectivity for the VEGF receptors has the potential to confer two important advantages:

Tolerability. In the clinical trials of tivozanib to date, we have observed low rates of unintended side effects, referred to as off-target toxicities, with hypertension and dysphonia being 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. As a result, in the phase 2 clinical trial of tivozanib, dose reductions due to side effects were required by 8% of patients, treatment interruptions due to side effects were required by 4% of patients and study discontinuation due to side effects were required by 9% of patients.

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. Sutent, Nexavar and Votrient, all relatively non-selective VEGF inhibitors, more potently inhibit other targets than they do the VEGF receptors. For example, Sutent and Votrient more potently inhibit the receptor known as c-Kit and Nexavar more potently inhibits the protein known as raf. The most commonly reported toxicities for Sutent and Nexavar are fatigue, rash and diarrhea, and a common toxicity for Votrient is diarrhea. Votrient has also been associated with severe, and sometimes fatal, liver toxicity. These drugs have high rates of a number of other side effects that can be very difficult for patients to tolerate, including: mucositis, a painful inflammation and ulceration of the mucous membranes lining the digestive tract; stomatitis, an inflammation of the mucous lining of the mouth, including the cheeks, gums, tongue, lips, throat and roof or floor of the mouth; and hand-foot syndrome, a blistering, burning, swelling and tenderness on the soles of the feet and palms of the hands that can interfere with a patient's ability to walk and/or use his or her hands. 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. These side effects can be difficult to manage, and result in high rates of dose reductions and discontinuations, as well as a reduced quality of life for patients. In clinical trials, more than 30% of patients receiving Sutent, more than 13% of patients receiving Nexavar and more than 40% of patients receiving Votrient have required dose reductions, and more than 35% of patients receiving Sutent, more than 20% of patients receiving Nexavar and more than 30% of patients receiving Votrient have required dose interruptions.

Combinability. While the approved VEGF pathway inhibitors have demonstrated improvements in outcomes in the patients with cancers they are used to treat, we believe an opportunity exists for significantly improved outcomes through the use of rational combinations of VEGF pathway inhibitors with other anti-cancer therapies. Because of the potency and selectivity of tivozanib, we believe that it

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has the potential to be more readily combined with other anti-cancer drugs at full dose and schedule, and therefore has the potential to significantly improve anti-cancer activity and clinical outcomes. In contrast, combining other anti-cancer drugs, each of which carries with it its own toxicity profile, can lead to high levels of side effects when administered at full dose, or the dose administered when the drugs are used alone, and schedule of dose administration, which can make the combination unsafe or difficult for patients to tolerate. For example, in a phase 1 clinical trial designed to test the safety and efficacy of Sutent in combination with Torisel, another drug approved to treat RCC, the trial had to be halted due to high levels of rash and thrombocytopenia, or an abnormal drop in blood cell count, resulting from this combination. This high toxicity level was observed despite both agents being administered at doses well below the standard doses that are used when administered alone. Similarly, in a phase 2 clinical trial in breast cancer patients designed to test the safety and efficacy of Nexavar in combination with Xeloda, a drug approved for the treatment of breast cancer, patients demonstrated clinical benefit from the combination, however, more than 40% of patients developed grade 3 hand-foot syndrome, which is the highest grade of hand-foot syndrome (there is no grade 4 or grade 5 for this side effect). Hand-foot syndrome is a serious skin reaction that interferes with patients' ability to conduct the normal activities of daily living.

We have commenced the following phase 1b clinical trials testing tivozanib in combination with other anti-cancer agents in multiple cancer types, including RCC, breast and gastrointestinal cancer:

In our recently completed phase 1b clinical trial evaluating the combination of tivozanib with Torisel in patients with RCC, tivozanib and Torisel were both administered at full dose and schedule. Preliminary data from the clinical trial presented in February 2011 indicate that the combination has been well-tolerated and resulted in disease control, defined as stable disease or tumor shrinkage, in 22 out of 28 evaluable patients (79%), with eight patients (29%) experiencing partial responses, which means the patients had a reduction in the sum of the longest diameter of the tumor, or the sum of all tumors, of at least 30% as compared to the longest diameters of the tumor(s) measured when the patient entered the trial.

In our ongoing phase 1b clinical trial evaluating the combination of tivozanib with FOLFOX6, a standard chemotherapy regimen, in patients with gastrointestinal cancers, including colorectal cancer, both tivozanib and FOLFOX6 have been administered at full dose and schedule. Preliminary data from the clinical trial presented in November 2010 indicate that the combination has been well-tolerated and resulted in disease control in 14 of 17 evaluable patients (82%), with six of 17 patients (35%) experiencing partial responses.

In our recently completed phase 1b clinical trial evaluating the combination of tivozanib with Taxol in patients with metastatic breast cancer, both tivozanib and Taxol have been administered at full dose and schedule. Preliminary data from the clinical trial presented in December 2010 indicate that the combination has been well-tolerated and resulted in disease control of at least 24 weeks in eight of 18 evaluable patients (44%), with five of 18 patients (28%) experiencing partial responses.

We are also evaluating two all-oral combinations of tivozanib and other cancer agents, including a combination of tivozanib with Xeloda in a phase 1b clinical trial in patients with breast and colorectal cancer, and a phase 1 investigator sponsored clinical trial in which tivozanib was combined with Afinitor in patients with advanced colorectal cancer, which was recently completed. The phase 2 portion of the trial was commenced in February 2011 and will enroll patients with refractory metastatic colorectal cancer.

Dosing Regimen. 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 maintain blockade

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of the VEGF receptors throughout the course of therapy, resulting in the potential for patients to experience a rebound effect, which can worsen their condition. 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 complete blockade of the relevant receptors and, accordingly, we dose tivozanib on a convenient, one-capsule, once-per-day schedule.

Renal Cell Cancer

Overview. We completed a 272-patient phase 2 clinical trial of tivozanib in advanced RCC in August of 2010. Final results from this trial show the overall median progression-free survival of patients was 11.7 months. In a retrospective analysis of the subset of 176 patients in our phase 2 clinical trial who had the clear cell type of RCC and who had undergone a prior nephrectomy, both of which are inclusion criteria for our phase 3 clinical trial of tivozanib, the median progression-free survival was 14.8 months. The most common treatment-related side effects seen in the phase 2 clinical trial were hypertension (44.9%) and dysphonia (21.7%). Additionally, the incidence of side effects in the phase 2 clinical trial, which are commonly associated with other VEGF receptor inhibitors, such as diarrhea, rash, mucositis, stomatitis, fatigue, and hand-foot syndrome, was notably low in comparison to clinical trial results of other VEGF receptor inhibitors. Severe (grade 3/4) incidences of these side effects that were considered by the investigator to be possibly related to tivozanib occurred in fewer than two percent of patients. Tivozanib was well-tolerated by patients and relatively few patients needed to discontinue or reduce their dose of tivozanib. In August 2010, we completed enrollment of our phase 3 clinical trial for tivozanib in patients with advanced clear cell RCC who have undergone a prior nephrectomy and who have not received any prior VEGF-targeted therapy. We anticipate receiving top-line data from this registration trial in mid-2011. Based on the data we have received from clinical trials conducted to date, we believe that tivozanib may offer a unique therapeutic alternative for the first-line treatment of advanced RCC.

Market Opportunity. Based on an epidemiology study reported in the Surveillance Epidemiology and End Results (SEER) Cancer Statistics Review conducted by the National Cancer Institute (NCI) (published in 2007), more than 200,000 new cases of kidney cancer will have been diagnosed in the world in 2010, and new cases of kidney cancer have been increasing steadily for the past 65 years. The NCI reports that there will have been more than 60,000 new cases of kidney cancer in the United States in 2010. According to a review article by R. Motzer et al. in the New England Journal of Medicine from 1996, RCC accounts for approximately 90% of all malignant kidney tumors. We estimate, based on publicly-available information, including 2010 quarterly and annual reports made publicly available by companies that market drugs approved for RCC, that the current worldwide RCC market for prescription drugs is over \$1.8 billion, with agents targeting the VEGF pathway representing over 80% 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, 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 recently 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

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patients compared to placebo or interferon. The reported progression-free survival in the treatment arms of the phase 3 clinical trials of these drugs in patients with advanced clear cell RCC is 11.0 months for Sutent, 5.5 months for Nexavar, 9.2 months for Votrient and 10.2 months for Avastin when Avastin is given in combination with interferon. In these trials, the percent of patients who had undergone a prior nephrectomy was 91% for Sutent, 94% for Nexavar, 89% for Votrient and 85% for Avastin. Torisel and Afinitor, drugs which target mTOR, have also been approved in RCC. In their respective phase 3 clinical trials, the reported median progression-free survival for Torisel was 5.5 months in patients with poor-prognosis RCC, and the reported median progression-free survival for Afinitor in patients who had progressed despite prior treatment with a VEGF receptor inhibitor was 4.9 months.

Despite the efficacy of the approved oral VEGF pathway inhibitors, these drugs 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 from the phase 3 clinical trials of these drugs in patients with advanced RCC is 32% for Sutent, 13% for Nexavar and 42% 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 38% for Sutent, 21% for Nexavar and 36% 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

Standard Response Evaluation Criteria in Solid Tumors (version 1.0), or RECIST, defines disease progression and tumor response based on changes of 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 1 Clinical Trials. In 2007, we completed a phase 1 clinical trial of tivozanib in 41 cancer patients. Results from the phase 1 clinical trial showed that patients were able to tolerate tivozanib at a dose of 1.5 mg/day given continuously for 4 weeks followed by a 2 week rest period, and that toxicities were reversible upon stopping treatment. The primary dose-limiting toxicity identified in the phase 1 clinical trial was hypertension, which is a common side effect of VEGF inhibitors and is considered an on-target side effect resulting from the blockade of the VEGF receptors. Hypertension was treated with standard anti-hypertensive agents such as calcium channel blockers or angiotensin converting enzyme inhibitors.

In the phase 1 clinical trial, nine of 41 patients had RCC, and all nine patients experienced clinical benefit from tivozanib. Two of these patients had a partial response, according to RECIST criteria, including one patient whose partial response lasted for over two years. The remaining seven RCC patients had stable disease lasting for at least two months. Stable disease was also observed in patients with other types of solid tumors including colorectal cancer, where four out of 10 patients who had progressed after prior chemotherapy demonstrated

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stable disease lasting for approximately six months during treatment with tivozanib. One patient with an acinar cell tumor of the pancreas that had progressed after prior treatment with gemcitabine received tivozanib for over two years with stable disease. Given the promising activity observed in the phase 1 clinical trial, we decided to move forward with the development of tivozanib in multiple solid tumors, with RCC being the leading program.

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 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.

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. The data reported in the following paragraph with respect to the percentage of patients remaining progression-free 12 weeks following random assignment as compared to placebo are based on final data from the tivozanib phase 2 clinical trial. 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 (Figure 1). 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. The vertical tick marks of the graphs below represent points during the clinical trial at which one or more patients were removed from the data analysis either because the patient was on treatment and still responding at the time of the data cut-off or because the patient withdrew from the clinical trial due to reasons other than disease progression or because the patient was randomized to placebo.

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Figure 1: Progression-Free Survival by Independent Radiological Review Assessments (Censored Dropouts, Intended to Treat (ITT) Population Excluding Subjects with Progressive Disease Prior to Randomization)

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Figure 2 shows the probability of a patient remaining alive without tumor progression while in the tivozanib phase 2 clinical trial. The overall median progression-free survival of patients in the phase 2 clinical trial was 11.7 months.

Figure 2: Progression-Free Survival by Independent Radiological Review Assessments (Censored Dropouts, All Treated Population)

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In the subset of 176 patients in the phase 2 clinical trial who had clear cell RCC and who had undergone a prior nephrectomy, both of which are inclusion criteria for our phase 3 clinical trial of tivozanib, the median progression-free survival was 14.8 months, calculated retrospectively using a Kaplan-Meier analysis, as shown in Figure 3.

Figure 3: Progression-Free Survival Throughout the Study by Independent Radiological Review Assessments (Censored Dropouts, All Treated Population, Subjects with Clear Cell Histology and Nephrectomy)

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.

The maximum percent change relative to baseline in the sum of the longest diameters at each tumor assessment for the 238 patients in the phase 2 clinical trial with at least one post-baseline CT scan is presented as a waterfall graph in Figure 4. The graph below shows the change in tumor size for each of these patients in the phase 2 clinical trial. Each vertical bar in the graph represents the percent change from the time when the patient entered the clinical trial (baseline) until the maximum change was observed for that patient. The changes in tumor size are based on independent radiological assessment.

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Figure 4: Waterfall Plot: Maximum Change in Tumor Size Throughout the Study (All Treated Population)

The most common treatment-related adverse events seen in our phase 2 clinical trial of tivozanib 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.

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 drug-related adverse events seen in >5% of patients and includes the number of patients in which these drug-related adverse events were seen. Grade 1 adverse events are characterized as mild, Grade 2 adverse events are moderate, Grade 3 adverse events are severe, Grade 4 adverse events are life-threatening, and Grade 5 adverse events are fatal.

The incidence of mucositis, stomatitis and hand-foot syndrome were less than 5%, with less than 1% Grade 3 or Grade 4 events reported. No Grade 5 events occurred.

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System Organ Class Preferred Term	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	All Grades Total
Combined Hypertension	15(5.5%)	74(27.2%)	31(11.4%)	1(0.4%)	0(0%)	122(44.9%)
Dysphonia	55(20.2%)	4(1.5%)	0(0%)	0(0%)	0(0%)	59(21.7%)
Diarrhea	21(7.7%)	7(2.6%)	5(1.8%)	0(0%)	0(0%)	33(12.1%)
Asthenia	7(2.6%)	14(5.1%)	7(2.6%)	0(0%)	0(0%)	28(10.3%)
Fatigue	9(3.3%)	8(2.9%)	5(1.8%)	0(0%)	0(0%)	22(8.1%)
Dyspnoea	6(2.2%)	7(2.6%)	3(1.1%)	0(0%)	0(0%)	16(5.9%)

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.

Phase 3 Clinical Trial. Based on the results of the phase 2 clinical trial of tivozanib and following discussions we have had with the FDA and European Medicines Agency, or EMA, we initiated a phase 3 clinical trial in patients with advanced clear cell RCC who have undergone a prior nephrectomy in December 2009, referred to as the TIVO-1 study. We commenced enrollment in this clinical trial in February 2010, and completed enrollment in August 2010. The TIVO-1 study enrolled 517 patients 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® (sorafenib) for first-line treatment in RCC. The TIVO-1 study is being conducted 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-targeted therapy. The primary endpoint for the trial is progression-free survival. Based on our discussions with the FDA and the EMA, we set the number of patients to be enrolled in the clinical trial based on standard statistical assumptions and an assumed difference in progression-free survival of three months or more between the treatment arms would be statistically significant. 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. 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.

Nexavar was approved in the United States in December 2005 as the first VEGF receptor inhibitor for the treatment of advanced RCC. Nexavar received marketing authorization by the European Commission in July 2006 for the treatment of patients with advanced RCC who have failed prior interferon-alpha or interleukin-2 based therapy or are considered unsuitable for such therapy. In the phase 3 clinical trial of Nexavar, patients with advanced clear cell RCC, 94% of whom had undergone a prior nephrectomy, treated with Nexavar had a median progression-free survival of 5.5 months and patients treated with placebo had a median progression-free survival of 2.8 months. 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.

In the TIVO-1 study, patients have been randomized in approximately equal numbers to treatment with tivozanib or Nexavar. Patients randomized to the tivozanib treatment arm receive 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 receive the approved dose of Nexavar, which is 400 mg twice a day. Patients randomized to the tivozanib treatment arm who develop documented disease progression will be discontinued from the clinical trial. Patients randomized to the Nexavar treatment arm who develop documented disease progression will be discontinued from the clinical trial and will be given the option to receive tivozanib by enrolling in a separate

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long-term treatment protocol. In order to meet FDA standards for assessing results in phase 3 trials, all radiology scans will be assessed by a single, centralized group of independent radiology reviewers in the United States who will be blinded to the assigned treatment. There can be no assurance that the efficacy and safety profile seen in prior clinical trials of Nexavar and of tivozanib will be reproduced in the TIVO-1 study.

In addition to the TIVO-1 study, we are conducting, or plan to conduct, or will seek waivers from conducting, a variety of other clinical trials that would support a New Drug Application, or NDA, including a mass balance study, a food effect study, a thorough QTc study, drug-drug interaction studies, special population studies, and a pediatric study. We are also conducting additional toxicology studies in non-human primates and 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. Based on preclinical studies we have conducted using our Human Response Platform, we believe that the combination of tivozanib and mTOR inhibitors may have enhanced anti-tumor activity in patients with RCC. We recently 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 for the treatment of advanced RCC in 2007, and is considered a standard of care for treatment of patients with poor-prognosis RCC.

Clinical trials have shown that Sutent cannot be used in combination with Torisel due to severe toxicities. A phase 1 clinical trial testing the combination of Sutent and Torisel was discontinued when two out of the first three patients treated in the first cohort with less than full doses of each drug (15 mg of Torisel and 25 mg of Sutent) developed serious dose-limiting toxicities such as rash and thrombocytopenia.

Nexavar has also had a significant challenge combining with Torisel at full doses due to a variety of dose-limiting 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 presented at the ASCO Annual Meeting in 2010 for the TORAVA trial, which tested the combination of Avastin and Torisel in patients with RCC, 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 and schedule, to date, the results of our recently completed phase 1b clinical trial indicate that tivozanib may be able to be used safely in combination with Torisel at full recommended dose and schedule. Preliminary data from the clinical trial reported in February 2011 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.

Breast Cancer. We believe that tivozanib can provide an improved therapy for women diagnosed with breast cancer. In 2010, approximately 207,000 women will have been diagnosed with invasive breast cancer, and 40,000 women will have died from breast cancer, in the United States, according to the American Cancer Society. 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.

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Avastin was approved by the FDA in 2008 for the treatment of metastatic breast cancer. In December 2010, the FDA moved to revoke 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. The drug remains approved in metastatic breast cancer in the U.S. while Avastin's manufacturer, Roche-Genentech, has appealed the FDA's decision. Despite the recent data, European regulators have decided to retain the approval of Avastin for advanced breast cancer when used in combination with paclitaxel.

In addition, previously presented phase 2 clinical trial data show that Nexavar when combined with Xeloda, an oral chemotherapy approved in breast cancer, improved outcomes in patients over Xeloda alone. However, overlapping toxicities have resulted in numerous side effects, including more than 40% of patients experiencing the highest grade of hand-foot syndrome, Grade 3.

We recently completed a phase 1b clinical trial of tivozanib in combination with a standard dose of Taxol in patients with metastatic breast cancer. Preliminary data from the clinical trial reported in December 2010 indicate that the combination has been well-tolerated and resulted in disease control of at least 24 weeks in eight of 18 evaluable patients (44%), with five of 18 patients (28%) experiencing partial responses.

Based on tivozanib's favorable toxicity profile, and minimal off-target toxicities with tivozanib monotherapy in clinical trials to date, we believe that tivozanib has the potential to be safely combined with Xeloda. Accordingly, we have initiated a phase 1b clinical trial evaluating the combination of tivozanib with Xeloda. The primary objectives of the trial are to determine the safety, tolerability and maximum tolerated dose of tivozanib when administered in combination with Xeloda. 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. We anticipate that the results of this trial will guide our future decisions regarding potential additional trials of this combination regimen.

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 2010, approximately 143,000 patients will have been diagnosed with colorectal cancer, and 51,000 patients will have died from this disease. Despite recent advances in chemotherapy, the American Cancer Society also reports that less than 10% of patients with metastatic colorectal cancer survive beyond 5 years. Therefore, there is a critical 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.

In 2008, 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 November 2010 indicate that the combination has been well-tolerated and resulted in disease control in 14 of 17 evaluable patients (82%), with six of 17 patients (35%) experiencing partial responses as assessed by RECIST. This clinical trial is currently enrolling patients for an expanded assessment of safety and activity in this patient population.

