

AVEO PHARMACEUTICALS INC
Form 10-K
March 11, 2013
Table of Contents

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

(Mark One)

ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the fiscal year ended: December 31, 2012

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.

(Exact Name of Registrant as Specified in Its Charter)

Edgar Filing: AVEO PHARMACEUTICALS INC - Form 10-K

Delaware
(State or Other Jurisdiction of

04-3581650
(I.R.S. Employer

Incorporation or Organization)

75 Sidney Street

Identification No.)

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 <input type="checkbox"/>	Accelerated filer <input checked="" type="checkbox"/>
Non-accelerated filer <input type="checkbox"/> (Do not check if a smaller reporting company)	Smaller reporting company <input type="checkbox"/>

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

The aggregate market value of the 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, 2012, was \$306,770,024. 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, 2013: 51,838,388

Documents incorporated by reference:

Portions of our definitive proxy statement for our 2013 annual meeting of stockholders are incorporated by reference into Part III of this Annual Report on Form 10-K.

Table of Contents

AVEO PHARMACEUTICALS, INC.

TABLE OF CONTENTS

	Page No.
<u>PART I</u>	2
Item 1. <u>Business</u>	2
Item 1A. <u>Risk Factors</u>	39
Item 1B. <u>Unresolved Staff Comments</u>	65
Item 2. <u>Properties</u>	65
Item 3. <u>Legal Proceedings</u>	65
Item 4. <u>Mine Safety Disclosures</u>	65
<u>PART II</u>	66
Item 5. <u>Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities</u>	66
Item 6. <u>Selected Financial Data</u>	68
Item 7. <u>Management's Discussion and Analysis of Financial Condition and Results of Operations</u>	70
Item 7A. <u>Quantitative and Qualitative Disclosures about Market Risk</u>	96
Item 8. <u>Financial Statements and Supplementary Data</u>	97
Item 9. <u>Changes in and Disagreements with Accountants on Accounting and Financial Disclosure</u>	134
Item 9A. <u>Controls and Procedures</u>	134
Item 9B. <u>Other Information</u>	137
<u>PART III</u>	138
Item 10. <u>Director, Executive Officers and Corporate Governance</u>	138
Item 11. <u>Executive Compensation</u>	138
Item 12. <u>Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters</u>	138
Item 13. <u>Certain Relationships and Related Person Transactions, and Director Independence</u>	138
Item 14. <u>Principal Accountant Fees and Services</u>	138
<u>PART IV</u>	139
Item 15. <u>Exhibits and Financial Statement Schedules</u>	139
<u>SIGNATURES</u>	140

Table of Contents

References to AVEO

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

Forward-Looking Information

This report contains forward-looking statements regarding, among other things, our future discovery and development efforts, our collaborations, our future operating results and financial position, our business strategy, and other objectives for our operations. You can identify these forward-looking statements by their use of words such as anticipate, believe, estimate, expect, forecast, intend, plan, project, and other words and 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.

Table of Contents**PART I****ITEM 1. Business
Overview**

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

On November 27, 2012, the U.S. Food and Drug Administration, or FDA, accepted for filing our New Drug Application, or NDA, for tivozanib, our lead product candidate, with the proposed indication for the treatment of patients with advanced renal cell carcinoma, or RCC. We have been informed by the FDA that its Oncologic Drugs Advisory Committee, or ODAC, which provides the FDA with independent expert advice and recommendations, will review our NDA for tivozanib on May 2, 2013. According to the timelines established by the Prescription Drug User Fee Act, or PDUFA, the review of the NDA is expected to be complete by July 28, 2013. We expect that our partner, Astellas Pharma Inc., or Astellas, will submit a Marketing Authorization Application, or MAA, with the European Medicines Agency, or EMA, in the second half of 2013. Tivozanib is a potent, selective, long half-life inhibitor of all three vascular endothelial growth factor, or VEGF, receptors that is designed to optimize VEGF blockade while minimizing off-target toxicities. Our clinical trials of tivozanib in more than 1,000 subjects to date have demonstrated a favorable safety and efficacy profile for tivozanib.