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 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

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cancer. A phase 1 investigator sponsored clinical trial was recently completed evaluating the combination of tivozanib with Afinitor, an oral mTOR inhibitor approved for the treatment of RCC, in patients with advanced colorectal cancer. The phase 2 portion of this all-oral clinical trial combining tivozanib and Afinitor commenced in February 2011 and will enroll patients with refractory metastatic colorectal cancer. If this clinical trial is successful, we believe that an all-oral regimen comprising a VEGF pathway inhibitor and an mTOR inhibitor would be an attractive drug combination worthy of further development in colorectal cancer.

Non-small Cell Lung Cancer. We believe that tivozanib could also provide an improved treatment for patients with advanced non-small cell lung cancer, or NSCLC. Lung cancer is the most deadly cancer in men and women, with approximately 223,000 new cases and 157,000 deaths in the United States in 2010, according to the American Cancer Society. Chemotherapy has shown modest activity in NSCLC and advanced lung cancer remains an incurable disease. Avastin, approved by the FDA for use in NSCLC in combination with chemotherapy, and various small molecular VEGF receptor inhibitors have demonstrated modest single-agent activity in lung cancer.

We recently completed a phase 1 clinical trial of tivozanib monotherapy in patients with advanced NSCLC, and we are in the process of aggregating and analyzing the data from this trial. This clinical trial is designed to test a continuous dosing regimen of tivozanib. We expect that the results will provide preliminary indications of activity in this cancer and further inform 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 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 (AV-299): Anti Hepatocyte Growth Factor (HGF) 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, bladder, breast, gastric, ovarian, prostate, colorectal, head and neck, certain sarcomas and in multiple myeloma and leukemias. There are no approved therapies that 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, a potent and functional inhibitor of HGF. 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 AMG-102 and TAK-701, the other anti-HGF antibodies currently in clinical development. Clinical trials will need to be conducted in order to determine whether the differences observed in these preclinical studies will contribute to greater efficacy in patients.

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Preclinical and clinical observations suggest that increased HGF and/or c-Met receptor amplification may confer resistance to epidermal growth factor receptor (EGFR) inhibitors. Recently, encouraging phase 2 clinical data were reported at the 2010 ASCO Annual Meeting with a third party small molecule c-Met inhibitor in combination with an EGFR tyrosine kinase inhibitor (TKI) in patients with advanced, refractory NSCLC. Additionally, phase 2 clinical data were reported at the 2010 35th Congress of the European Society for Medical Oncology (ESMO) 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.

In 2008, we commenced a phase 1 clinical trial of ficlatuzumab, which has completed enrollment, in patients with a variety of solid tumors to establish the safety, tolerability, pharmacokinetics, maximum tolerated dose and the recommended phase 2 clinical trial dose of ficlatuzumab as a monotherapy, and to determine the safety, tolerability, and maximum tolerated dose of ficlatuzumab in combination with Tarceva, an approved EGFR inhibitor. 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 up to the highest dose tested, 20mg/kg, for the monotherapy cohorts. One patient dosed with ficlatuzumab, 20mg/kg, in combination with Tarceva, experienced inflammation of the mucous lining of the mouth. The most frequently observed adverse events were mild fatigue, hypokalemia, or low blood potassium, tissue swelling, also referred to as edema, and nausea. A preliminary review of 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, as shown in the chart below. Review of response data for the ficlatuzumab/Tarceva cohort is underway.

We are also conducting a phase 1 clinical trial in cancer patients with liver metastases in order to evaluate the activity of ficlatuzumab in HGF pathway activation in metastatic tumors.

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In May 2010, we commenced a phase 2 clinical trial testing a combination of ficlatuzumab with Iressa® (gefitinib), an EGFR inhibitor, randomized 1:1 versus Iressa alone in patients with newly diagnosed non-small-cell lung cancer. Patients who demonstrate disease progression during treatment with Iressa alone will have the opportunity to be treated with ficlatuzumab in combination with Iressa provided that safety is maintained and the patient continues to meet trial eligibility criteria. This 170-patient, randomized clinical trial, which is being conducted in Asia, will study response rate and progression-free survival in two distinct patient subsets: those with activating EGFR mutations and those with wild-type EGFR. We expect to receive top-line efficacy data from the phase 2 trial in 2012.

We are also using our Human Response Platform to identify 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 a novel inhibitor of the pathway. We believe that these preclinical models will provide us with an advantage over other competitive programs.

In March 2007, we entered into a collaboration agreement with Merck (through its subsidiary Schering Corporation) under which we granted Merck worldwide rights to develop and commercialize ficlatuzumab. Pursuant to the terms of the collaboration agreement, Merck funded all research, development and manufacturing expenses, subject to an agreed-upon budget, was responsible for manufacturing ficlatuzumab for clinical use and was required to pay us development milestones and royalties on the sale of ficlatuzumab. On September 28, 2010, we received notice from Merck of termination of the collaboration agreement effective as of December 27, 2010, at which point we became responsible for the performance and funding of all future research, development, manufacturing and commercialization activities for 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 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 selected AV-203 as our lead development candidate in March 2010, and have commenced process development for manufacturing of this candidate in preparation for preclinical studies and human clinical trials. We have not yet submitted to the FDA an investigational new drug application for AV-203, and anticipate initiating phase 1 development with AV-203 in 2012.

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In March 2009, 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. The targets we have focused on to date are the Notch receptors, FGF receptors and the RON receptor, as more fully described below.

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, Notch2 and Notch3 that prevent ligand binding and activation of the receptors. The program has generated functional inhibitory antibodies against the Notch1 and Notch3 receptors. Our team has demonstrated proof of concept with our lead Notch1 antibody candidate in preclinical models of angiogenesis and preclinical testing is ongoing. In

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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. Because the blockade of Notch1 signaling results in a potent inhibition of angiogenesis by a mechanism which differs from VEGF inhibition, we believe that blockade of both pathways simultaneously might increase the efficacy of anti-angiogenesis therapy. We are also exploring preclinical models to determine which tumors might be uniquely dependent on Notch1 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.

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.

Recently, the human Cancer Genome Sequencing project 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 FGFR1, FGFR2, FGFR3 and FGFR4 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.

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.

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.

Our scientists have identified antibodies which can inhibit the growth of RON-driven tumors created through our Human Response Platform. Preclinical testing of these antibodies is ongoing.

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Our Human Response Platform

Our scientific founders, Ronald A. DePinho, M.D. and Lynda Chin, M.D., both 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 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.

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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 and Biogen Idec. 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.

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

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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.

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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, the tumors that arise from those cells are no longer sensitive to drugs that inhibit HER2, but are sensitive to drugs

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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.

Recently, 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.

Similar efforts to identify candidate biomarkers for our other development programs are also underway. For instance, 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 activation.

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.

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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, 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 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 2010 sales estimated to be in excess of \$10.0 billion worldwide, based on 2010 quarterly and annual reports made publicly available by companies marketing such drugs. There are currently four 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, HER2-negative metastatic breast 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 three FDA-approved oral small molecule VEGF receptor inhibitors: Nexavar, marketed by Bayer and Onyx Pharmaceuticals, Inc.; Sutent, marketed by Pfizer; and Votrient, marketed by GSK. These approved drugs are non-specific and target other receptors more potently than 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 and for gastrointestinal stromal tumors. Votrient is approved as a monotherapy for advanced RCC. Other recently 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. We believe the only other VEGF pathway inhibitor in late-stage development in RCC is Pfizer's AG013736 (axitinib), which was recently reported to have met its primary endpoint in a phase 3 registration clinical trial for the second-line treatment of advanced RCC. Other VEGF pathway inhibitors 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 (intedanib), Bristol-Myers Squibb Company's BMS-582664 (brivanib alaninate), Exelixis Inc.'s XL-184 (cabozantinib), ImClone LLC's IMC-1121b (ramucirumab), Onco Therapy Science Inc.'s OTS-102 (elpamotide) 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 MetMab (5D5 Fab), ArQule, Inc.'s / Daiichi Sankyo, Inc.'s ARQ-197, MethylGene, Inc.'s MGCD-265, Exelixis' and GSK's XL-880 (foretinib), Incyte Corp.'s and Novartis' INCB-028060, Pfizer's PF-2341066 (crizotinib) and Exelixis' XL-184 (cabozantinib).

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' MM-121, which is

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currently in phase 2 clinical development, and Daiichi Sankyo and Amgen, Inc. s U3-1287 / AMG-888, which is also in phase 2 clinical development. Other clinical-stage competitors include PharmaMar s elisidepsin, Merrimack s MM-111, and AstraZeneca 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, 2010, 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 Agreement	Subject Matter	Payments	
			Received as of December 31, 2010 ⁽¹⁾⁽²⁾	
Kyowa Hakko Kirin	December 2006	Tivozanib ⁽³⁾		N/A
OSI Pharmaceuticals	September 2007	Target and Biomarker Identification	\$	62.0 million
Biogen Idec	March 2009	AV-203	\$	55.0 million ⁽⁴⁾
Merck	November 2003	Target Identification	\$	22.3 million
Merck	August 2005	Biomarker Identification	\$	6.5 million

- (1) Includes up-front payments, equity investments, research and development funding and milestone payments.
- (2) The foregoing table does not include receipt of the initial cash payment from Astellas in March 2011 of an aggregate of \$125 million, of which we expect to retain net proceeds of approximately \$96 million, in connection with the execution of a collaboration and license agreement with Astellas.
- (3) In December 2006, we in-licensed the rights to our lead product candidate, tivozanib, in all territories of the world, except for Asia.
- (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.

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

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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.

Astellas Pharma Inc.

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 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' 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, 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

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we will be 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, 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.

The collaboration activities in North America and Europe will be 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 will be 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 clinical supply and commercial supply agreements 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, including the filing of an NDA in the United States to treat patients with RCC, 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 expect to retain net proceeds of approximately \$96 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 \$575 million in milestone payments upon achievement of specified clinical development and 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 (ii) 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.

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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.

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 provides 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. Our strategic partnership with OSI is primarily focused 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. We are currently working with OSI 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. The research program portion of our strategic partnership began in October 2007 and will expire at the end of June 2011 unless the agreement is terminated earlier by either party. Key elements of our strategic partnership with OSI include:

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

generating 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

applying 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.

We are required to devote, and OSI is required to fund, a mutually agreed minimum number of individuals to the research program each year.

Under the terms of our agreement, OSI may, but has no obligation to, elect 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.

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

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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 is expected to be completed in July 2011.

During the remainder of the research program, which will expire in June 2011, neither we nor our affiliates has the right to conduct validation or biomarker research with respect to certain pre-agreed targets that are being, or may be, pursued under our strategic partnership, or to grant any such rights to any third party. Further, during the remainder of the research program, we cannot grant any third party rights to intellectual property used in creating the tumor models and archives to which we granted OSI an option, except that we may grant rights in this intellectual property and these archives to our affiliates and to third parties in connection with the partnering of our existing drug discovery and development programs. We also retain the right to use this intellectual property and these archives for our internal research purposes, including internal use for the benefit of our existing and future third party strategic partners.

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. On December 1, 2010, we announced that OSI had exercised its option under the parties July 2009 expansion of the agreement to obtain a non-exclusive, perpetual license to certain elements of our propriety technology platform and that OSI will pay us \$25 million in license expansion fees. We received \$12.5 million upon delivery of the notice of option exercise, with the remaining \$12.5 million to be paid following the successful transfer of the applicable technology from us to OSI, which is expected to be completed in July 2011. As of December 31, 2010, we have received approximately \$13.7 million in research and development funding under the agreement, and we will continue to receive research funding to support all individuals we devote to the strategic partnership until expiration of the research program. To date, we have received milestone payments under the agreement in the amount of \$15.3 million, which includes the payment of \$12.5 million in connection with the exercise by OSI of its option to obtain a non-exclusive license to certain elements of our technology platform. 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. In addition, OSI is required to make payments to us upon our completion of additional deliverables under the research plan. 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, we will retain 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

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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 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).

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 are collectively referred 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 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

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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.

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 and April 2010, we received a \$5.0 million milestone payment for achievement of the first two pre-clinical discovery milestones under the agreement. We could also receive (i) additional pre-clinical discovery and development milestone payments of \$5.0 million in the aggregate, and (ii) if Biogen Idec exercises its option to obtain exclusive rights to commercialize ErbB3 antibody products in its territory, an option exercise fee and regulatory milestone payments of \$50.0 million in the aggregate. 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,

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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 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.

Merck

Target Identification Collaboration

In November 2003, we entered into a license and collaboration agreement with Merck to discover and validate oncology targets. During the research program portion of the collaboration, which concluded in November 2006, we used our proprietary cancer models to identify and subsequently validate essential tumor maintenance genes suitable as targets for small molecule drug development. During the research program, Merck exercised its option with respect to, and we granted Merck an exclusive, worldwide license, with the right to grant sublicenses, to six molecular targets, and associated data, discovered and validated by us under the research

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collaboration, to develop, manufacture and commercialize small molecule products directed to such targets for therapeutic use. In conjunction with the exclusive license granted to Merck, we granted Merck non-exclusive licenses, with the right to grant sublicenses, to (1) develop, manufacture and commercialize products and compounds directed at certain targets for diagnostic use, and (2) develop, manufacture and use biological products (antibodies, proteins, polypeptides, etc.) directed at certain targets solely for the research or development of products for therapeutic and/or diagnostic use. We also granted Merck a non-exclusive right to use data generated during the collaboration, not related to the six collaboration targets exclusively licensed by Merck, solely for Merck's and its affiliates' internal research purposes. Except for the six collaboration targets selected by Merck, we retain all of our rights to targets that were explored under the research collaboration. Merck is solely responsible for drug discovery, clinical development and commercialization of the products directed to the six collaboration targets it selected.

Upon entering into the agreement with Merck, we received a \$7.0 million cash up-front payment. Over the course of the three-year research program, we received approximately \$6.0 million in research funding, and as of December 31, 2010, we have received milestone payments of approximately \$300,000. The collaboration was expanded in April 2005, and as part of that expansion, we received a \$5.0 million equity investment. We also received cash payments of \$2.0 million in each of May 2005 and April 2006 in return for providing Merck with rights to advance a pre-agreed number of targets into high-throughput screening. In addition, if all development and regulatory milestones are reached with respect to each of the six targets, potential additional milestone payments could total, in the aggregate, \$249.0 million. We are also eligible to receive tiered royalties from Merck based on the sales of products that are directed to or use the collaboration targets selected by Merck. Merck'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.

Our agreement with Merck will remain in effect for the length of Merck's royalty obligation to us, determined on a product-by-product and country-by-country basis. Merck has the right to terminate the agreement at any time, in its sole discretion, upon 120 days' prior written notice to us. 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 Merck terminates the agreement at will, or if we terminate the agreement due to Merck's material breach of the agreement, Merck's licenses to develop, manufacture, and commercialize products directed to or using the collaboration targets will terminate, and we will be permitted to use the data generated under our collaboration to research, develop and commercialize products directed to such targets.

Biomarker Identification Collaboration

In August 2005, we entered into our second collaboration with Merck, a license and research collaboration agreement relating to the use of our Human Response Platform. The collaboration concluded in December 2007 and was focused on the identification of genetic profiles that correlate with drug response to certain cancer compounds then under development at Merck, in order to more effectively guide Merck's clinical and market development of these compounds.

Under the terms of the agreement, Merck obtained exclusive rights to all inventions and discoveries developed in the conduct of the collaborative research program that relate to Merck's proprietary cancer compounds, including gene expression patterns that correlate with a response to Merck's compounds. We and Merck jointly own the rights to all inventions and discoveries developed in the conduct of the collaborative research program that relate to control compounds (i.e. non-Merck compounds), including gene expression patterns that correlate with a response to the control compounds. Upon entering into the license and research collaboration agreement with Merck, we received a \$2.0 million equity investment, and over the course of the collaborative research program we received approximately \$4.5 million in research funding. If all development and regulatory milestones under the agreement are achieved, potential milestone payments could total, in the aggregate, \$4.9 million.

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Either party may terminate the agreement in the event of an uncured material breach by, or a bankruptcy event of, the other party. If Merck terminates the agreement due to our material breach of the agreement, Merck's payment obligations to us will also terminate. Merck may terminate the agreement at any time for convenience by providing us with at least 120 days' prior written notice, however, Merck's payment obligations to us will continue after such termination if the applicable milestone events are achieved. If the license and research collaboration agreement is not terminated as described above, the agreement will continue in effect until the expiration of all of Merck's payment obligations to us under the agreement.

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: 5 issued; 1 pending; expirations ranging from 2018 to 2030

European patents: 3 granted; none pending; expirations ranging from 2018 to 2023

Canadian patents: none granted; 1 pending; expiration 2022

Australian patents: 1 granted; none pending; expiration 2022

International applications: 3 pending; expirations ranging from 2029 to 2030

our antibody product pipeline and related technologies

U.S. patents: 3 issued; 8 pending; expirations ranging from 2027 to 2031

European patents: 1 granted; 4 pending; expirations 2027 to 2029

International applications: none pending

various facets of our technology platform

U.S. patents: 4 issued; 2 pending; expirations ranging from 2020 to 2025

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European patents: 1 granted; 3 pending; expirations ranging from 2022 to 2026

Australian patents: 2 granted; 2 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 a pending application 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, and methods of making and using those antibodies. We are prepared to file patent applications on the other antibodies in our antibody product pipeline soon after the experimental data necessary for an application becomes available.

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.

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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, or may be shortened if a patent is terminally disclaimed 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, our patent portfolio contains a number of 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. Furthermore, 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. 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 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

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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.

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.

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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. 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. 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 and establish contractual relationships with them to secure supply on a commercial basis. 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, we may not be able to successfully produce and market tivozanib.

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. Pursuant to the terms of our agreement with Merck, we are currently in discussions with Merck regarding the purchase of amounts of clinical supply of ficlatuzumab which supply we expect will allow us to complete our ongoing phase 1 and phase 2 clinical trials of ficlatuzumab. While we believe that the existing batches we expect will be purchased from Merck are adequate to support the ongoing clinical trials, we will need to identify a third party manufacturer capable of producing quantities of drug substance and drug product to support other clinical trials, including planned phase 3 clinical trials and commercial quantities. If we are unable to arrange for purchase of sufficient amounts of clinical supply of ficlatuzumab from Merck or identify a third-party manufacturing source, or fail to do so on commercially reasonable terms, we may not be able to successfully further develop and market ficlatuzumab.

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.

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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 recently entered into a strategic partnership with Astellas in connection with which we and Astellas will 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, as well as internal and outsourced commercial groups including sales 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 will share with our partner, Astellas. To develop the appropriate commercial infrastructure, 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. In Europe, although Astellas will 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 U.S. Food and Drug Administration, or 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.

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.

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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 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.

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

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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;

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.

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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.

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

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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 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.

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.

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.

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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, Special Protocol Assessment or Protocol Assistance 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 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 subject to 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 Community. 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

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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.

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 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,

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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, which sets the target date for FDA action on the application at 6 months. 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. 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

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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 or cost-effective. 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.

The Medicare Part D outpatient prescription drug benefit went into effect in 2006. Such government payment for some of the costs of prescription drugs may increase demand for any products for which we receive marketing approval. However, coverage under Medicare Part D is provided primarily through private entities, which act as plan sponsors and negotiate price concessions from pharmaceutical manufacturers, thus limiting the payment we may be able to receive for our products for which we receive marketing approval, if any.

In 2010, Congress enacted sweeping health care reform legislation. This legislation is expected to substantially change the way that health care is financed by both governmental and private insurers and significantly affect the pharmaceutical industry. Among the provisions of the legislation are provisions governing enrollment in federal health care 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 health care providers and to the distribution of product samples to health care providers. In addition, the federal government has been given additional enforcement authority.

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 health care legislation and regulations, including regulations that will be issued to implement provisions of the health care reform legislation. The recently 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 Community, governments influence the price of pharmaceutical products through their pricing and reimbursement rules and control of national health care 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 health care 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.

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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.

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. 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. All of our activities are potentially subject to federal and state consumer protection and unfair competition laws.

Employees

As of December 31, 2010, we had 147 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.

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Our research and development costs were \$86.3 million in 2010, \$51.8 million in 2009, and \$41.8 million in 2008. 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.

Executive Officers

The following table lists the positions, names and ages of our executive officers as of March 1, 2011:

Executive Officers

Tuan Ha-Ngoc	58	Chief Executive Officer, President and Director
David Johnston	55	Chief Financial Officer
Elan Ezickson	47	Executive Vice President, Chief Business Officer
William Slichenmyer, M.D., Sc.M.	53	Chief Medical Officer
Michael P. Bailey	45	Chief Commercial Officer
Jeno Gyuris, Ph.D.	51	Senior Vice President, Head of Research

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, the Boston Philharmonic Orchestra, 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 Executive Vice President effective as of July 1, 2010 and has served as 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 sits on the Board of Directors of the Greater Boston Food Bank. 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, M.D., Sc.M. 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 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.

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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 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, Ph.D. was named Senior Vice President, Head of Research in January 2010, 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 and as our Senior Vice President, Drug Discovery from January 2007 to January 2010. 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.

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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.

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, which is in phase 3 development.

To date, we have invested a significant portion of our efforts and financial resources in the research and development of tivozanib. We are currently conducting our phase 3 registration clinical trial for tivozanib, referred to as TIVO-1, as well as a phase 2 clinical trial and five phase 1 clinical trials, four of which focus on tivozanib in combination with other known anti-cancer agents.

Our near-term prospects, including our ability to finance our company and to generate strategic partnerships and 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:

successful completion of our phase 3 clinical trial and timely enrollment in, and completion of, our other on-going or planned clinical trials;

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 trials, including without limitation TIVO-1;

the prevalence and severity of adverse side effects;

timely receipt of necessary marketing approvals from the FDA and similar foreign regulatory authorities;

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

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;

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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; and

a continued acceptable safety profile of the product following approval.

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

Positive results in our phase 2 clinical trial of tivozanib may not be predictive of the results in our phase 3 clinical trial. If the results of our phase 3 clinical trial are not positive, or are not sufficient for approval of tivozanib, our business will be adversely affected.

Positive results in early clinical trials of a drug candidate may not be replicated in later clinical trials. A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials even after achieving promising results in earlier-stage development. Although the results of our phase 2 clinical trial of tivozanib for the treatment of advanced RCC were positive, we cannot assure you that the phase 3 clinical trial for the treatment of advanced RCC will achieve positive results. A number of factors could contribute to a lack of positive results in our phase 3 clinical trial of tivozanib.

For example, in our phase 2 clinical trial, we compared tivozanib to treatment with placebo. In our phase 3 clinical trial, the primary endpoint is a comparison of progression-free survival of patients treated with tivozanib to the progression-free survival of patients treated with Nexavar. Nexavar is a VEGF receptor inhibitor which has been approved by the FDA and the European Medicines Agency, or the EMA, for the treatment of advanced RCC, as well as the treatment of hepatocellular carcinoma. Based on our discussions with the FDA and the EMA, we set the number of patients to be enrolled in the clinical trial at a number we expect will be sufficient to demonstrate that a difference in progression-free survival of three months or more between the treatment arms would be statistically significant. 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.

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, including Votrient, which was approved by the FDA in October 2009, 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.

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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 RCC. We are also conducting phase 1b 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 and phase 2 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.

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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;

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.

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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.

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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 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 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.

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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 never achieve or sustain profitability, which would depress the market price of our common stock.

We have incurred net losses since our inception, including net losses of \$58.8 million, \$44.1 million and \$32.5 million for the years ended December 31, 2010, 2009 and 2008, respectively. As of December 31, 2010, we had an accumulated deficit of \$236.5 million. We do not know whether or when we will achieve or sustain profitability. To date, we have not commercialized any products or generated any revenues from the sale of products. 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, research, development and commercialization activities, including the phase 3 clinical development and planned commercialization of our lead product candidate, tivozanib, and the continued clinical development of our phase 2 product candidate, ficlatuzumab, to which we recently regained rights from Merck.

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 a phase 3 and phase 2 clinical trial of tivozanib, with which we share expenses with Astellas, and a phase 2 clinical trial of ficlatuzumab, 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, including the upfront payments we received under the Astellas agreement, will allow us to fund our operating plan through 2012. 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;

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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.

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 agreements with Astellas, OSI Pharmaceuticals and Biogen Idec.

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 Pharmaceuticals and Biogen Idec. 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 our product candidates would 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.

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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 68.

Fluctuations in our quarterly operating losses could adversely affect the price of our common stock.

Our quarterly operating losses may fluctuate significantly. Some of the factors that may cause our operating losses 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;

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 losses 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, 2010, we had \$140.2 million of cash, cash equivalents and marketable securities consisting of money market funds, U.S. treasuries, U.S. government agency securities, corporate debt and 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 the general economic downturn.

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Risks Related to Our Business and Industry

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, as an early stage company, 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 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.

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, marketed by Pfizer Inc., Votrient, marketed by GlaxoSmithKline plc, Torisel, marketed by Pfizer, 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. 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;

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.

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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.

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 Business 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, Head of Research, as well as other senior scientists on our management team. Although none of these individuals has informed us to date that he intends to retire or resign in the near future, the loss of services of any of these individuals or one or more of our other members of senior 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.

Although we have not historically experienced unique difficulties attracting and retaining qualified employees, we could experience such problems in the future. For example, 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 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

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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 would 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;

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

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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:

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.

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, health care 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, health care 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;

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the clinical indications for which the drug is approved;

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

with respect to tivozanib, the results obtained in our phase 3 clinical trial for the treatment of advanced clear cell RCC and the extent to which the results 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, 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.

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 health care 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;

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 health care 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.

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As a result of legislative proposals and the trend towards managed health care in the United States, third-party payors are increasingly attempting to contain health care 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 health care, 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 health care services to contain or reduce health care 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 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 health care 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

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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 health care 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 health care 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 recently 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 a strategic partnership with OSI, 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.

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.

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, Merck terminated its collaboration agreement with us related to ficlatuzumab effective December 27, 2010, at which point we assumed responsibility for funding and

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performance of all research and clinical development manufacturing and future commercialization of ficlatuzumab. 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.

Our strategic partnership agreements with OSI and Biogen 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 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.

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 or OSI Pharmaceuticals 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

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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;

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.

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. 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 and establish contractual relationships with them to secure supply on a commercial basis. If we are unable to validate our third-party manufacturing sources' ability to supply on a commercial basis and fail to establish commercially reasonable terms for commercial supply, we may not be able to successfully produce and market tivozanib or would be delayed in doing so.

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Pursuant to the terms of our collaboration agreement with Merck, we are currently negotiating to purchase supply of ficlatuzumab, which supply we expect will support clinical trials of ficlatuzumab through at least phase 2 clinical trials. As of December 27, 2010, the effective date of the termination of our collaboration with Merck, we became responsible for manufacturing future batches of ficlatuzumab for additional clinical trials or for commercial use. If we are unsuccessful in acquiring sufficient amounts of ficlatuzumab from Merck to complete the ongoing phase 1 and phase 2 clinical trials, transferring the ficlatuzumab manufacturing technology from Merck, including any proprietary processes useful in such manufacturing, or engaging a third party to manufacture ficlatuzumab on terms acceptable to us, 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 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 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.

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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 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

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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 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.

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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 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.

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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 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.

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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.

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.

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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, Congress may pass patent reform legislation. 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. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has

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created uncertainty with respect to the value of patents, once obtained. 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 would 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, 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, as well as 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;

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;

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, 2010, our executive officers, directors, entities affiliated with such executive officers and directors, and certain other significant stockholders, owned approximately 43% of our

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common stock, including shares subject to outstanding options and warrants that are exercisable within 60 days after December 31, 2010. 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 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.

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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 initial cost to us as well as ongoing increases in our legal, audit and financial compliance costs.

Failure to achieve and 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, to review and evaluate our internal controls, and requires our independent registered public accounting firm to attest to the effectiveness of our internal controls. Both we and our independent registered public accounting firm will begin attesting to the effectiveness of our internal controls over financial reporting in connection with the filing of our Annual Report on Form 10-K for the year ending December 31, 2011 with the SEC. To achieve compliance with Section 404 within the prescribed period, we are engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to dedicate internal resources, engage outside consultants and adopt a detailed work plan to (a) assess and document the adequacy of internal control over financial reporting, (b) take steps to improve control processes where appropriate, (c) validate through testing that controls are functioning as documented, and (d) implement a continuous reporting and improvement process for internal control over financial reporting. 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 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

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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 the phase 3 clinical trial of tivozanib, our lead product candidate, 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 April 2012, and approximately 14,214 square feet of office space located at 12 Emily Street, Cambridge, Massachusetts, which sublease expires in May 2015. We believe that our existing facilities are sufficient for our current needs for the foreseeable future.

ITEM 3. Legal Proceedings

None.

ITEM 4. (Removed and Reserved)

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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:

	High	Low
2010		
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

HOLDERS

At February 28, 2011, there were approximately 121 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 EQUITY SECURITIES

Set forth below is information regarding certain shares of common stock, preferred stock and warrants issued by us within the past three years 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 warrants and information relating to the section of the Securities Act, or rule of the SEC, under which exemption from registration was claimed.

- (1) On March 18, 2009 and July 16, 2009, we sold an aggregate of 11,250,000 shares of our series E convertible preferred stock at a price per share of \$4.00 to accredited investors, for an aggregate purchase price of \$45,000,000.
- (2) On March 18, 2008, we sold an aggregate of 125,000 shares of our common stock to an accredited investor affiliated with a director at a price per share of \$0.004, for an aggregate purchase price of \$500.
- (3) On May 15, 2008, we issued warrants to accredited investors, in connection with debt financings completed with such accredited investors, to purchase up to an aggregate of 189,000 shares of our series D convertible preferred stock, each at an exercise price of \$2.50 per share.
- (4) From January 1, 2008 through March 17, 2010, we issued an aggregate of 149,849 shares of our common stock at prices ranging from \$0.48 to \$12.24 per share to certain of our employees, consultants and directors pursuant to the exercise of stock options under our 2002 stock plan for an aggregate purchase price of \$340,524.

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No underwriters were involved in the foregoing issuances of securities. The securities described in paragraphs (1) through (3) above were issued to accredited investors in reliance upon the exemption from the registration requirements of the Securities Act, as set forth in Section 4(2) under the Securities Act, and, in certain cases, in reliance on Regulation D promulgated thereunder, relative to transactions by an issuer not involving any public offering, to the extent an exemption from such registration was required. The securities described in paragraph (4) above were issued pursuant to written compensatory plans or arrangements with our employees, directors and consultants in reliance on the exemption provided by Rule 701 promulgated under Section 3(b) of the Securities Act, or pursuant to Section 4(2) under the Securities Act, relative to transactions by an issuer not involving any public offering, to the extent an exemption from such registration was required.

All of the purchasers of shares of our convertible preferred stock described above, the purchaser of shares of our common stock affiliated with a director described above, and the parties to which warrants were issued described above represented to us in connection with their respective acquisitions described above that they were accredited investors and that they were acquiring the applicable securities for investment and not distribution and to the effect that they could bear the risks of the investment. Such parties received written disclosures that the applicable 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.

All of the foregoing securities are deemed restricted securities for purposes of the Securities Act. The certificates representing the issued shares of capital stock and the warrants described above included appropriate legends setting forth that the applicable securities have 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, 2010, we estimate that we have used approximately \$48.8 million 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. We have invested the unused proceeds from the offering in short-term interest-bearing, investment grade securities. There has been no material change in our planned use of proceeds from the initial public offering from that described in the final prospectus filed with the SEC on March 12, 2010.

Table of Contents**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
AVEO Pharmaceuticals	\$ 100.00	\$ 100.00	\$ 78.56	\$ 123.78	\$ 162.44
NASDAQ Composite Index	\$ 100.00	\$ 102.23	\$ 89.45	\$ 100.45	\$ 112.50
NASDAQ Biotechnology Index	\$ 100.00	\$ 100.23	\$ 85.39	\$ 95.57	\$ 103.56

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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, 2010 and 2009 and the Statement of Operations Data for each of the three years ended December 31, 2010 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, 2008, 2007 and 2006, and the Statement of Operations Data for each of the two years in the period ended December 31, 2007 have been derived from the audited Consolidated Financial Statements for such years not included in this Annual Report on Form 10-K.

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

	2010	2009	Years Ended December 31, 2008		2007	2006
			(in thousands, except per share data)			
Statement of operations data:						
Revenue	\$ 44,682	\$ 20,719	\$ 19,660	\$ 11,034	\$ 7,783	
Operating expenses:						
Research and development	86,345	51,792	41,820	29,248	26,845	
General and administrative	14,763	10,120	9,165	6,502	5,161	
Total operating expenses	101,108	61,912	50,985	35,750	32,006	
Loss from operations	(56,426)	(41,193)	(31,325)	(24,716)	(24,223)	
Other income and expense:						
Other income (expense), net	900	(333)	(230)			
Interest expense	(3,389)	(2,811)	(2,086)	(2,437)	(1,591)	
Interest income	126	144	1,168	2,171	909	
Other expense, net	(2,363)	(3,000)	(1,148)	(266)	(682)	
Net loss before benefit for income taxes	(58,789)	(44,193)	(32,473)	(24,982)	(24,905)	
Benefit for income taxes		100				
Net loss	\$ (58,789)	\$ (44,093)	\$ (32,473)	\$ (24,982)	\$ (24,905)	
Net loss per share - basic and diluted	\$ (2.30)	\$ (27.43)	\$ (21.08)	\$ (17.89)	\$ (18.73)	
Weighted average number of common shares used in net loss per share calculation - basic and diluted						
	25,582	1,607	1,541	1,396	1,330	
	2010	2009	As of December 31, 2008		2007	2006
			(in thousands)			
Balance sheet data:						
Cash, cash equivalents, and marketable securities	\$ 140,198	\$ 51,301	\$ 32,364	\$ 61,742	\$ 16,748	
Working capital	103,360	18,789	16,073	42,542	3,674	
Total assets	151,048	59,844	40,087	67,654	22,448	
Loans payable, including current portion, net of discount	23,402	19,745	21,055	15,078	19,365	
Preferred stock warrant liability		1,459	1,211	905	727	
Convertible preferred stock		156,705	123,720	123,720	66,223	
Accumulated deficit	(236,514)	(177,725)	(133,631)	(101,158)	(76,176)	
Total stockholders' equity (deficit)	71,770	(170,291)	(128,688)	(98,458)	(74,547)	

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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. Tivozanib, our lead product candidate, which we recently partnered with Astellas Pharma Inc., or 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. Our clinical trials of tivozanib to date have demonstrated a favorable safety and efficacy profile for tivozanib. We have completed a successful 272-patient phase 2 clinical trial of tivozanib in patients with advanced renal cell cancer, or RCC. In this trial, we measured, among other things, each patient's progression-free survival, 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. Final data from the trial show the overall median progression-free survival of patients in the phase 2 clinical trial was 11.7 months. In a retrospective analysis of the subset of 176 patients in our phase 2 clinical trial who had the clear cell type of RCC and who had undergone prior removal of their affected kidney, referred to as a nephrectomy, both of which are inclusion criteria for our phase 3 clinical trial of tivozanib, the median progression-free survival was 14.8 months. 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, which are commonly associated with other VEGF receptor inhibitors, such as diarrhea, rash, mucositis, stomatitis, fatigue, and hand-foot syndrome, was notably low in comparison to clinical trial results of other VEGF receptor inhibitors. Severe (grade 3/4) incidences of these side effects that were considered by the investigator to be possibly related to tivozanib occurred in fewer than two percent of patients. In February 2010, we initiated enrollment in our global, phase 3 clinical trial comparing the efficacy and safety of tivozanib with Nexavar® (sorafenib), 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 and who have not received any prior VEGF-targeted therapy. In August 2010, we completed enrollment in the TIVO-1 study with 517 patients. We anticipate receiving top-line data from the TIVO-1 study in mid-2011. Nexavar is an oral VEGF receptor inhibitor approved for the treatment of RCC. In its phase 3 clinical trial in patients with advanced clear cell RCC, 94% of whom had undergone a prior nephrectomy, Nexavar demonstrated a median progression-free survival of 5.5 months. Progression-free survival is the primary endpoint in the TIVO-1 study. The TIVO-1 study is designed so that a difference in progression-free survival of three months or more between the treatment arms would be statistically significant.

In addition to the TIVO-1 study, we are evaluating tivozanib in multiple clinical trials including: a completed phase 1b clinical trial in combination with Torisel® (temsirolimus), an approved inhibitor of the receptor known as mammalian target of rapamycin, or mTOR, in patients with advanced RCC; a phase 1b clinical trial in combination with the FOLFOX6 chemotherapy regimen in patients with advanced gastrointestinal cancers, including colorectal cancer; a recently completed phase 1b clinical trial in combination with Taxol® (paclitaxel) in patients with metastatic breast cancers; a phase 1b clinical trial in combination with Xeloda® (capecitabine), an oral chemotherapeutic agent, in patients with breast and colorectal cancers; a completed phase

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1b clinical trial as a monotherapy in patients with non-small cell lung cancer; and a phase 2 clinical trial designed to evaluate biomarkers of tivozanib in patients with RCC. In addition, a phase 1 investigator sponsored clinical trial was recently completed in which tivozanib was combined with Afinitor® (everolimus), an approved inhibitor of the mTOR receptor, in patients with advanced colorectal cancer. The phase 2 portion of this investigator sponsored trial combining tivozanib with Afinitor was recently initiated in February 2011 and will enroll patients with refractory metastatic colorectal cancer. We expect that the results of these 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, *Astellas Pharma, Inc.*, we recently 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, a novel method of building preclinical models of human cancer, which are intended to more accurately represent cancer biology in patients. Ficlatusumab (AV-299), our next most advanced product candidate, is an antibody which binds to hepatocyte growth factor, or HGF, thereby blocking its function. Through the use of our Human Response Platform, our scientists have observed that the HGF/c-Met pathway is a significant driver of tumor growth. We have completed a phase 1 clinical trial of ficlatusumab and initiated a phase 2 clinical trial in patients with non-small cell lung cancer in May 2010. In 2007, we entered into an agreement with Merck and Co., Inc., or Merck (through its subsidiary Schering Corporation), under which we granted Merck exclusive worldwide rights to develop and commercialize ficlatusumab. Pursuant to the agreement, Merck funded all research, development and manufacturing expenses, subject to an agreed-upon budget, and under which Merck was obligated to pay development milestones to us, and, as applicable, royalties on product sales. On September 28, 2010, we received notice from Merck of termination of the collaboration agreement effective as of December 27, 2010, at which point we became responsible for the performance and funding of all future research, development, manufacturing and commercialization activities for ficlatusumab.

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 antibody discovery programs underway focusing 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), as well as programs directed toward the RON receptor, the Notch receptors and the Fibroblast Growth Factor receptors.

Our 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

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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.

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 and, through December 31, 2010, have principally funded our operations through:

\$134.4 million of non-dilutive capital in the form of license fees, milestone payments and research and development funding received from our strategic partners;

\$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.; and

\$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.

We have never been profitable and, as of December 31, 2010, we had an accumulated deficit of \$236.5 million. We incurred net losses of approximately \$58.8 million, \$44.1 million and \$32.5 million during the years ended December 31, 2010, 2009 and 2008, respectively. We expect to incur significant operating costs for the foreseeable future as we advance our product candidates from discovery through preclinical studies and clinical trials to seek regulatory approval and eventual commercialization.

Strategic Partnerships

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, pharmaceutical compositions thereof and associated biomarkers. Our exclusive license covers all territories in the world, except for Asia. Kyowa Hakko Kirin has retained rights to tivozanib in Asia. 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.

Upon entering into the license agreement with Kyowa Hakko Kirin, we made a one-time cash payment in the amount of \$5.0 million. We also made a \$10.0 milestone payment to Kyowa Hakko Kirin in March 2010 in connection with the initial dosing of patients in our phase 3 clinical trial of tivozanib. In addition, we may be required to make up to an aggregate of \$50.0 million in additional milestone payments upon the achievement of specified regulatory milestones. We are also required to pay Kyowa Hakko Kirin tiered royalty payments on net sales we make of tivozanib in North America. The royalty rates under the agreement range from the low to mid teens as a percentage of our net sales of tivozanib. In connection with the execution of our collaboration agreement with Astellas discussed below, we are required to pay Kyowa Hakko Kirin a specified percentage of

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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.