We have announced detailed data from our global, phase 3 clinical trial comparing the efficacy and safety of tivozanib with Nexavar® (sorafenib), an approved therapy, for first-line treatment in advanced RCC, which we refer to as the TIVO-1 (Tivozanib Versus Sorafenib in 1st line Advanced RCC) study. The TIVO-1 study was conducted in patients with advanced clear cell RCC who had undergone a prior nephrectomy (kidney removal) and who had not received any prior VEGF- or mTOR-targeted therapy. In this trial, we measured, among other things, each patient's progression-free survival, or PFS, which refers to the period of time that began when a patient entered the clinical trial and ended when either the patient died or the patient's cancer had grown by a specified percentage or spread to a new location in the body. PFS was the primary endpoint in the TIVO-1 study. Secondary endpoints included overall survival, for which patients continue to be followed, and safety. Key data from the TIVO-1 study include:

Tivozanib demonstrated a statistically significant improvement in PFS over Nexavar with a median PFS of 11.9 months for tivozanib compared to a median PFS of 9.1 months for Nexavar in the overall study population (HR=0.797, 95% confidence interval, or CI, 0.639-0.993; P=0.042).

Tivozanib also demonstrated a statistically significant improvement in PFS with a median PFS of 12.7 months compared to a median PFS of 9.1 months for Nexavar in the pre-specified subpopulation of patients who received no prior systemic anti-cancer therapy for metastatic disease—a subpopulation that comprised approximately 70% of the total study population (HR=0.756, 95% CI 0.580-0.985; P=0.037).

Tivozanib demonstrated a well-tolerated safety profile as evidenced by a lower rate of dose reductions (11.6% vs. 42.8%; p<0.001) and interruptions (17.8% vs. 35.4%; p<0.001) due to adverse events and discontinuations (4.2% vs. 5.4%; p=0.683) due to drug-related adverse events compared to Nexavar.

The most commonly reported side effect for tivozanib was hypertension (44% for tivozanib vs. 34% for Nexavar), and for Nexavar was hand-foot syndrome (13% for tivozanib vs. 54% for Nexavar). Other side effects that are commonly associated with other VEGF receptor inhibitors included: diarrhea (22% for tivozanib vs. 32% for Nexavar), dysphonia, or hoarseness of voice (21% for tivozanib vs. 5% for Nexavar), fatigue (18% for tivozanib vs. 16% for Nexavar), and neutropenia, a condition of having a lower than normal number of white blood cells (10% for tivozanib vs. 9% for Nexavar).

Table of Contents

The final, protocol-specified analysis of overall survival, or OS, at 24 months since last patient enrolled showed a median OS of 28.8 months (95% CI: 22.5 NA) for the tivozanib arm versus a median OS of 29.3 months (95% CI: 29.3 NA) for the Nexavar arm. No statistical difference between the two arms (HR=1.245, p=0.105) was observed. A one-sided crossover for patients randomized to the Nexavar arm was offered pursuant to a separate, long-term treatment protocol to allow trial participants originally treated in the Nexavar arm to receive tivozanib upon disease progression. This resulted in a substantial difference in the use of subsequent therapies. Of 189 patients who discontinued their initial therapy on the tivozanib arm, 36% received some form of subsequent therapy, including 10% who received subsequent anti-VEGF therapy. Of 226 patients who discontinued their initial therapy on the Nexavar arm, 74% received some form of subsequent therapy, including 70% who received subsequent anti-VEGF therapy (98% of whom received tivozanib).