Astellas Pharma Inc.

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 planned 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 (excluding 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 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. We have not yet completed our assessment of our accounting for the Astellas arrangement; 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.

The collaboration activities in North America and Europe will be 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 will be 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' requirements for tivozanib pursuant to clinical supply and commercial supply agreements 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 AVEO's manufacturing costs for supply of tivozanib for North America and Europe, and Astellas' 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.

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Each party is obligated to use commercially reasonable efforts to develop and commercialize tivozanib in each of the United States, Mexico and Canada, including the filing of an NDA in the United States to treat patients with RCC, 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.

Under 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 expect to retain net proceeds of approximately \$96 million of the initial cash payments 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 \$575 million in milestone payments upon achievement of specified clinical development and 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 (ii) 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' 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 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.

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. Our strategic partnership with OSI 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. We are currently working with OSI 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

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development activities. The research program portion of our strategic partnership began in October 2007 and will expire at the end of June 2011 unless the agreement is terminated earlier by either party. Under the terms of our agreement, OSI may, but has no obligation to, elect 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. 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.

In September 2007, OSI paid us an up-front payment of \$7.5 million, which was recorded in deferred revenue and is being amortized over our period of substantial involvement, which is now determined to be through 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 are recognizing 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 is being amortized over our remaining period of substantial involvement. 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 are recognizing the premium of \$3.9 million 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 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. In connection with the exercise of the option, OSI is 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 are in the process of transferring the relevant technology to OSI. The remaining \$12.5 million will be paid following the successful transfer of the applicable technology, which is expected to be completed in July 2011. We have deferred the initial \$12.5 million payment, and are recognizing the full \$25 million relating to the option exercise by OSI over the period of substantial involvement, which is now determined to be through July 2011.

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. These milestones are not considered to be at risk and substantive, therefore, the milestone payments are being deferred and will be recognized on a straight-line basis over the remaining estimated period of substantial involvement.

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Under the amended 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. In addition, we are eligible to receive up to \$3.0 million in milestones for certain deliverables and research milestones, and up to \$24.0 million in biomarker related milestones.

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.

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 will recognize 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 and at risk, 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. This milestone was considered substantive and at risk and was included in revenue for the quarter ended March 31, 2010. We could also receive (i) a \$5.0 million pre-clinical discovery and development milestone payment, and (ii) if Biogen Idec exercises its option to obtain exclusive rights to commercialize ErbB3 antibody products in its territory, an option exercise fee and regulatory milestone payments of \$50.0 million in the aggregate.

Schering-Plough (now Merck)

In March 2007, we 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 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. We also are using our Human Response Platform to conduct translational research to guide the clinical development of ficlatuzumab. Merck was responsible for all costs related to the clinical development of ficlatuzumab and clinical and commercial

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manufacturing. On September 28, 2010, we received notice from Merck of termination of the collaboration agreement effective as of December 27, 2010, at which point we became responsible for the performance and funding of all future research, development, manufacturing and commercialization activities for ficlatuzumab. As provided for under the license agreement, we are currently in discussions with Merck regarding the purchase of amounts of clinical supply of ficlatuzumab which supply we expect will allow us to complete our ongoing phase 1 and phase 2 clinical trials of ficlatuzumab.

Under the agreement, Merck paid us an up-front payment of \$7.5 million in May 2007, which is 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 has been 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 and at risk, it has been included in revenue for the year ended December 31, 2010.

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 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;

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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 and regulatory approvals.

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.

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, 2010, 2009 and 2008:

	Years Ended December 31,		
	2010	2009	2008
	(in thousands)		
Tivozanib	\$ 52,653	\$ 23,399	\$ 14,231
Ficlatuzumab	9,855	6,498	5,671
AV-203 program	3,044	1,763	992
Platform collaborations	3,259	2,960	2,836
Antibody pipeline	6,044	5,523	5,176
Other research and development	1,299	2,358	3,437
Overhead	10,191	9,291	9,477
Total research and development expenses	\$ 86,345	\$ 51,792	\$ 41,820

Tivozanib

We have completed a phase 2 clinical trial for tivozanib and in August 2010 completed enrollment of our 517-patient phase 3 clinical trial for tivozanib in advanced RCC. We are also conducting phase 1 clinical trials of tivozanib in various combinations and dosing regimens in advanced RCC and additional solid tumor indications. 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, the timing of the regulatory process, and the success of the ongoing phase 3 clinical trial. We recently entered into a collaboration and license agreement with Astellas 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, will be shared equally between the parties. Our current estimate for the cost of the phase 3 clinical trial program, including the cost of the comparator drug, Nexavar, is approximately \$67.0 million, excluding the effect of our cost sharing arrangement with Astellas. In the first quarter of 2010, we paid Kyowa Hakko Kirin a \$10.0 million milestone in connection with the initiation of our

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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 Kyowa Hakko Kirin upon the achievement of specified regulatory milestones. Further, we are 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. In connection with the execution of our collaboration agreement with Astellas, 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 expect to pay the amount owed to Kyowa Hakko Kirin related to Astellas' license fee in the second quarter of the fiscal year ending December 31, 2011.

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 are currently conducting phase 1 clinical trials of ficlatuzumab and initiated a phase 2 clinical trial in the second quarter of 2010, for which we earned an \$8.5 million milestone payment from Merck. On September 28, 2010, we received notice from Merck of termination of the collaboration agreement effective as of December 27, 2010, at which point we became responsible for the performance and funding of all future research, development, manufacturing and commercialization activities for ficlatuzumab. Pursuant to the terms of our collaboration agreement with Merck, we are currently negotiating to purchase supply of ficlatuzumab, which supply we expect will support clinical trials of ficlatuzumab through at least phase 2 clinical trials. 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.

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. 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. 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. We commenced process development for manufacturing of this candidate in September 2010 in preparation for preclinical and human clinical trials.

Platform Collaborations

We perform research services for OSI Pharmaceuticals using our Human Response Platform. 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 are fully supported by the revenue from that agreement.

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 and additional personnel are added to these projects. 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.

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Other Research and Development

Other research and development includes expenses related to AV-412, a product candidate for which we have decided not to pursue further development, and certain funding related to our Human Response Platform, which is not specifically related to a particular product candidate or a specific strategic partnership. 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 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 complete the commercialization of tivozanib and to fund the development of ficlatuzumab 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, auditing and tax services.

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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 may also begin to incur expenses related to the sales and marketing of our product candidates in anticipation of commercial launch before we receive regulatory approval of a product candidate; and

as a result of increased payroll, expanded infrastructure and higher consulting, legal, accounting and investor relations costs, and directors and officers insurance premiums, associated with being a public company.

Interest Income and Interest Expense

Interest income consists of interest earned on our cash and 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.

Critical Accounting Policies and Significant Judgments and Estimates

Our discussion and analysis of our financial condition and results of operations are based on our 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 accrued 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 which may include (i) licenses, or options to obtain licenses, to our technology and (ii) research and development activities to be performed on behalf of the collaborative partner. 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.

When evaluating multiple element arrangements, we consider whether the components of the arrangement represent separate units of accounting. This evaluation requires subjective determinations and requires management to make judgments about the individual elements and whether such elements are separable from the other aspects of the contractual relationship. In determining the units of accounting, we evaluate whether the licenses provided to collaborative partners have standalone value based on the consideration of the relevant facts and circumstances for each arrangement. Factors considered in this determination include, among other things, the collaborative partner's experience and capabilities and the nature of the research and development activities to be provided.

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We typically receive up-front, non-refundable payments when licensing our intellectual property in conjunction with a research and development agreement. We believe that these payments generally are not separable from the activity of providing research and development services because the license generally does not have stand-alone value separate from the research and development services that we provide under our agreements. Accordingly, we generally account for these elements as one unit of accounting and recognize up-front, non-refundable payments as revenue on a straight-line basis over our contractual or estimated performance period, which is typically the term of our research and development obligations. If we cannot reasonably estimate when our performance obligation ends, then revenue is deferred until we 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 strategic partnership agreement. Such a change could have a material impact on the amount of revenue we record in future periods.

We receive payments and reimbursements for development activities undertaken by us for the benefit of our strategic partners and present them on a gross basis when we are acting as the principal in the arrangement, 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.

Our strategic partnership agreements may also contain milestone payments. Revenues from milestones, if they are non-refundable and considered substantive, are recognized upon successful accomplishment of the milestones. If not considered substantive, milestones are initially deferred and recognized over the remaining performance obligation.

We have not received any royalty revenues to date.

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

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amounts that are too high or too low in any particular period. Based on our level of clinical trial expenses as of December 31, 2010, 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 \$284,000.

Stock-Based Compensation

Effective January 1, 2006, we adopted the fair value recognition provisions of Financial Accounting Standards Board Accounting Standards Codification, or ASC, 718 Accounting for Stock Based Compensation (formerly Statement of Financial Accounting Standards No. 123(R), Share-Based Payments), which we refer to as ASC 718, using the prospective transition method. Under the prospective transition method, nonvested awards outstanding at the date of adoption continue to be accounted for in the same manner as they had been accounted for prior to adoption. All awards granted, modified or settled after the date of adoption 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 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 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 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.

The fair value of stock options was estimated at the grant date using the following assumptions:

	Years Ended December 31,		
	2010	2009	2008
Volatility	63.92%-66.81%	70.35%-72.04%	68.70%
Expected Term (in years)	5.50-6.25	5.50-6.25	5.61
Risk-Free Interest Rates	1.59%-2.92%	1.98%-3.04%	1.55%-3.34%
Dividend Yield			

We recognized stock-based compensation expense of approximately \$4.1 million, \$2.4 million and \$2.3 million for the years ended December 31, 2010, 2009, and 2008, respectively, in accordance with ASC 718. As of December 31, 2010, we had approximately \$5.7 million of total unrecognized stock-based compensation expense, net of related forfeiture estimates, which we expect to recognize over a weighted-average period of approximately 2.4 years.

Upon the adoption of ASC 718, we were 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 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.

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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 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.

The following table presents the grant dates and related exercise prices of stock options granted to employees since December 18, 2008 through the date of our initial public offering:

Date	Number of Shares Subject to Options Granted	Exercise Price	Reassessed Fair Value of Common Stock Per Share at Date of Grant	Intrinsic Value at Date of Grant
December 18, 2008	2,500	\$ 6.88	\$ 7.12	\$ 0.24
January 30, 2009	114,437	\$ 8.00	\$ 8.60	\$ 0.60
April 1, 2009	145,526	\$ 8.48	\$ 9.28	\$ 0.80
June 16, 2009	94,300	\$ 8.72	\$ 10.04	\$ 1.32
July 17, 2009	10,000	\$ 8.72	\$ 10.04	\$ 1.32
October 8, 2009	208,025	\$ 9.64	\$ 10.40	\$ 0.76
December 17, 2009	18,887	\$ 11.32	N/A	N/A
February 2, 2010	398,182	\$ 12.24	N/A	N/A
Total	991,857			

The exercise price for stock options granted above was set by our board of directors based upon our valuation models. 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 on December 18, 2008, January 30, 2009, April 1, 2009, June 16, 2009, July 17, 2009, October 8, 2009, December 17, 2009 and February 2, 2010 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. These valuations considered the following scenarios for achieving shareholder liquidity:

an IPO;

sale of the company at an equity value greater than the aggregate liquidation preference of the preferred stock; and

sale of the company at an equity value equal to or less than the aggregate liquidation preference of the preferred stock.

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. In connection with that reexamination, we prepared retrospective valuation reports of the fair value of our common stock for financial reporting purposes as of November 28, 2008, January 15, 2009, March 20, 2009, June 1, 2009 and September 25, 2009. We believe that the valuation methodologies used in the retrospective valuations and the contemporaneous valuations are reasonable and

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consistent with the Practice Aid. We also believe that the preparation of the retrospective valuations was necessary due to the fact that the timeframe and probability for a potential IPO had accelerated significantly since the time of our initial contemporaneous valuations.

In the IPO scenario for our retrospective and contemporaneous valuations, on November 28, 2008 and January 15, 2009, we applied the guideline transactions method under the market approach as provided in the Practice Aid and for the subsequent valuations, we applied the guideline public company method under the market approach as provided in the Practice Aid due to the very limited number of biotechnology company IPOs in 2008 and 2009. Our selection of guideline companies included companies deemed comparable because of their disease focus (oncology), stage of clinical trials, and size.

In the sale above liquidation preference scenario for each of our retrospective and contemporaneous valuations, we applied the guideline transactions method under the market approach as provided in the Practice Aid. Our selection of guideline transactions took into account the timing of the transactions and the characteristics of the acquired companies. We selected target companies which were deemed comparable because of their disease focus (oncology), stage of clinical trials, and size.

In the liquidation scenario for each of our retrospective and contemporaneous valuations, we assumed a sale or liquidation of the company at an equity value equal to the aggregate liquidation preference of our preferred stock.

Future values for each scenario are converted to present value by applying a discount rate estimated using a size-adjusted capital asset pricing model, or CAPM. As described in the Practice Aid, the CAPM takes into account risk-free rates, an equity risk premium, the betas of selected public guideline companies and a risk premium for size. The estimated discount rate includes a premium for company-specific risk as well.

In our application of CAPM, on each of the valuation dates disclosed, we assumed a risk-free rate of 3.17% to 4.56% based on long-term U.S. Treasuries, a supply-side equity-risk premium of 5.0% to 6.2% based on Ibbotson's *SBBi Valuation Yearbook* and *PPC's Guide to Business Valuation*, a beta of 1.27 to 1.71 based on historical trading data for our guideline public companies and a risk premium for size of 2.71% to 5.82% based on Ibbotson's *SBBi Valuation Yearbook* and company-specific risk of 5.5% to 10.0%. Changes in the risk-free rate, the equity-risk premium and beta reflect changes in market conditions. Market volatility in late 2008 and early 2009 corresponded to a decline in guideline public company betas. Changes in the risk premium for size reflect changes in the value of the company relative to the categories of size reported by Ibbotson. The company-specific risk premium reflects the significant overall business risk associated with our pre-commercial stage of development prior to the IPO and also includes our:

dependence on the success of our lead drug candidate, tivozanib, which is currently in phase 3 development;

short operating history and history of operating losses since inception;

need for substantial additional financing to achieve our goals; and

dependence on a limited number of collaboration partners.

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In our retrospective valuations for the period from November 2008 to September 2009 and our contemporaneous valuations for December 2009 and January 2010, we estimated the following probabilities and future sale and IPO dates:

Appraisal Date	11/28/08	1/15/09	3/20/09	6/1/09	9/25/09	12/17/09	2/2/10
Exercise price per share of options	\$ 6.88	\$ 8.00	\$ 8.48	\$ 8.72	\$ 9.64	\$ 11.32	\$ 12.24
Reassessed fair value of common stock per share at date of grant	\$ 7.12	\$ 8.60	\$ 9.28	\$ 10.04	\$ 10.40	N/A	N/A
Probabilities							
IPO in Q1 2010	20%	25%	35%	40%	25%	35%	35%
IPO in Q2 2010					25%	35%	35%
Sale above liquidation preference	70%	70%	60%	55%	45%	25%	25%
Sale below liquidation preference	10%	5%	5%	5%	5%	5%	5%
Future sale date	12/31/09	12/31/10	12/31/10	9/30/11	9/30/11	9/30/11	9/30/11
1 st IPO date	12/31/09	12/31/09	3/31/10	3/31/10	3/31/10	3/31/10	3/31/10
2 nd IPO date					6/30/10	6/30/10	6/30/10
Discount rate	24%	24%	24%	24%	24%	24%	24%

The estimated fair market value of our common stock at each valuation date is equal to the sum of the probability weighted present values for each scenario.

We have incorporated the fair values calculated in the retrospective valuations into the Black-Scholes option pricing model when calculating the stock-based compensation expense to be recognized for the stock options granted during the period November 2008 to September 2009. The retrospective valuations generated per share fair values of common stock of \$7.12, \$8.60, \$9.28, \$10.04 and \$10.40, respectively, at November 2008 and January, March, June and September 2009, respectively. This resulted in intrinsic values of \$0.24, \$0.60, \$0.80, \$1.32 and \$0.76 per share, respectively, at each grant date.

The retrospective fair values of our common stock increased throughout 2009 thereby reducing the difference between the fair value of our common stock and the estimated IPO price range. The increases were caused by business and scientific milestones, financing transactions and the proximity to a potential IPO. The retrospective fair value of our common stock underlying options to purchase 2,500 shares granted on December 18, 2008 was determined to be \$7.12 per share. The fair value of the common stock on that date took into account changes in the following factors:

initiation of a phase 1 clinical trial for ficlatuzumab, for which the first patient dosed triggered a \$3.0 million milestone payment from Merck; and

because of the unfavorable conditions in the public markets, we deemed the probability of an IPO to be low, or 20%.

The retrospective fair value of our common stock underlying options to purchase 114,437 shares granted on January 30, 2009 was determined to be \$8.60 per share. The increase in value from the November 2008 valuation was primarily due to the following:

we received a term sheet for the Biogen Idec agreement for ErbB3 that included a proposed \$30.0 million investment in new series E convertible preferred stock which would be priced at a premium to our other series of convertible preferred stock;

the expected proceeds from the Biogen Idec agreement would improve our position for funding future cash needs;

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due to our progress, including continued progress of our phase 2 clinical trial of tivozanib showing a favorable safety profile in patients with advanced RCC, we deemed that the probability of an IPO increased to 25% and the probability of a sale below the liquidation preference decreased to 5%; and

the timeline for a sale above the liquidation preference was extended due to expected timing of enrollment of our phase 3 clinical trial of tivozanib.

The retrospective fair value of our common stock underlying options to purchase 145,526 shares granted on April 1, 2009 was determined to be \$9.28 per share. The increase in value from the January 2009 valuation was primarily due to the following:

execution of the agreement with Biogen Idec, which included a \$30.0 million investment in series E convertible preferred stock at \$4.00 per share and a \$5.0 million up-front payment;

we initiated a phase 1b/2a clinical trial of tivozanib as a monotherapy for the treatment of non-small cell lung cancer; and

due to our progress, including continued progress of our phase 2 clinical trial of tivozanib showing a favorable safety profile in patients with advanced RCC, we deemed that the probability of an IPO increased to 35%, although the assumed timing was adjusted to March 31, 2010 due to our assessment of current market conditions.

The retrospective fair value of our common stock underlying options to purchase 94,300 shares granted on June 16, 2009 was determined to be \$10.04 per share. The increase in value from the March 2009 valuation was primarily due to the following:

in May 2009, we announced additional data from our phase 2 clinical trial of tivozanib, which demonstrated an overall median progression-free survival of patients of 11.8 months and a favorable safety profile in patients with advanced RCC;

due to our progress with respect to tivozanib, including the data noted above, we deemed that the probability of an IPO increased to 40%; and

the timeline for a sale above the liquidation preference was extended to September 30, 2011, which is closer to the date we anticipated that data would become available from our phase 3 clinical trial of tivozanib.

The retrospective fair value of our common stock underlying options to purchase 208,025 shares granted on October 8, 2009 was determined to be \$10.40 per share. The increase in value from the June 2009 valuation was primarily due to the following:

execution of an agreement with OSI which included a \$15.0 million investment in Series E convertible preferred stock at \$4.00 per share and a \$5.0 million up-front payment;

our plans to commence the phase 3 clinical trial of tivozanib; and

due to our progress and plans to commence a phase 3 clinical trial of tivozanib, we deemed that the probability of an IPO increased to 50%, with a 25% probability of an IPO being completed in the first quarter of 2010 and a 25% probability of an IPO being completed in the second quarter of 2010.

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The fair value of our common stock underlying options to purchase 18,887 shares granted on December 17, 2009 was determined to be \$11.32 per share. The increase in value from the October 2009 valuation was primarily due to the following:

initiation of the phase 3 clinical trial of tivozanib; and

due to our progress and initiation of the phase 3 clinical trial of tivozanib, we deemed that the probability of an IPO increased to 70%, with a 35% probability of an IPO being completed in the first quarter of 2010 and a 35% probability of an IPO being completed in the second quarter of 2010.

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The fair value of our common stock underlying options to purchase 398,182 shares granted on February 2, 2010 was determined to be \$12.24 per share. The increase in value from the December valuation was primarily due to a reduction in the period of time before the expected completion of an IPO.

On February 9, 2010, we and the underwriters for our IPO determined the range for the IPO. The midpoint of the range was \$14.00 per share as compared to \$12.24 per share, which was based on management's contemporaneous valuation prepared on January 22, 2010, of the estimated fair value of our common stock. The \$12.24 was used on February 2, 2010, the date of our then most recent grant of stock options. This estimated fair value represents a discount of approximately 12.6% from the midpoint of the range and an increase of 8% from the estimated fair value of our common stock on December 17, 2009. We noted that, as is typical in initial public offerings, the range was not derived using a formal determination of fair value, but was determined based upon discussions between us and the underwriters. Among the factors considered in setting this range were prevailing market conditions and estimates of our business potential. In addition to this difference in purpose and methodology, we believe that the difference in value reflected between the midpoint of the range and management's determination of the estimated fair value of our common stock on January 22, 2010 is primarily the result of the following factors:

The contemporaneous valuation we prepared on January 22, 2010 contained multiple scenarios including two IPO scenarios with an aggregate probability of 70% and two sale scenarios. If we had considered only a single scenario with 100% probability and that assumed that the IPO will be completed as of March 31, 2010, the contemporaneous valuation would have resulted in a fair value determination of \$14.48 per share.

On February 2, 2010, Ironwood Pharmaceuticals completed its IPO, which we believed demonstrated a significant improvement in the market for initial public offerings in the U.S. in the biopharmaceutical industry. We noted, however, that Ironwood's initial public offering was completed at \$11.25 per share, or a 25% discount from the midpoint of its filing range.

Our February 2010 discussions with the underwriters for our IPO took into account our and the underwriters' perceptions of significantly increased optimism regarding the market for initial public offerings, and confirmed our and our underwriters' expectations that we would complete our initial public offering by the end of the first quarter of 2010. As noted above, our January 22, 2010 contemporaneous valuation included a scenario with a 35% probability that the IPO would not be completed until the end of the second quarter of 2010.

History has shown that it is reasonable to expect that the completion of an IPO will increase the value of stock as a result of the significant increase in the liquidity and ability to trade/sell such securities. However, it is not possible to measure such increase in value with precision or certainty.

The IPO price of our common stock was \$9.00 per share. The difference between the estimated fair value of our common stock of \$12.24 per share in January 2010 and the IPO price took into account several factors considered by our board of directors and underwriters, including:

an analysis of the typical valuation ranges seen in initial public offerings for companies in our industry with similar market capitalization;

a deterioration in financial markets with accompanying decrease in market capitalization of companies comparable to ours;

increased difficulty in raising equity financing with accompanying financing uncertainty;

a review of the then current market conditions and the results of operations, competitive position and the stock performance of our competitors; and

consideration of our history as a private company and previous valuation reports received by independent valuation firms. As of December 31, 2010, 3,605,718 shares of our common stock were issuable upon exercise of stock options.

Table of Contents**Results of Operations****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)	%
Revenue	2010	2009		
	(in thousands)			
Strategic Partner:				
Schering-Plough (Merck)	\$ 22,561	\$ 10,853	\$ 11,708	108%
OSI Pharmaceuticals	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%

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

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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.

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 Capital Inc., or Hercules Technology Growth Capital, 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.

Table of Contents**Comparison of Years Ended December 31, 2009 and 2008**

The following tables summarize the results of our operations for each of the years ended December 31, 2009 and 2008, together with the changes in those items in dollars and as a percentage:

	Years Ended December 31,		Increase/ (decrease)	%
	2009	2008		
	(in thousands)			
Revenue	\$ 20,719	\$ 19,660	\$ 1,059	5%
Operating expenses:				
Research and development	51,792	41,820	9,972	24%
General and administrative	10,120	9,165	955	10%
Total operating expenses	61,912	50,985	10,927	21%
Loss from operations	(41,193)	(31,325)	(9,868)	32%
Other income (expense), net	(333)	(230)	(103)	(45)%
Interest expense	(2,811)	(2,086)	(725)	35%
Interest income	144	1,168	(1,024)	(88)%
Net loss before benefit for income taxes	(44,193)	(32,473)	(11,720)	36%
Benefit for income taxes	100		100	
Net loss	\$ (44,093)	\$ (32,473)	\$ (11,620)	36%

Revenue	Years Ended December 31,		Increase/ (decrease)	%
	2009	2008		
	(in thousands)			
Strategic Partner:				
Schering-Plough (Merck)	\$ 10,853	\$ 13,349	\$ (2,496)	(19)%
OSI Pharmaceuticals	9,788	6,144	3,644	59%
Kyowa Hakko Kirin	78		78	
Eli Lilly		167	(167)	(100)%
	\$ 20,719	\$ 19,660	\$ 1,059	5%

Revenue. Revenue for the year ended December 31, 2009 was \$20.7 million compared to \$19.7 million for the year ended December 31, 2008, an increase of approximately \$1.1 million or 5%. Revenue for the year ended December 31, 2008 included a \$3.0 million milestone payment from Schering-Plough (now Merck) for the first human dosed in the phase 1 clinical trial of ficlatuzumab. There was no corresponding milestone in 2009. Excluding the \$3.0 million milestone payment in 2008, revenue for the year ended December 31, 2009 increased \$4.1 million over the same period in 2008. The increase was attributable to an increase in amortization of deferred revenue associated with the amended OSI agreement in the amount of \$2.4 million; an increase in research revenue earned under the OSI agreement of \$1.3 million; additional research and development revenue of \$1.0 million earned under the agreement with Schering-Plough (now Merck); and a \$0.1 million reimbursement by Kyowa Hakko Kirin for our supply of tivozanib to Kyowa Hakko Kirin to be used in a phase 1 clinical trial which Kyowa Hakko Kirin is conducting in Japan. These increases were partially offset by a decrease of \$0.5 million in amortization of deferred revenue under the agreement with Schering-Plough (now Merck) due to a change in the estimated period of our substantial involvement and \$0.2 million in revenue from Eli Lilly and Company pursuant to our agreement with Eli Lilly and Company which ended in 2008.

Research and development. Research and development expense for the year ended December 31, 2009 was \$51.8 million compared to \$41.8 million for the year ended December 31, 2008, an increase of \$10.0 million or 24%. The increase was primarily attributable to a \$3.0 million purchase of Nexavar, the comparator drug used in

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our phase 3 clinical trial of tivozanib; an increase in clinical trial costs of \$2.1 million resulting primarily from costs for the phase 3 clinical trial of tivozanib offset by a reduction in costs of the phase 2 clinical trial for tivozanib as it winds down; an increase in spending for toxicology supporting tivozanib of \$1.4 million; a \$1.4 million increase in salaries and benefits mainly due to an increase in personnel primarily supporting development activities for tivozanib and our antibody pipeline; a \$1.0 million increase in contract manufacturing for tivozanib to support an increasing number of trials, including our phase 3 clinical trial; a \$0.8 million increase in costs related to ficlatuzumab which were reimbursed by Merck but recorded on a gross basis; a \$0.5 million increase in outsourced services primarily supporting research activities for the antibody pipeline; a \$0.4 million increase in lab supplies and mice; a \$0.4 million increase in stock-based compensation expenses for employees and nonemployees; and a \$0.2 million increase in facility expenses as result of our lease in September 2008 of an additional 7,407 square foot of space. These increases were partially offset by a decrease in licensing costs of \$0.8 million as a result of a license of a third party drug discovery technology in 2008 which was fully expensed in 2008; and a \$0.3 million decrease in contract manufacturing costs for the AV-412 program which has been discontinued.

Included in research and development expense were stock-based compensation expenses of \$1.2 million and \$0.8 million for the years ended December 31, 2009 and 2008, respectively.

General and administrative. General and administrative expense for the year ended December 31, 2009 was \$10.1 million compared to \$9.2 million for the year ended December 31, 2008, an increase of \$1.0 million or 10%. The increase was primarily a result of \$0.8 million in salaries and benefits mainly due to an increase in personnel needed to support increased research and development; a \$0.2 million increase in consulting associated with finance and marketing; a \$0.1 million increase in patent expenses related to ficlatuzumab which are reimbursed by Merck but are recorded on a gross basis; a \$0.1 million increase in legal expenses primarily related to the support of our phase 3 clinical trial of tivozanib; and a \$0.1 million increase in public relations expense. Such increases were partially offset by a \$0.4 million decrease in stock-based compensation expense. The decrease in stock-based compensation expense results from a \$0.8 million share-based expense for a stock issuance in 2008 to a former consultant and an entity affiliated with a board member after a warrant held by such entity expired unexercised.

Included in general and administrative expense were stock-based compensation expenses of \$1.1 million and \$1.5 million for the years ended December 31, 2009 and 2008, respectively. Stock-based compensation expenses for 2008 included a \$0.8 million share-based expense for a stock issuance in 2008 to a former consultant and an entity affiliated with a board member after a warrant held by such entity expired unexercised.

Other income (expense), net. Other income (expense), net for the year ended December 31, 2009 was \$(0.3) million compared to \$(0.2) million for the year ended December 31, 2008, a decrease of \$0.1 million. The decrease was largely a result of a charge for the increase in the value of warrants to purchase preferred stock resulting from an increase in value of the underlying stock.

Interest expense. Interest expense for the year ended December 31, 2009 was \$2.8 million compared to \$2.1 million for the year ended December 31, 2008, an increase of \$0.7 million or 35%. The increase was due to an increase in the average loan balance in 2009 due to a drawdown of \$10.0 million in September 2008 which was outstanding for the full period of 2009.

Interest income. Interest income for the year ended December 31, 2009 was \$0.1 million compared to \$1.2 million for the year ended December 31, 2008, a decrease of \$1.0 million or 88%. Although the average cash balances were higher for the year ended December 31, 2009, interest rates decreased to only slightly above 0% in 2009 causing the significant decrease in interest income.

Table of Contents**Liquidity and Capital Resources**

We have funded our operations principally through the sale of equity securities sold in connection with our initial public offering, the private placement of equity securities, revenue from strategic partnerships, debt financing and interest income. As of December 31, 2010, 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, and \$169.6 million from the sale of convertible preferred stock, including \$32.9 million from the sale of 11,250,000 shares of series E convertible preferred stock in 2009. As of December 31, 2010, we had received an aggregate of \$134.4 million in cash from our three agreements with Merck and our agreements with OSI Pharmaceuticals, Biogen Idec, and Eli Lilly, and \$25.0 million in funding from our debt financing with Hercules Technology Growth Capital and certain of its affiliates. As of December 31, 2010, we had cash, cash equivalents and marketable securities of approximately \$140.2 million. We expect to retain net proceeds of approximately \$96 million of the initial cash payment from Astellas, after payments to KHK and strategic, legal and financial advisors. Currently, our funds are invested in money market funds, U.S. government agency securities, corporate debt and commercial paper. The following table sets forth the primary sources and uses of cash for each of the periods set forth below:

	2010	Years Ended December 31, 2009	2008
	(in thousands)		
Net cash used in operating activities	\$ (51,825)	\$ (9,973)	\$ (35,301)
Net cash (used in) provided by investing activities	(90,506)	3,414	28,151
Net cash provided by financing activities	142,832	31,035	6,881
 Net increase (decrease) in cash and cash equivalents	 \$ 501	 \$ 24,476	 \$ (269)

During the years ended December 31, 2010, 2009 and 2008, our operating activities used cash of \$51.8 million, \$10.0 million and \$35.3 million, respectively. The use of cash in all periods primarily resulted from our net losses adjusted for non-cash items, which have increased each year as we have incurred additional research and development spending as we advance development of our product candidates. The variance in cash used in operating activities during the years ended December 31, 2010, 2009 and 2008, respectively, is primarily due to an increased deferred revenue balance at December 31, 2009 due to our license agreements with OSI and Biogen. 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 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. The cash used in operating activities for the year ended December 31, 2008 was primarily the result our net loss adjusted for non-cash items and an increase in research and development activities, and a decrease in deferred revenue of \$6.6 million related to the recognition of previously deferred revenue.

During the years ended December 31, 2010, 2009 and 2008, our investing activities provided (used) cash of \$(90.5) million, \$3.4 million and \$28.2 million, respectively. The cash used in investing activities for the year ended December 31, 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 \$1.7 million. The cash provided by investing activities for the years ended December 31, 2009 and 2008 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 and \$1.4 million, respectively.

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During the years ended December 31, 2010, 2009 and 2008, our financing activities provided \$142.8 million, \$31.0 million and \$6.9 million, respectively. 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 Capital, 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. The cash provided by financing activities in 2008 was a result of the net proceeds of \$10.7 million from the refinancing of loans payable related to our original loan with Hercules Technology Growth Capital, partially offset by principal payments on loans payable of \$3.8 million.

On October 29, 2010, we received notification from the Internal Revenue Service that we were 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 have been made with respect to certain of our qualifying research and development programs. We have received the full amount related to these grants during the fourth quarter of 2010, and this amount has been recorded as other income in the statement of operations for the year ended December 31, 2010.

Credit Facilities. On May 15, 2008, we entered into a \$21.0 million financing agreement with Hercules Technology Growth Capital and Comerica Bank, referred to as the prior loan agreement. The full amount of the loan was drawn down in 2008. On May 28, 2010, we 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 Capital, 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 the prior loan agreement. 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 April 1, 2011, provided, however, that such date will be extended under certain circumstances specified in the new loan agreement. 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. 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 entire 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 September 1, 2013, provided, however, such amounts will be due and payable on a later date under certain circumstances specified in the new loan agreement.

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, 2010, the principal balance outstanding was \$25.0 million.

In November 2003, we entered into a \$7.5 million financing agreement with General Electric Capital Corporation for an equipment capital expenditure line, which we refer to as the equipment line, and a refinancing

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line of existing equipment debt, which we refer to as the refinancing line. Borrowings under the equipment line were repayable over 54 months, the first six of which were interest only at fixed interest rates ranging from 8.39% to 10.11%, with a 10% end-of-term balloon payment (guaranteed purchase option). The aggregate principal outstanding under the equipment line and the refinancing line was fully paid in June 2010. There is no remaining ability to borrow under the equipment line and refinancing line with General Electric Capital Corporation.

Operating Capital Requirements. Assuming we successfully complete clinical trials and obtain requisite regulatory approvals, we anticipate commercializing our first product in 2013 at the earliest. Therefore, we anticipate that we will continue to incur significant operating costs for the next several years as we incur expenses to complete our clinical trial programs for tivozanib, build commercial capabilities, develop our antibody pipeline and expand our corporate infrastructure. We believe that our existing cash and cash equivalents, marketable securities, and committed research and development funding and milestone payments that we expect to receive under our existing strategic partnership and license agreements, including the upfront payments we received under the Astellas agreement, will allow us to fund our operating plan through 2012.

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.

Table of Contents**Contractual Obligations and Commitments**

The following table summarizes our contractual obligations at December 31, 2010:

	Total	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)	\$ 32,342	\$ 9,452	\$ 22,890	\$	\$
Operating lease obligations	7,317	2,452	4,497	368	
Other License Agreements ⁽¹⁾	925	525	350	50	
Total contractual cash obligations	\$ 40,584	\$ 12,429	\$ 27,737	\$ 418	\$

(1) 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 \$475,000 per year. We have included one milestone payment of \$50,000 in the table above, but have not included any additional milestone payments 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 call for 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.

In connection with the collaboration and license agreement we entered into with Astellas on February 16, 2011, we are obligated to pay approximately \$29 million to KHK and strategic, legal and financial advisors. Pursuant to the terms of our collaboration agreement with Merck, we are currently negotiating to purchase supply of ficlatuzumab, which we expect will support clinical trials of ficlatuzumab through at least phase 2 clinical trials.

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 October 2009, the FASB issued Accounting Standards Update (ASU) Update No. 2009-13, *Revenue Recognition (Topic 605): Multiple-Deliverable Revenue Arrangements (ASU 2009-13)*. The consensus in ASU 2009-13 supersedes certain guidance in Topic 605 (formerly EITF Issue No. 00-21, *Multiple-Element Arrangements*) and requires an entity to allocate arrangement consideration at the inception of an arrangement to all of its deliverables based on their relative selling prices. The consensus eliminates the use of the residual method of allocation and requires the use of the relative-selling-price method in all circumstances in which an entity recognizes revenue for an arrangement with multiple deliverables subject to ASC 605-25. ASU 2009-13 establishes a relative-selling-price hierarchy for determining the selling price of a deliverable, which includes: (1) vendor-specific objective evidence of fair value if available; (2) third party evidence if vendor-specific objective evidence of fair value is not available; and (3) estimated selling price if neither vendor-specific objective evidence of fair value or third party evidence is available. Prior to ASU 2009-13, Topic 605 required that the fair value of an undelivered item be determined by reference to vendor-specific objective evidence of fair value or third party evidence. This was difficult to determine when a deliverable was not individually sold because of its unique features. 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. ASU 2009-13 is effective

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prospectively for revenue arrangements entered into or materially modified in fiscal years beginning on or after June 15, 2010. This standard may impact our accounting for collaborative agreements entered into or materially modified after January 1, 2011.

In February 2010, the FASB issued amended guidance on subsequent events. Under this amended guidance, SEC filers are no longer required to disclose the date through which subsequent events have been evaluated in originally issued and revised financial statements. This guidance was effective immediately and we adopted these new requirements upon issuance of this guidance.

In April 2010, the FASB issued ASU No. 2010-17, *Revenue Recognition Milestone Method* (ASU 2010-017). ASU 2010-017 provides guidance in applying the milestone method of revenue recognition to research or development arrangements. This guidance concludes 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. The guidance is effective for fiscal years, and interim periods within those years, beginning on or after June 15, 2010. The adoption of this accounting standard is not expected to impact our financial position or results of operations.

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, 2010 and December 31, 2009, we had cash and cash equivalents and marketable securities of \$140.2 million and \$51.3 million, respectively, consisting of money market funds, U.S. treasuries, U.S. government agency securities, foreign government agency securities, corporate debt and 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 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.

We contract with contract research organizations and investigational sites globally. We may be subject to fluctuations in foreign currency rates in connection with these agreements. We do not hedge our foreign currency exchange rate risk.

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, 2010, we would have a decrease in future annual cash flows of approximately \$219,000 over the next twelve month period.

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ITEM 8. Financial Statements and Supplementary Data

AVEO PHARMACEUTICALS, INC.

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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, 2010 and 2009, and the related consolidated 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, 2010. These consolidated financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these consolidated 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. We were not engaged to perform an audit of the Company's internal control over financial reporting. Our audits included consideration of internal control over financial reporting as a basis for designing audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion. An audit also includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, and 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, 2010 and 2009, and the consolidated results of its operations and its cash flows for each of the three years in the period ended December 31, 2010 in conformity with U.S. generally accepted accounting principles.

/s/ Ernst & Young LLP

Boston, Massachusetts

March 11, 2011

Table of Contents**AVEO Pharmaceuticals, Inc.****Consolidated Balance Sheets****(in thousands, except par value amounts)**

	2010	2009
Assets		
Current assets:		
Cash and cash equivalents	\$ 45,791	\$ 45,290
Marketable securities	94,407	6,011
Accounts receivable	391	487
Prepaid expenses and other current assets	4,864	1,306
Total current assets	145,453	53,094
Property and equipment, net	4,532	4,197
Other assets	456	1,946
Restricted cash	607	607
Total assets	\$ 151,048	\$ 59,844
Liabilities and stockholders equity (deficit)		
Current liabilities:		
Accounts payable	\$ 9,247	\$ 7,491
Accrued expenses (Note 5)	10,121	7,389
Loans payable, net of discount	5,766	7,467
Deferred revenue	16,693	11,782
Deferred rent	266	176
Total current liabilities	42,093	34,305
Loans payable, net of current portion and discount	17,636	12,278
Deferred revenue, net of current portion	16,509	23,320
Deferred rent, net of current portion	553	819
Other liabilities	2,487	1,249
Warrants to purchase convertible preferred stock		1,459
Commitments and contingencies (Note 8)		
Convertible preferred stock, \$.001 par value: 0 and 80,624 shares authorized at December 31, 2010 and 2009, respectively; 0 and 75,917 shares issued and outstanding at December 31, 2010 and 2009, respectively (Note 10)		156,705
Stockholders deficit:		
Preferred stock, \$.001 par value: 5,000 and 0 shares authorized at December 31, 2010 and 2009, respectively; no shares issued and outstanding at December 31, 2010 and 2009, respectively		
Common stock, \$.001 par value: 100,000 and 25,500 shares authorized at December 31, 2010 and 2009, respectively; 35,604 and 1,641 shares issued and outstanding at December 31, 2010 and 2009, respectively	36	2
Additional paid-in capital	308,268	7,432
Accumulated other comprehensive income	(20)	
Accumulated deficit	(236,514)	(177,725)
Total stockholders equity (deficit)	71,770	(170,291)

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Total liabilities and stockholders' equity (deficit)	\$ 151,048	\$ 59,844
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See accompanying notes

Table of Contents**AVEO Pharmaceuticals, Inc.****Consolidated Statements of Operations****(in thousands, except per share amounts)**

	Year Ended December 31,		
	2010	2009	2008
Collaboration revenue	\$ 44,682	\$ 20,719	\$ 19,660
Operating expenses:			
Research and development	86,345	51,792	41,820
General and administrative	14,763	10,120	9,165
	101,108	61,912	50,985
Loss from operations	(56,426)	(41,193)	(31,325)
Other income and expense:			
Other income (expense), net	900	(333)	(230)
Interest expense	(3,389)	(2,811)	(2,086)
Interest income	126	144	1,168
Other income (expense), net	(2,363)	(3,000)	(1,148)
Net loss before benefit for income taxes	(58,789)	(44,193)	(32,473)
Benefit for income taxes		100	
Net loss	\$ (58,789)	\$ (44,093)	\$ (32,473)
Net loss per share basic and diluted	\$ (2.30)	\$ (27.43)	\$ (21.08)
Weighted-average number of common shares used in net loss per share basic and diluted	25,582	1,607	1,541

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, 2007	64,639	123,720	1,434	2	2,583	115	(101,159)	(98,459)	
Exercise of stock options			28		33			33	
Issuance of common stock			125		805			805	
Stock-based compensation expense related to stock options granted to employees					1,369			1,369	
Stock-based compensation expense related to restricted common stock and stock options granted to nonemployees					132			132	
Vesting of restricted stock					2			2	
Change in unrealized gain/loss on investments						(97)		(97)	\$ (97)
Net loss							(32,473)	(32,473)	(32,473)
Comprehensive loss									\$ (32,570)
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 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	

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(Note 11)

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	

See accompanying notes

Table of Contents**AVEO Pharmaceuticals, Inc.****Consolidated Statements of Cash Flows**

(in thousands)

	Year Ended December 31,		
	2010	2009	2008
Operating activities			
Net loss	\$ (58,789)	\$ (44,093)	\$ (32,473)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	1,350	1,289	1,321
Stock-based compensation	4,085	2,387	2,306
Noncash interest expense	1,434	686	724
Loss on disposal of property and equipment	1		10
Remeasurement of warrants to purchase convertible preferred stock	(713)	333	(7)
Amortization of (premium) discount on investments	404	373	(496)
Changes in operating assets and liabilities:			
Accounts receivable	96	1,594	(1,460)
Prepaid expenses and other current assets	(3,595)	(155)	(211)
Other noncurrent assets	1,490	(1,825)	(146)
Accounts payable	1,756	3,636	1,437
Accrued expenses	2,732	3,981	417
Deferred rent	(176)	(141)	(116)
Deferred revenue	(1,900)	21,962	(6,607)
Net cash used in operating activities	(51,825)	(9,973)	(35,301)
Investing activities			
Purchases of property and equipment	(1,686)	(1,734)	(1,356)
Purchases of marketable securities	(167,706)	(35,927)	(28,645)
Proceeds from maturities and sales of marketable securities	78,886	41,075	58,152
Net cash (used in) provided by investing activities	(90,506)	3,414	28,151
Financing activities			
Proceeds from issuance of common stock, net of issuance costs	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	1,632	159	34
Proceeds from issuance of loans payable	7,555		10,655
Principal payments on loans payable	(3,278)	(1,986)	(3,808)
Net cash provided by financing activities	142,832	31,035	6,881
Net increase (decrease) in cash and cash equivalents	501	24,476	(269)
Cash and cash equivalents at beginning of period	45,290	20,814	21,083
Cash and cash equivalents at end of period	\$ 45,791	\$ 45,290	\$ 20,814
Supplemental cash flow and noncash investing and financing activities			
Issuance of warrants	\$ 900	\$	\$ 314
Conversion of convertible preferred stock	\$ 156,686	\$	\$

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Conversion of preferred stock warrants	\$ 745	\$	\$
Cash paid for interest	\$ 2,453	\$ 2,125	\$ 1,559
Cash paid for income taxes	\$	\$	\$
Vesting of restricted common stock	\$	\$	\$ 2

See accompanying notes

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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 recently partnered with Astellas Pharma Inc., 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. The Company also has a pipeline of monoclonal antibodies, including ficlatuzumab (AV-299), 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 subsidiary.

The Company has generated an accumulated deficit as of December 31, 2010 of approximately \$236.5 million since inception, and will require substantial additional capital for research and product development. At December 31, 2010, the Company believes that its cash, cash equivalents and marketable securities totaling approximately \$140.2 million, as well as the net proceeds of approximately \$96 million of the initial cash payment from Astellas (note 17), are sufficient to fund its operations through at least the next 12 months.

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 which may include (i) licenses, or options to obtain licenses, to the Company's technology and (ii) research and development activities to be performed on behalf of the collaborative partner. 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.

When evaluating multiple element arrangements, the Company considers whether the components of the arrangement represent separate units of accounting. This evaluation requires subjective determinations and requires management to make judgments about the individual elements and whether such elements are separable from the other aspects of the contractual relationship. In determining the units of accounting, management evaluates whether the licenses provided to collaborative partners have standalone value based on the consideration of the relevant facts and circumstances for each arrangement. Factors considered in this determination include, among other things, the collaborative partner's experience and capabilities and the nature of the research and development activities to be provided.

The Company typically receives up-front, non-refundable payments when licensing its intellectual property in conjunction with a research and development agreement. Management generally believes that these payments are not separable from the activity of providing research and development services because the license generally does not have stand-alone value separate from the research and development services to be provided under the agreements. Accordingly, the Company generally accounts for these elements as one unit of accounting and recognizes up-front, non-refundable payments as revenue on a straight-line basis over the Company's contractual

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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. 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 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, specifically reviewing factors such as the scientific and other risks that must be overcome to achieve the milestone, as well as the level of effort and investment required. Revenues from 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.

Principles of Consolidation

The Company's consolidated financial statements include the Company's accounts and the accounts of the Company's wholly owned subsidiary, AVEO Pharma Limited. 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, contracted services, license fees, and other external costs.

On January 1, 2008, the Company adopted the provisions of Accounting Standards Codification (ASC) 730-20-25-13, which requires that nonrefundable advance payments for goods and services that will be used in future research and development activities be expensed when the activity has been performed or when the goods have been received rather than when the payment is made.

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, 2010 and 2009 consist of money market funds, commercial paper, corporate bonds and U.S. government agency securities.

Marketable Securities

Marketable securities at December 31, 2010 and 2009 primarily consist of U.S. Treasuries, U.S. government agency securities, foreign government agency securities, commercial paper and corporate debt maintained by an investment manager. Credit risk is minimized as a result of the Company's policy to limit the amount invested in any one issue. Marketable securities consist primarily of investments which have original maturities at the date of purchase in excess of three months, but not longer than 24 months. The Company classifies these investments as

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available-for-sale. Unrealized gains and losses are included in other comprehensive loss as a component of stockholders' deficit until realized. The cost of securities sold is based on the specific identification method. The Company sold one security in 2010 and one security in 2008 for gross proceeds of \$4.5 million, and \$3.0 million, respectively, and recognized a gain of \$1,853 and \$20,800, respectively.

All marketable securities at December 31, 2010 and 2009 had maturities of one year or less.

Available-for-sale securities at December 31, 2010 and 2009 consist of the following:

	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
(in thousands)				
December 31, 2010:				
Corporate debt securities	\$ 71,615	\$ 19	\$ (27)	\$ 71,607
U.S. Treasuries	5,178		(1)	5,177
Government agency securities	13,503		(6)	13,497
Foreign government agency security	4,131		(5)	4,126
	\$ 94,427	\$ 19	\$ (39)	\$ 94,407

(in thousands)				
December 31, 2009:				
U.S. Treasuries	\$ 2,003	\$	\$	\$ 2,003
Government agency securities	4,009			4,009
	\$ 6,011	\$	\$	\$ 6,011

The aggregate fair value of securities in an unrealized loss position for less than 12 months at December 31, 2010 was \$50.3 million, representing eighteen securities. There were no securities that were in an unrealized loss position for greater than 12 months at December 31, 2010. 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.

Marketable securities in an unrealized loss position at December 31, 2010 consists of the following:

	Aggregate Fair Value	Unrealized Losses
(in thousands)		
December 31, 2010:		
Corporate debt securities due in less than one year	\$ 27,536	\$ (27)
U.S. Treasury due in less than one year	5,177	(1)
Government agency securities due in less than one year	13,497	(6)
Foreign government agency security due in less than one year	4,126	(5)
	\$ 50,336	\$ (39)

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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, 2010.

There were no marketable securities in an unrealized loss position at December 31, 2009.

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.

Fair Value

The carrying amounts of the Company's financial instruments, which include cash and cash equivalents, marketable securities, accounts receivable and payable, warrants and loans payable, approximate their fair values at December 31, 2010 and 2009.

On January 1, 2008, the Company adopted Financial Accounting Standards Board (FASB) ASC Topic 820, *Fair Value Measurements and Disclosures* (formerly FASB Statement No. 157, *Fair Value Measurements*), which provides guidance for using fair value to measure assets and liabilities. ASC 820 applies whenever other standards require (or permit) assets or liabilities to be measured at fair value but does not expand the use of fair value in any new circumstances. ASC 820 also requires expanded disclosure of the effect on earnings for items measured using unobservable data, establishes a fair value hierarchy that prioritizes the information used to develop those assumptions and requires separate disclosure by level within the fair value hierarchy.

The Company records cash equivalents, marketable securities and warrants to purchase preferred stock at fair value. ASC 820 establishes a fair value hierarchy for those instruments measured at fair value that distinguishes between assumptions based on market data (observable inputs) and 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.

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 U.S. agency securities, including direct issuance bonds and corporate bonds.

Level 3 Unobservable inputs developed using estimates and assumptions developed by the Company, which reflect those that a market participant would use. The fair value of the warrants to purchase convertible preferred stock is valued based on Level 3 inputs at December 31, 2009. In connection with the initial public offering consummated by the Company in March 2010, such warrants to purchase convertible preferred stock were converted into warrants to purchase common stock.

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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, 2010 and 2009.

	Fair Value Measurements of Cash Equivalents and Marketable Securities as of December 31, 2010			
	Level 1	Level 2	Level 3	Total
	(in thousands)			
Cash equivalents	\$ 28,767	\$ 14,015	\$	\$ 42,782
Marketable securities	5,177	89,230		94,407
	\$ 33,944	\$ 103,245	\$	\$ 137,189

	Fair Value Measurements of Cash Equivalents and Marketable Securities as of December 31, 2009			
	Level 1	Level 2	Level 3	Total
	(in thousands)			
Cash equivalents	\$ 38,404	\$	\$	\$ 38,404
Marketable securities		6,011		6,011
	\$ 38,404	\$ 6,011	\$	\$ 44,415

The Company's Level 2 securities in 2010 and 2009 include commercial paper, corporate bonds, U.S. government agency securities, and a foreign government agency 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.

Preferred Stock Warrant Liability

At December 31, 2009, warrants to purchase the Company's convertible preferred stock are classified as liabilities and are recorded at their estimated fair value. At each reporting period, any change in fair value of the freestanding warrants was recorded as other income (expense). In connection with the initial public offering consummated by the Company in March 2010, such warrants to purchase convertible preferred stock were converted into warrants to purchase common stock and are now recorded in equity.

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 periodically assesses the impairment of long-lived assets in accordance with ASC Topic 360, *Property, Plant, and Equipment*. 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, 2010.

Table of Contents*Comprehensive Income (Loss)*

Comprehensive income (loss) is defined as the change in equity of a business enterprise during a period from transactions and other events and circumstances from non-owner sources. Accumulated other comprehensive income consists entirely of unrealized gains/losses on available-for-sale securities.

	2010	Years Ended December 31, 2009 (in thousands)	2008
Net loss	\$ (58,789)	\$ (44,093)	\$ (32,473)
Unrealized loss on marketable securities	(20)	(18)	(97)
Total comprehensive loss	\$ (58,809)	\$ (44,111)	\$ (32,570)

Stock-Based Compensation

Effective January 1, 2006, the Company adopted the provisions of ASC Topic 718, *Compensation-Stock Compensation*, using the prospective-transition method. Under the prospective-transition method, nonvested awards outstanding at the date of adoption continue to be accounted for in the same manner as they had been accounted for prior to adoption. All awards granted, modified or settled after the date of adoption 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, 2010, 2009 and 2008, the Company recorded the following stock-based compensation expense:

	2010	Years Ended December 31, 2009 (in thousands)	2008
Research and development	\$ 1,825	\$ 1,245	\$ 811
General and administrative	2,260	1,142	1,495
Total stock-based compensation expense	\$ 4,085	\$ 2,387	\$ 2,306

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.

On January 1, 2009, the Company adopted FASB Interpretation No. 48, *Accounting for Uncertainty In Income Taxes* (codified within ASC Topic 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.

Table of Contents*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 October 2009, the FASB issued Accounting Standards Update (ASU) Update No. 2009-13, *Revenue Recognition (Topic 605): Multiple-Deliverable Revenue Arrangements* (ASU 2009-13). The consensus in ASU 2009-13 supersedes certain guidance in Topic 605 (formerly EITF Issue No. 00-21, *Multiple-Element Arrangements*) and requires an entity to allocate arrangement consideration at the inception of an arrangement to all of its deliverables based on their relative selling prices. The consensus eliminates the use of the residual method of allocation and requires the use of the relative-selling-price method in all circumstances in which an entity recognizes revenue for an arrangement with multiple deliverables subject to ASC 605-25. ASU 2009-13 establishes a relative-selling-price hierarchy for determining the selling price of a deliverable, which includes: (1) vendor-specific objective evidence of fair value (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 ASU 2009-13, Topic 605 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. 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. ASU 2009-13 is effective prospectively for revenue arrangements entered into or materially modified in fiscal years beginning on or after June 15, 2010. This standard may impact the Company's accounting for collaborative agreements entered into or materially modified after January 1, 2011.

In February 2010, the FASB issued amended guidance on subsequent events. Under this amended guidance, SEC filers are no longer required to disclose the date through which subsequent events have been evaluated in originally issued and revised financial statements. This guidance was effective immediately and the Company adopted these new requirements upon issuance of this guidance.

In April 2010, the FASB issued ASU No. 2010-17, *Revenue Recognition Milestone Method* (ASU 2010-17). ASU 2010-17 provides guidance in applying the milestone method of revenue recognition to research or development arrangements. This guidance concludes 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. The guidance is effective for fiscal years, and interim periods within those years, beginning on or after June 15, 2010. The adoption of this accounting standard is not expected to impact the Company's financial position or results of operations.

Subsequent Events

The Company has evaluated all events or transactions that occurred after December 31, 2010 up through the date the Company issued these financial statements. See Note 17 for a description of all subsequent events.

Table of Contents**3. Net Loss Per Common Share**

Basic net loss per share is calculated by dividing the net loss attributable to common stockholders by the weighted-average number of common shares outstanding during the period, without consideration for common stock equivalents. Diluted net loss per share is computed by dividing the net loss attributable to common stockholders by the weighted-average number of common share equivalents outstanding for the period determined using the treasury-stock method. For purposes of this calculation, convertible preferred stock, stock options and warrants are considered to be common stock equivalents and are only included in the calculation of diluted net loss per share when their effect is dilutive.

	Years Ended December 31,		
	2010	2009	2008
	(in thousands, except per share amounts)		
Historical net loss per share			
Numerator:			
Net loss	\$ (58,789)	\$ (44,093)	\$ (32,473)
Denominator:			
Weighted average common shares outstanding	25,582	1,607	1,541
Basic and diluted net loss per share	\$ (2.30)	\$ (27.43)	\$ (21.08)

4. Property and Equipment

Property and equipment consists of the following:

	Estimated Useful Life	December 31, 2010	December 31, 2009
		(in thousands)	
Laboratory equipment	5 years	\$ 8,075	\$ 7,160
Computer equipment and software	3 years	1,595	1,390
Office furniture	5 years	189	189
Leasehold improvements	Shorter of asset's useful life or remaining term of lease	4,109	3,768
Construction in process		318	464
		14,286	12,971
Less accumulated depreciation and amortization		(9,754)	(8,774)
Property and equipment, net		\$ 4,532	\$ 4,197

Depreciation expense for the years ended December 31, 2010, 2009 and 2008 was \$1,350,000, \$1,289,000 and \$1,321,000 respectively.

5. Accrued Expenses

Accrued expenses consisted of the following:

	December 31, 2010	December 31, 2009
	(in thousands)	
Salaries and benefits	\$ 3,696	\$ 2,142
Clinical expenses	5,676	4,612
Other	749	635

\$ 10,121 \$ 7,389

Table of Contents**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 Capital, and Comerica Bank, referred to as the prior loan agreement. The full amount of the loan was drawn down in 2008. 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 is 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, provided, however, that such date will be extended under certain circumstances specified in the new loan agreement. 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 payments on the loan each month following the date of borrowing under the new loan agreement. The entire principal balance and all accrued but unpaid interest will be due and payable on September 1, 2013, provided, however, such amounts will be due and payable on a later date under certain circumstances specified in the new loan agreement. 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. 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. These warrants expire seven years from issuance. 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 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 Capital 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, 2010, there have been no events of default under the loan. As of December 31, 2010, the principal balance outstanding was \$25.0 million.

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Future minimum payments under the loans payable outstanding as of December 31, 2010 are as follows (amounts in thousands):

Years Ending December 31:	
2011	\$ 9,451
2012	12,860
2013	10,030
	32,341
Less amount representing interest	(4,855)
Less discount	(1,597)
Less deferred charges	(2,487)
Less current portion	(5,766)
Loans payable, net of current portion	\$ 17,636

7. Collaboration and License Agreements*(a) Out-License Agreements**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 is also using its Human Response Platform to conduct translational research 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 was considered substantive and at risk, it has been included in revenue for the year ended December 31, 2010.

Under the agreement, the Company received cash payments related to upfront license fees, milestone payments, research and development funding, and equity of \$19,785,000, \$10,576,000, and \$9,522,000, and

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recorded revenue of \$22,461,000, \$10,853,000, and \$13,349,000, for the years ended December 31, 2010, 2009 and 2008, respectively. 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 (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 provides 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 biomarker research to further develop and advance OSI's small molecule drug discovery and translational research related to cancer and other diseases. Under the agreement, OSI paid the Company an up-front payment of \$7.5 million, which was recorded in deferred revenue and is being amortized over the Company's period of substantial involvement which is now determined to be through July 2011. 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 is recognizing the premium of \$917,000 as additional license revenue on a straight-line basis over the period of substantial involvement.

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 a Company 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. In consideration for such additional rights, under the amended agreement, OSI paid the Company an up-front payment of \$5.0 million, which was recorded in deferred revenue and will be amortized over the Company's remaining period of substantial involvement. 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. 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. The valuation used the Market Approach to estimate the Company's enterprise value and the Probability Weighted Expected Return Method (PWERM) to allocate the enterprise value to each class of the Company's equity securities; accordingly, the Company is recognizing the premium of \$3,900,000 as additional license revenue on a straight-line basis over the period of substantial involvement.

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 received \$12.5 million upon delivery of the notice of option exercise, and is in the process of transferring the relevant technology to OSI. The remaining \$12.5 million will be paid following the successful transfer of the applicable technology, which is expected to be completed in July 2011. The Company has deferred the initial \$12.5 million payment, and is recognizing the full \$25 million relating to the option exercise by OSI over the period of substantial involvement, which is now determined to be through July 2011. Upon

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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 or delivery of cell lines. These milestones are not considered to be at risk and substantive, therefore, the milestone payments are being deferred and will be recognized on a straight-line basis over the remaining estimated period of substantial involvement.

Under the amended 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. In addition, the Company is eligible to receive up to \$3.0 million in milestones for certain deliverables and research milestones, and up to \$24.0 million in biomarker related milestones.

Under these agreements, the Company received cash payments related to upfront license fees, milestone payments, research and development funding, and equity of \$17,943,000, \$26,546,000, and \$1,989,000, and recorded revenue of \$16,186,000, \$9,787,000, and \$6,145,000, for the years ended December 31, 2010, 2009 and 2008, 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. 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. 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. The valuation used the Market Approach to estimate the Company's enterprise value and the Probability Weighted Expected Return Method (PWERM) to allocate the enterprise value to each class of the Company's equity securities; accordingly, the Company is recognizing the premium of \$8,175,000 as revenue on a straight-line basis over the period of substantial involvement.

In June 2009, the Company 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 is a near term milestone and not considered to be substantive and at risk, the revenue is being amortized as additional license revenue over the Company's period of substantial involvement. The Company also earned a second \$5.0 million milestone payment upon selection of a development candidate in March 2010. This milestone was considered substantive and at risk and has been included in revenue for the year ended December 31, 2010. The Company could also receive (i) an additional pre-clinical discovery and development milestone payment of \$5.0 million, and (ii) if Biogen Idec exercises its option to obtain exclusive rights to commercialize ErbB3 antibody products in its territory, an option exercise fee and regulatory milestone payments of \$50.0 million in the aggregate. Once a development candidate was selected in March 2010, the Company began amortizing all license revenue under the agreement over the projected patent life of the candidate.

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.

Under the agreement, the Company received cash payments related to upfront license fees, milestone payments, and equity of \$5,000,000 and \$40,000,000 for the years ended December 31, 2010 and 2009, respectively, and recorded revenue of \$5,757,000 for the year ended December 31, 2010.

Table of Contents*(b) In-license Agreements**Kirin Brewery Co. Ltd. (Kirin)*

In December 2006, the Company entered into an exclusive license agreement with Kirin Brewery Co. Ltd. (now Kyowa Hakko Kirin) 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. Upon entering into the license agreement, the Company made a cash payment in the amount of \$5.0 million. In March 2010, the Company made a \$10.0 million milestone payment to Kyowa Hakko Kirin in connection with the dosing of the first patient in the Company's phase 3 clinical trial of tivozanib. In addition, the Company may be required to make up to an aggregate of \$50.0 million in additional milestone payments upon the achievement of specified regulatory milestones. The Company is also required to pay tiered royalty payments on net sales it makes of tivozanib in its territory. The royalty rates under the agreement range from the low to mid teens as a percentage of the Company's net sales of tivozanib.

The Company also has the right to grant sublicenses under the license agreement, subject to certain restrictions. In the event the Company sublicenses the rights licensed to it as part of the agreement, the Company is required to pay Kyowa Hakko Kirin a specified percentage of any amounts the Company receives from any third party sublicenses, other than amounts it receives in respect of research and development funding or equity investments, subject to certain limitations.

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. Certain of these arrangements related to the humanization and discovery of the Company's antibody products required the Company to pay an aggregate of \$1.5 million for the year ended December 31, 2008 in up-front licensing fees and milestones payments. There were no up-front licensing fees and milestone payments in 2010 or 2009. The Company is also 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 call for 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.

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 \$0.40 million, \$0.44 million and \$0.46 million, for the years ended December 31, 2010, 2009 and 2008, 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 \$2.18 million, \$2.18 million and \$2.03 million for the years ended December 31, 2010, 2009 and 2008, 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. 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

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issued the letter of credit and has been automatically extended through July 12, 2011. The Company has classified this money market account within restricted cash on its balance sheets at December 31, 2010 and 2009. The Company received six free months of rent under this arrangement and has straight-lined the total rent payments over the lease term resulting in deferred rent of approximately \$799,000 and \$969,000 at December 31, 2010 and 2009, respectively.

In September 2008, the Company entered into a sublease agreement with Alkermes, Inc., to sublease 7,407 square feet of office space. The sublease will expire on April 30, 2012. In conjunction with the lease, the Company entered into a standby letter of credit in the amount of \$55,392 to expire on May 30, 2011 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. The Company has classified this money market account within restricted cash on its balance sheets at December 31, 2010 and 2009. The Company received six free weeks of rent under this arrangement and has straight-lined the total rent payments over the lease term resulting in deferred rent of approximately \$20,200 and \$26,800 at December 31, 2010 and 2009, respectively.

Future annual minimum lease payments under all noncancelable operating leases at December 31, 2010 are as follows (amounts in thousands):

Years Ending December 31:	
2011	\$ 2,452
2012	2,289
2013	2,208
2014	368
2015	
	\$ 7,317

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 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 upon the position of the key employee.

9. Income Taxes

The Company accounts for income taxes under the provisions of ASC Topic 740, *Income Taxes*. For the 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. The Company did not record a federal or state tax provision for the year ended December 31, 2008.

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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, 2010, 2009 and 2008:

	December 31, 2010	December 31, 2009	December 31, 2008
Income tax computed at federal statutory tax rate	34.0%	34.0%	34.0%
State taxes, net of federal benefit	5.3%	6.3%	6.3%
Research and development credits	2.5%	2.5%	4.1%
Permanent differences	(0.3)%	(1.0)%	(1.5)%
Other	(3.5)%	%	(3.9)%
Change in valuation allowance	(38.0)%	(41.6)%	(39.0)%
Total	0.0%	0.2%	0.0%

The Company has incurred net operating losses from inception. At December 31, 2010, the Company had domestic federal and state net operating loss carryforwards of approximately \$187,776,000 and \$141,384,000, 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 2011 and continue through 2015. The Company also had federal and state research and development tax credit carryforwards of approximately \$4,629,000 and \$2,554,000, respectively, available to reduce future tax liabilities and which expire at various dates. The federal credits expire beginning in 2022 through 2030 and the state credits begin to expire in 2011. 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, 2010 and 2009 are as follows:

	2010	2009
	(in thousands)	
NOL carryforwards	\$ 71,309	\$ 50,921
Research and development credits	6,314	4,829
Deferred revenue	13,042	14,136
Other temporary differences	3,898	2,368
Valuation allowance	(94,563)	(72,254)
	\$	\$

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 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 increased by \$22,309,000 during 2010, primarily due to an increase in net operating loss carryforwards related to the Company's net loss.

In June 2006, FASB issued Interpretation No. 48, *Accounting for Uncertainty in Income Taxes, an interpretation of FAS 109* (codified within ASC Topic 749, *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. The implementation did not have a material impact on the Company's consolidated financial statements, results of operations or cash flows. 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

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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, 2010 and 2009:

	Year ended December 31, 2010	Year ended December 31, 2009
	(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 has 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 have been made with respect to certain of the Company's qualifying research and development programs. The Company has received the full amount related to these grants during the fourth quarter of 2010, and this amount has been recorded as other income in the statement of operations for the year ended December 31, 2010.

10. Convertible Preferred Stock*Conversion*

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 approximately \$5.7 million in underwriters' discounts were approximately \$72.2 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.

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The Company's Convertible Preferred Stock consisted of the following (in thousands, except par value amounts):

	December 31, 2009
Series A convertible preferred stock, \$.001 par value: 12,448 shares authorized; 12,428 shares issued and outstanding at December 31, 2009 (at liquidation value)	\$ 15,560
Series B convertible preferred stock, \$.001 par value: 27,215 shares authorized; 26,906 shares issued and outstanding at December 31, 2009 (at liquidation value)	43,723
Series C convertible preferred stock, \$.001 par value: 4,167 shares authorized, issued and outstanding at December 31, 2009 (at liquidation value)	11,583
Series D convertible preferred stock, \$.001 par value: 21,794 shares authorized at December 31, 2009; 21,166 shares issued and outstanding at December 31, 2009 (at liquidation value).	52,914
Series E convertible preferred stock, \$.001 par value: 15,000 shares authorized; 11,250 shares issued and outstanding at December 31, 2009 (at liquidation value)	32,925
	\$ 156,705

In March 2009, the Company issued 7,500,000 shares of Series E Convertible Preferred Stock to Biogen Idec (see Note 7) at a price per share of \$4.00, resulting in gross proceeds to the Company of \$30.0 million. Additionally, in July 2009, the Company issued 3,750,000 shares of Series E Convertible Preferred Stock to OSI (see Note 7) at \$4.00 per share, resulting in gross proceeds to the Company of \$15.0 million. The Series E Convertible Preferred Stock carries the same terms and conditions as the Series A, B, and D Preferred Stock.

The holders of the Series A, Series B, Series C, Series D and Series E Preferred Stock (the Preferred Stock) had the following rights prior to the Company's Initial Public Offering:

Dividends

The holders of the Preferred Stock were entitled to receive dividends when, and as declared by, the Board.

Voting

The holders of the Preferred Stock were entitled to the number of votes equal to the number of shares of common stock into which each share of Preferred Stock was convertible at the time of such vote.

Liquidation

In the event of voluntary or involuntary liquidation, dissolution, or winding-up of the Company, the holders of Preferred Stock were entitled to receive, on a pari passu basis, in preference to the holders of common stock: (i) in the case of Series A Preferred Stock, an amount equal to the greater of (a) \$1.25 per share, adjusted for certain dilutive events, plus any accrued and unpaid dividends, or (b) an amount per share as would have been payable had each share been converted to common stock immediately prior to a liquidation event; (ii) in the case of Series B Preferred Stock, an amount equal to the greater of (a) \$1.625 per share, adjusted for certain dilutive events, plus any accrued and unpaid dividends, or (b) an amount per share as would have been payable had each share been converted to common stock immediately prior to a liquidation event; (iii) in the case of Series C Preferred Stock, an amount equal to the greater of (a) \$3.00 per share, adjusted for certain dilutive events, plus any accrued and unpaid dividends, or (b) an amount per share as would have been payable had each share been converted to common stock immediately prior to a liquidation event; (iv) in the case of Series D Preferred Stock, an amount equal to the greater of (a) \$2.50 per share, adjusted for certain dilutive events, plus any accrued and unpaid dividends, or (b) an amount per share as would have been payable had each share been converted to

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common stock immediately prior to a liquidation event; (v) in the case of Series E Preferred Stock, an amount equal to the greater of (a) \$4.00 per share, adjusted for certain dilutive events, plus any accrued and unpaid dividends, or (b) an amount per share as would have been payable had each share been converted to common stock immediately prior to a liquidation event. Any remaining assets would have been allocated ratably to the holders of the common stock. As the Preferred Stock may have become redeemable upon an event that was outside of the control of the Company, the value of the Preferred Stock has been classified outside of permanent equity.

11. Warrants and Common Stock

As of December 31, 2010, the Company had the following warrants outstanding:

	Number of Shares	Exercise Price	Expiration Date
Common Stock	311,841	\$ 6.50-\$10.00	2013-2018
	311,841		

On February 18, 2010, the Company effected a 1-for-4 reverse stock split of all outstanding shares of common stock. All common share and per share data presented in the accompanying consolidated financial statements and the notes thereto have been retroactively restated to reflect this event.

As of December 31, 2010, the Company had 100,000,000 authorized shares of common stock, \$0.001 par value, of which 35,604,112 shares were issued and outstanding.

Initial Public Offering

In March 2010, the Company received \$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 underwriting discounts and commissions and approximately \$3.1 million in offering related expenses, 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.

12. 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. This 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 46,565 shares of common stock at an exercise 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 \$99,000 during the year ended December 31, 2010.

Table of Contents**13. Preferred Stock Warrant Liability**

In connection with its initial public offering in March 2010, the Company reclassified its liability related to warrants to purchase convertible preferred stock into additional paid-in capital as a result of the conversion of such warrants to purchase convertible preferred stock into warrants to purchase common stock.

At December 31, 2009, warrants for shares of redeemable instruments were required to be accounted for as liabilities. Increases or decreases in fair value were recorded as other income or expense in the statements of operations. As a result, the Company's outstanding preferred stock warrants were revalued at the end of each reporting period using the Black-Scholes option pricing valuation model. Changes in fair value, based on the fair value of the Company's convertible preferred stock and other valuation assumptions, were reflected in the Company's statements of operations as other income or expense. As of December 31, 2009, each share of Series B and D Preferred Stock was convertible into one share of common stock. All preferred stock warrants were immediately exercisable upon their issuance.

The following table sets forth the fair values of preferred stock warrants as of December 31, 2009 (amounts in thousands):

Series	Fair Value as of 12/31/2009
Series B	207
Series D	1,252
Total	\$ 1,459

The fair value of the preferred stock warrants was determined using the Black-Scholes valuation model with the following weighted-average assumptions:

	Year Ended December 31, 2009
Risk-free interest rate	2.20%-3.85%
Dividend yield	
Expected term (years)	4-9
Volatility	70.35%

14. 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. The Company has reserved 1,950,140 shares of common stock under the Plan, and at December 31, 2010, the Company has 1,492,857 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.

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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,		
	2010	2009	2008
Risk-free interest rate	1.59%-2.92%	1.98%-3.04%	1.55%-3.34%
Dividend yield			
Expected term (years)	5.50-6.25	5.50-6.25	5.61
Volatility	63.92%-66.81%	70.35%-72.04%	68.70%

The risk-free interest rate is determined based upon the United States Treasury's 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 did not have sufficient historical data to support its 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 periods prior to 2009, the Company used an average of several peer companies with the characteristics described above to calculate its expected term given its limited history. For 2009 and 2010, 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, 2010, 2009, and 2008 was \$7.17, \$6.48 and \$4.00 per share, respectively.

The Company has historically granted stock options at exercise prices not less than the fair market value of its common stock. Prior to the Company's initial public offering in March 2010, the fair value of the Company's common stock was determined by the Company's board of directors, with input from management, as there was no public market for our common stock at that time. Prior to the Company's initial public offering, the Company's board of directors had historically determined the estimated fair value of its 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 the Company sold shares of convertible preferred stock, the superior rights and preferences of securities senior to its common stock at the time of each grant, the results of operations, financial position, status of its research and development efforts, its stage of development and business strategy and the likelihood of achieving a liquidity event such as an initial public offering or sale of the Company.

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The following table presents grant dates and related exercise prices of stock options granted to employees through the date of the Company's initial public offering:

Date	Number of Options Granted	Exercise Price	Reassessed Fair Value of Common Stock Per Share at Date of Grant	Intrinsic Value at Date of Grant
December 18, 2008	2,500	\$ 6.88	\$ 7.12	\$ 0.24
January 30, 2009	114,437	\$ 8.00	\$ 8.60	\$ 0.60
April 1, 2009	145,526	\$ 8.48	\$ 9.28	\$ 0.80
June 16, 2009	94,300	\$ 8.72	\$ 10.04	\$ 1.32
July 17, 2009	10,000	\$ 8.72	\$ 10.04	\$ 1.32
October 8, 2009	208,025	\$ 9.64	\$ 10.40	\$ 0.76
December 17, 2009	18,887	\$ 11.32	N/A	N/A
February 2, 2010	398,182	\$ 12.24	N/A	N/A
Total	991,857			

The exercise price for stock options granted prior to April 1, 2010 was set by the Company's board of directors based upon its valuation models. The Company's 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* (Practice Aid). The exercise prices for stock options granted on December 18, 2008, January 30, 2009, April 1, 2009, June 16, 2009, July 17, 2009, October 8, 2009, December 17, 2009 and February 2, 2010 were determined by the results of its contemporaneous valuations completed in November 2008, January 2009, March 2009, June 2009, September 2009, December 2009 and January 2010, respectively. These valuations considered the following scenarios for achieving shareholder liquidity:

an initial public offering (IPO);

sale of the Company at an equity value greater than the combined liquidation preference of the preferred shares; and

sale of the Company at an equity value equal to or less than the combined liquidation preference of the preferred shares.

In connection with the preparation of the consolidated financial statements for the year ended December 31, 2009 and in preparing for the Company's IPO, the Company reexamined the contemporaneous valuations of its common stock during the period November 2008 to September 2009. In connection with that reexamination, the Company prepared retrospective valuation reports of the fair value of its common stock for financial reporting purposes as of November 28, 2008, January 15, 2009, March 20, 2009, June 1, 2009 and September 25, 2009. The Company believes that the valuation methodologies used in the retrospective valuations and the contemporaneous valuations are reasonable and consistent with the Practice Aid. The Company also believes that the preparation of the retrospective valuations was necessary due to the fact that the timeframe and probability for a potential IPO had accelerated significantly since the time of the Company's initial contemporaneous valuations.

In the IPO scenario of the Company's retrospective and contemporaneous valuations on November 28, 2008 and January 15, 2009 the Company applied the guideline transactions method under the market approach as provided in the Practice Aid and for subsequent valuations, the Company applied the guideline public company method under the market approach as provided in the Practice Aid due to the limited number of biotechnology company IPOs in 2008 and 2009. The Company's selection of guideline companies included companies deemed comparable because of their disease focus (oncology), stage of clinical trials, and size.

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In the sale above liquidation preference scenario for each of the Company's retrospective and contemporaneous valuations, the Company applied the guideline transactions method under the market approach as provided in the Practice Aid. The Company's selection of guideline transactions took into account the timing of the transactions and the characteristics of the acquired companies. The Company selected target companies which were deemed comparable because of their disease focus (oncology), stage of clinical trials, and size.

In the liquidation scenario for each of the Company's retrospective and contemporaneous valuations, it assumed sale or liquidation of the Company at an equity value equal to the liquidation preference of the Company's preferred shares.

Future values for each scenario are converted to present value by applying a discount rate estimated using a size-adjusted capital asset pricing model, or CAPM. As described in the Practice Aid, the CAPM takes into account risk-free rates, an equity risk premium, the betas of selected public guideline companies and a risk premium for size. The estimated discount rate includes a premium for company-specific risk as well.

In the Company's application of CAPM, on each of the valuation dates disclosed, the Company assumed a risk-free rate of 3.17% to 4.56% based on long-term U.S. Treasuries, a supply-side equity-risk premium of 5.0% to 6.2% based on Ibbotson's *SBBI Valuation Yearbook* and *PPC's Guide to Business Valuation*, a beta of 1.27 to 1.71 based on historical trading data for the Company's guideline public companies and a risk premium for size of 2.71% to 5.82% based on Ibbotson's *SBBI Valuation Yearbook* and company-specific risk of 5.5% to 10.0%. Changes in the risk-free rate, the equity-risk premium and beta reflect changes in market conditions. Market volatility in late 2008 and early 2009 corresponded to a decline in guideline public company betas. Changes in the risk premium for size reflect changes in the value of the company relative to the categories of size reported by Ibbotson. The company-specific risk premium reflects the significant overall business risk associated with the Company's pre-commercial stage of development prior to the IPO and also includes the Company's:

dependence on the success of its lead drug candidate, tivozanib, which is currently in phase 3 development;

short operating history and history of operating losses since inception;

need for substantial additional financing to achieve its goals; and

dependence on a limited number of collaboration partners.

In the Company's retrospective valuations for the period November 2008 to September 2009 and the Company's contemporaneous valuations for December 2009 and January 2010, it estimated the following probabilities and future sale and IPO dates:

Appraisal Date	11/28/08	1/15/09	3/20/09	6/1/09	9/25/09	12/17/09	2/2/10
Exercise price per share of options	\$ 6.88	\$ 8.00	\$ 8.48	\$ 8.72	\$ 9.64	\$ 11.32	\$ 12.24
Reassessed fair value of common stock per share at date of grant	\$ 7.12	\$ 8.60	\$ 9.28	\$ 10.04	\$ 10.40	N/A	N/A
Probabilities							
IPO in Q1 2010	20%	25%	35%	40%	25%	35%	35%
IPO in Q2 2010					25%	35%	35%
Sale above liquidation preference	70%	70%	60%	55%	45%	25%	25%
Sale below liquidation preference	10%	5%	5%	5%	5%	5%	5%
Future sale date	12/31/09	12/31/10	12/31/10	9/30/11	9/30/11	9/30/11	9/30/11
1 st IPO date	12/31/09	12/31/09	3/31/10	3/31/10	3/31/10	3/31/10	3/31/10
2 nd IPO date					6/30/10	6/30/10	6/30/10
Discount rate	24%	24%	24%	24%	24%	24%	24%

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The estimated fair market value of the Company's common stock at each valuation date is equal to the sum of the probability weighted present values for each scenario.

The Company has incorporated the fair values calculated in the retrospective valuations into the Black-Scholes option pricing model when calculating the stock-based compensation expense to be recognized for the stock options granted during the period November 2008 to September 2009. The retrospective valuations generated per share fair values of common stock of \$7.12, \$8.60, \$9.28, \$10.04 and \$10.40, respectively, at November 2008 and January, March, June and September 2009, respectively. This resulted in intrinsic values of \$0.24, \$0.60, \$0.80, \$1.32 and \$0.76 per share, respectively, at each grant date.

The retrospective fair values of the Company's common stock increased throughout 2009 thereby reducing the difference between the fair value of the Company's common stock and the estimated initial public offering price range. The increases were caused by business and scientific milestones, financing transactions and the proximity to a potential initial public offering. The retrospective fair value of the Company's common stock underlying 2,500 shares granted on December 18, 2008 was determined to be \$7.12 per share. The fair value of the common stock on that date took into account the following:

initiation of a phase 1 clinical trial for ficlatuzumab, for which the first patient dosed triggered a \$3 million milestone payment from Merck; and

because of the unfavorable conditions in the public markets, the Company deemed the probability of an IPO to be low or 20 percent. The retrospective fair value of the Company's common stock underlying options for 114,437 shares granted on January 30, 2009 was determined to be \$8.60 per share. The increase in value from the November 2008 valuation was primarily due to the following:

the Company received a term sheet for the Biogen agreement for ErBb3 that included a proposed \$30 million investment in new Series E Convertible Preferred Stock which would be priced at a premium to its other classes of preferred stock;

the expected proceeds from the Biogen agreement would improve the Company's position for funding future cash needs;

due to the Company's progress, including continued progress of its phase 2 clinical trial showing a favorable safety profile in patients with advanced RCC, the Company deemed that the probability of an IPO increased to 25% and the probability of a sale below liquidation preference decreased to 5%; and

the timeline for sale above liquidation preference was extended due to expected timing of enrollment of its phase 3 clinical trial of tivozanib.

The retrospective fair value of the Company's common stock underlying options for 145,526 shares granted on April 1, 2009 was determined to be \$9.28 per share. The increase in value from the January 2009 valuation was primarily due to the following:

execution of the agreement with Biogen, which included a \$30 million investment in Series E Convertible Preferred Stock at \$4.00 per share and a \$5 million upfront payment;

the Company initiated a phase 1b/2a clinical trial of tivozanib as a monotherapy for the treatment of non-small cell lung cancer; and

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due to the Company's progress including continued progress of its phase 2 clinical trial showing a favorable safety profile in patients with advanced RCC, the Company deemed that the probability of an IPO increased to 35%, although the assumed timing was adjusted to March 31, 2010 due to its assessment of current market conditions.

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The retrospective fair value of the Company's common stock underlying options for 94,300 shares granted on June 16, 2009 was determined to be \$10.04 per share. The increase in value from the March 2009 valuation was primarily due to the following:

in May 2009, the Company announced additional data from the Company's phase 2 clinical trial of tivozanib, which demonstrated an overall median progression-free survival of patients of 11.8 months and a favorable safety profile in patients with advanced RCC;

due to the Company's progress in its lead program and data noted above, the Company deemed that the probability of an IPO increased to 40%; and

the timeline for sale above liquidation preference was extended to September 30, 2011, which is closer to the date the Company anticipated that data would become available from its phase 3 clinical trial of tivozanib.

The retrospective fair value of the Company's common stock underlying options for 208,025 shares granted on October 8, 2009 was determined to be \$10.40 per share. The increase in value from the June 2009 valuation was primarily due to the following:

execution of an agreement with OSI which included a \$15 million investment in Series E Convertible Preferred Stock at \$4.00 per share and a \$5 million upfront payment;

the Company's plans to commence the phase 3 clinical trial of tivozanib; and

due to the Company's progress and plans for commencement of a phase 3 clinical trial, the Company deemed that the probability of an IPO increased to 50%, with a 25% probability of an IPO being completed in the first quarter of 2010 and a 25% probability of an IPO being completed in the second quarter of 2010.

The fair value of the Company's common stock underlying options for 18,887 shares granted on December 17, 2009 was determined to be \$11.32 per share. The increase in value from the September 2009 valuation was primarily due to the following:

initiation of the phase 3 clinical trial of tivozanib; and

due to the Company's progress and the initiation of the phase 3 clinical trial of tivozanib, the Company deemed that the probability of an IPO increased to 70%, with a 35% probability of an IPO being completed in the first quarter of 2010 and a 35% probability of an IPO being completed in the second quarter of 2010.

The fair value of the Company's common stock underlying options for 398,182 shares granted on February 2, 2010 was determined to be \$12.24 per share. The increase in value from the December 2009 valuation was primarily due to a reduction in the period of time before the expected completion of an IPO.

On February 9, 2010, the Company and the underwriters for the Company's IPO determined the range for the IPO. The midpoint of the range was \$14.00 per share as compared to \$12.24 per share, which was based on management's contemporaneous valuation prepared on January 22, 2010, of the estimated fair value of the Company's common stock. The \$12.24 was used on February 2, 2010, the date of the Company's then most recent grant of stock options. This estimated fair value represented a discount of approximately 12.6% from the midpoint of the range and an increase of 8% from the estimated fair value of the Company's common stock on December 17, 2009. The Company noted that, as is typical in initial public offerings, the range was not derived using a formal determination of fair value, but was determined based upon discussions between the Company and the underwriters. Among the factors considered in setting this range were prevailing market conditions and estimates of the Company's business potential. In addition to this difference in purpose and methodology, the Company believed that the difference in value reflected between the midpoint of the range and management's determination of the estimated fair value of the Company's common stock

on January 22, 2010 was primarily the result of the following factors:

The contemporaneous valuation the Company prepared on January 22, 2010 contained multiple scenarios including two IPO scenarios with an aggregate probability of 70% and two sale scenarios. If

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the Company had considered only a single scenario with 100% probability and that assumed that the IPO would be completed as of March 31, 2010, the contemporaneous valuation would have resulted in a fair value determination of \$14.48 per share.

On February 2, 2010, Ironwood Pharmaceuticals completed its IPO, which the Company believed demonstrated a significant improvement in the market for initial public offerings in the U.S. in the biopharmaceutical industry. The Company noted, however, that Ironwood's IPO was completed at \$11.25 per share, or a 25% discount from the midpoint of its filing range.

The Company's February 2010 discussions with the underwriters for the Company's IPO took into account the Company's and the underwriters' perceptions of significantly increased optimism regarding the market for initial public offerings, and confirmed the Company's and the Company's underwriters' expectations that the Company would complete the initial public offering by the end of the first quarter of 2010. As noted above, the Company's January 22, 2010 contemporaneous valuation included a scenario with a 35% probability that the IPO would not be completed until the end of the second quarter of 2010.

History has shown that it is reasonable to expect that the completion of an IPO will increase the value of stock as a result of the significant increase in the liquidity and ability to trade/sell such securities. However, it is not possible to measure such increase in value with precision or certainty.

The IPO price of the Company's common stock was \$9.00 per share. The difference between the estimated fair value of the Company's common stock of \$12.24 per share in January 2010 and the IPO price took into account several factors considered by the Company's board of directors and underwriters, including:

an analysis of the typical valuation ranges seen in initial public offerings for companies in the Company's industry with similar market capitalization;

a deterioration in financial markets with accompanying decrease in market capitalization of companies comparable to the Company;

increased difficulty in raising equity financing with accompanying financing uncertainty;

a review of the then current market conditions and the results of operations, competitive position and the stock performance of the Company's competitors; and

consideration of the Company's history as a private company and previous valuation reports received by independent valuation firms. Valuation models require the input of highly subjective assumptions. Because the Company's common stock prior to its IPO had characteristics significantly different from that of publicly traded common stock and because changes in the subjective input assumptions can materially affect the fair value estimate, in management's opinion, the existing models did not necessarily provide a reliable, single measure of the fair value of the Company's common stock. The foregoing valuation methodologies are not the only valuation methodologies available and have not been used to value the Company's common stock subsequent to the IPO.

As of December 31, 2010, the total unrecognized compensation expense, net of related forfeiture estimates, was \$5.7 million which the Company expects to recognize over a weighted-average period of approximately 2.4 years. The intrinsic value of options exercised during the years 2010, 2009 and 2008 was \$3,411,011, \$326,500 and \$147,700, respectively.

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The following table summarizes the activity of the Company's stock option plan for the year ended December 31, 2010:

	Number of Options	Weighted- Average Exercise Price	Weighted- Average Remaining Contractual Life (in years)	Aggregate Intrinsic Value
Outstanding at December 31, 2009	3,275,906	\$ 4.56		
Granted	865,965	\$ 11.67		
Exercised	(448,236)	\$ 2.76		
Forfeited	(87,917)	\$ 6.93		
Outstanding at December 31, 2010	3,605,718	\$ 6.44	6.84	\$ 29,524,606
Exercisable at December 31, 2010	2,491,702	\$ 4.69	5.95	\$ 24,731,094
Vested or expected to vest at December 31, 2010	3,507,373	\$ 6.29	6.78	\$ 29,235,879

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 2010 and 2009. The Company valued these grants using the Black-Scholes option-pricing model and recognizes expense related to these awards using the graded-vesting method. For the valuation for the years ended December 31, 2010, 2009 and 2008 option grants, the Company has assumed risk-free rates of return of 2.25% to 3.85% expected option lives equal to the contractual term, no dividends and stock price volatility of 66.81%, 70.35% and 68.70%, respectively, in calculating the options' fair values. 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. The Company recorded a reversal of stock-based compensation expense related to stock options granted to nonemployees of \$4,000 during the year ended December 31, 2010. Compensation expense of approximately \$266,600, and \$123,300 was recorded during the years ended December 31, 2009 and 2008, respectively, relating to nonemployee stock option awards.

Restricted Stock

The Company has sold or issued shares of restricted stock to nonemployee founders, consultants and certain executives from time to time between 2002 and 2005. Generally, the terms of the restricted stock agreements provide that the Company has the right to purchase from the individuals, at the original purchase price, some or all of the unvested shares upon certain conditions such as discontinuance of employment or consulting services. The Company determines the value of such awards as the difference between the exercise price and the fair value of the underlying stock on the date of grant. This value, if any, is recognized on a straight-line basis as compensation expense over the period in which the restrictions lapse. The vesting of the awards is determined by the board of directors and all awards generally vest over a period of four years. The Company periodically reassesses the value of each nonemployee award through the remaining vesting period, which may result in additional charges to expense in the future. Compensation expense, relating to restricted stock, of \$9,100 was recorded in the year ended December 31, 2008. All restricted stock was fully vested, therefore, there was no compensation expense relating to restricted stock for the years ended December 31, 2010 and 2009.

15. 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

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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 \$304,000, \$301,300, and \$253,700 for the years ended December 31, 2010, 2009, and 2008, respectively.

16. Quarterly Results (Unaudited)

	March 31, 2010	Three Months Ended June 30, 2010 September 30, 2010		December 31, 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)

	March 31, 2009	Three Months Ended June 30, 2009 September 30, 2009		December 31, 2009
		(in thousands, except per share data) (unaudited)		
Collaboration revenue	\$ 3,670	\$ 5,096	\$ 5,917	\$ 6,036
Operating Expenses	12,300	14,495	19,035	16,082
Loss from operations	(8,630)	(9,399)	(13,118)	(10,046)
Other expense, net	(777)	(836)	(680)	(707)
Net Loss	\$ (9,407)	\$ (10,235)	\$ (13,735)	\$ (10,716)
Net loss per share basic and diluted	\$ (5.92)	\$ (6.41)	\$ (8.53)	\$ (6.57)

17. Subsequent Events*Tivozanib Collaboration and License Agreement*

On February 16, 2011, the Company, together with its wholly owned subsidiary, entered into a Collaboration and License Agreement (the *Astellas Agreement*) with Astellas Pharma Inc., and its indirect wholly owned subsidiaries (the *Astellas*), 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 the joint development plan and joint commercialization plan, respectively. Throughout the rest of the world (the *Royalty Territory*), excluding Asia, where Kyowa Hakko Kirin (the *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.

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 the Company responsible for conducting fifty percent (50%) of the medical affairs activities in the major European countries. The Company has not yet completed its assessment of the accounting for the *Astellas*

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arrangement, however, the Company expects 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 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 expects to retain net proceeds of approximately \$96 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 \$575 million in milestone payments upon achievement of specified clinical development and 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 renal cell carcinoma in the United States and Europe, and (ii) up to approximately \$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 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 to KHK a specified percentage of milestones and royalties it may receive from Astellas in connection with Astellas' development and commercialization activities in Europe and the Royalty Territory.

Sublease

On February 28 2011, the Company entered into a sublease agreement with Acceleron Pharma, Inc., to sublease 14,214 square feet of office space. 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 to expire on May 31, 2012 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. The Company will classify this money market account within restricted cash on its balance sheet.

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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, 2010. The term disclosure controls and procedures, as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act, means controls and other procedures of a company that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the SEC's rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to the company's management, including its principal executive and principal financial officers, as appropriate to allow timely decisions regarding required disclosure. Management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Based on the evaluation of our disclosure controls and procedures as of December 31, 2010, our Chief Executive Officer and Chief Financial Officer concluded that, as of such date, our disclosure controls and procedures were effective at the reasonable assurance level.

Management's Annual Report on Internal Control Over Financial Reporting

This Form 10-K does not include a report of management's assessment regarding internal control over financial reporting or an attestation report of the company's independent registered public accounting firm due to a transition period established by rules of the Securities and Exchange Commission for newly public companies.

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, 2010 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

ITEM 9B. Other Information

None.

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PART III

ITEM 10. Directors, Executive Officers and Corporate Governance

The information required by this Item 10 will be contained in the sections entitled Management and Section 16(a) Beneficial Ownership Reporting Compliance appearing in the definitive proxy statement we will file in connection with our 2011 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 Officer Compensation, Compensation Committee Interlocks and Insider Participation and Compensation Committee Report appearing in the definitive proxy statement we will file in connection with our 2011 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 Principal Stockholders and Equity Compensation Plan Information appearing in the definitive proxy statement we will file in connection with our 2011 Annual Meeting of Stockholders and is incorporated by reference herein.

ITEM 13. Certain Relationships and Related 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 2011 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 Independent Registered Public Accounting Firm Fees and Services appearing in the definitive proxy statement we will file in connection with our 2011 Annual Meeting of Stockholders and is incorporated by reference herein.

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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
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 11, 2011

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 Tuan Ha-Ngoc	President, Chief Executive Officer and Director <i>(Principal Executive Officer)</i>	March 11, 2011
/s/ DAVID B. JOHNSTON David B. Johnston	Chief Financial Officer <i>(Principal Financial and Accounting Officer)</i>	March 11, 2011
/s/ KENNETH M. BATE Kenneth M. Bate	Director	March 11, 2011
/s/ DOUGLAS G. COLE Douglas G. Cole	Director	March 11, 2011
/s/ RONALD A. DEPINHO Ronald A. DePinho	Director	March 11, 2011
/s/ ANTHONY B. EVNIN Anthony B. Evnin	Director	March 11, 2011
/s/ NICHOLAS GALAKATOS Nicholas Galakatos	Director	March 11, 2011
/s/ RUSSELL HIRSCH Russell Hirsch	Director	March 11, 2011
/s/ RAJU KUCHERLAPATI	Director	March 11, 2011

Raju Kucherlapati

/s/ KENNETH E. WEG

Director

March 11, 2011

Kenneth E. Weg

/s/ ROBERT C. YOUNG

Director

March 11, 2011

Robert C. Young

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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	S-1/A	333-163778	02/23/2010	10.5	
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	
10.13	Severance and Change in Control Agreement, dated as of December 11, 2009, by and between the Registrant and Jenő Gyuris	S-1	333-163778	12/16/2009	10.12	

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Exhibit Number	Description of Exhibit	Form	Incorporated by Reference		Exhibit Number	Filed Herewith
			File Number	Date of Filing		
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	11/05/10	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	11/05/10	10.2	
10.19	Consultation and Scientific Advisory Board Agreement, effective as of January 1, 2010, by and between the Registrant and Lynda Chin					X
	<i>Material Contracts Financing Agreements</i>					
10.20	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	06/04/10	10.1	
	<i>Material Contracts Leases</i>					
10.21	Sublease, dated as of July 2004, by and between the Registrant and Millennium Pharmaceuticals, Inc.	S-1	333-163778	12/16/2009	10.19	
10.22	Sublease, dated as of September 2, 2008, by and between the Registrant and Alkermes, Inc.	S-1	333-163778	12/16/2009	10.20	
	<i>Material Contracts License and Strategic Partnership Agreements</i>					
10.23	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	
10.24	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	
10.25	First Amended and Restated License and Research Collaboration Agreement, dated as of April 13, 2005, by and between the Registrant and Merck & Co., Inc.	S-1/A	333-163778	03/09/2010	10.24	

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Exhibit Number	Description of Exhibit	Form	Incorporated by Reference		Exhibit Number	Filed Herewith
			File Number	Date of Filing		
10.26	License and Research Collaboration Agreement, dated as of August 30, 2005, by and between the Registrant and Merck & Co., Inc., as amended by Letter Amendment, dated March 5, 2007, as amended by Amendment No. 1, dated August 12, 2007	S-1	333-163778	12/16/2009	10.24	
10.27	Research, Development and License Agreement, dated as of March 23, 2007, by and between the Registrant and Schering Corporation, acting through its Schering-Plough Research Institute division	S-1	333-163778	12/16/2009	10.25	
10.28	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	
10.29	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 001-34655	03/09/2010 08/06/2010	10.28 10.1	
10.30	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					X
<i>Material Contracts Miscellaneous</i>						
10.31	Securities Purchase Agreement, among the Registrant and the Purchasers thereto, dated October 28, 2010	8-K	001-34655	11/3/2010	10.1	
10.32	Registration Rights Agreement, between the Registrant and the Holders thereto, dated October 28, 2010	8-K	001-34655	11/3/2010	10.2	
10.33	Registration Rights Agreement dated June 23, 2010 by and among the Registrant, Hercules Technology II, L.P. and Hercules Technology III, L.P.	8-K	001-34655	06/29/10	10.1	
10.34	Warrant dated as of June 2, 2010 issued by the Registrant to Hercules Technology II, L.P.	8-K	001-34655	06/04/10	10.2	
10.35	Warrant dated as of June 2, 2010 issued by the Registrant to Hercules Technology III, L.P.	8-K	001-34655	06/04/10	10.3	

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Exhibit Number	Description of Exhibit	Incorporated by Reference			Exhibit Number	Filed Herewith
		Form	File Number	Date of Filing		
10.36	Fourth Amended and Restated Investor Rights Agreement dated March 18, 2009 by and among the Registrant and the Purchasers named therein	S-1	333-163778	12/16/2009	10.28	
10.37	Warrant Agreement to Purchase Shares of Preferred Stock, issued to Hercules Technology Growth Capital, Inc., March 29, 2006	S-1	333-163778	12/16/2009	10.30	
10.38	Warrant Agreement to Purchase Shares of Stock, issued to Hercules Technology Growth Capital, Inc., May 15, 2008	S-1	333-163778	12/16/2009	10.31	
10.39	Warrant Agreement to Purchase Shares of Stock, issued to Comerica Bank, May 15, 2008 (assigned to Comerica Ventures Incorporated)	S-1	333-163778	12/16/2009	10.32	
Additional Exhibits						
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

Confidential treatment has been requested as to certain portions, which portions have been omitted and separately filed with the Securities and Exchange Commission.