In addition to the TIVO-1 study, we have an ongoing clinical study which we refer to as TAURUS (Tivozanib Use versus Sunitinib in advanced RCC: Patient Preference), seeking to demonstrate patient preference of tivozanib compared to Sunitinib[®] (sunitinib) as a first-line therapy in patients with advanced RCC. We are also evaluating tivozanib in multiple clinical trials including our BATON (Biomarker Assessment of Tivozanib in ONcology) program, a series of clinical trials assessing biomarkers in solid tumors that may be predictive of a clinical response to tivozanib. The BATON trials include:

BATON-RCC, a phase 2 exploratory biomarker study in patients with advanced RCC;

BATON-CRC, a phase 2 clinical trial being conducted by Astellas evaluating tivozanib in combination with modified FOLFOX6 (mFOLFOX6) compared to Avastin[®] (bevacizumab) in combination with mFOLFOX6 as first-line therapy in patients with advanced metastatic colorectal cancer, or CRC; and

BATON-BC, a phase 2 clinical trial evaluating the efficacy of tivozanib in combination with paclitaxel, compared to placebo in combination with paclitaxel in patients with locally recurrent or metastatic triple negative breast cancer who have received no prior systemic therapy.

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

We acquired exclusive rights to develop and commercialize tivozanib worldwide outside of Asia pursuant to a license agreement we entered into with Kirin Brewery Co. Ltd. (now Kyowa Hakko Kirin), or KHK, in 2006. Under the license agreement, we obtained an exclusive license to research, develop, manufacture and commercialize tivozanib, pharmaceutical compositions thereof and associated biomarkers for the diagnosis, prevention and treatment of any and all human diseases and conditions outside of Asia. KHK has retained all rights to tivozanib in Asia. We have obligations to make milestone and royalty payments to KHK. The royalty rates range from the low to mid-teens as a percentage of our net sales of tivozanib. We are also obligated to pay a specified percentage of certain amounts we receive from any third party sublicensees, including Astellas. As discussed below under the heading Strategic Partnerships, we entered into a strategic collaboration with Astellas in which we have agreed to share responsibility, including all profits and losses, with Astellas for continued development and commercialization of tivozanib in the United States, Mexico and Canada, or 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. Ficlatazumab is an antibody which binds to hepatocyte growth factor, or HGF, thereby blocking its function. In September 2012, we announced detailed data from our phase 2 study comparing the combination of ficlatazumab and Iressa[®] (gefitinib) to Iressa monotherapy in previously untreated Asian subjects

Table of Contents

with non-small cell lung cancer. In the intent-to-treat population, the addition of ficlatuzumab to Iressa did not result in statistically significant improved overall response rate. Given that our current priority is the anticipated registration and planned commercialization of tivozanib, we intend to focus our efforts on further ficlatuzumab development through external collaborations.

AV-203 is a monoclonal antibody that targets the ErbB3 receptor, which we have partnered outside of North America with Biogen Idec International GmbH, a subsidiary of Biogen Idec Inc., which we collectively refer to herein as Biogen Idec. In May 2012, we announced the initiation of a phase 1 clinical trial examining the safety, tolerability and preliminary efficacy of AV-203 along with exploratory biomarkers in patients with metastatic or advanced solid tumors.

Our proprietary Human Response Platform was designed to overcome many of the limitations of traditional approaches to modeling human cancer, as we use patented genetic engineering techniques to grow populations of spontaneous tumors in animals containing human-relevant, cancer-causing mutations and tumor variations 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. The identification and development of potential biomarkers through our Human Response Platform is a core component of our oncology drug development efforts.

Recent Developments

On January 23, 2013, we closed an underwritten public offering of our common stock. The total number of shares sold was 7,667,050, comprised of 6,667,000 shares of common stock initially offered and an additional 1,000,050 shares of common stock sold pursuant to the underwriters' exercise of their over-allotment option, at the public offering price of \$7.50 per share. Aggregate net proceeds to the company were approximately \$53.6 million, after deducting underwriting discounts and commissions and estimated offering expenses. J.P. Morgan Securities LLC acted as sole book-running manager for the offering, with RBC Capital Markets, LLC and Canaccord Genuity Inc. acting as co-lead managers.

Tivozanib: A Potent, Selective and Long Half-life Inhibitor of VEGF Receptors 1, 2 & 3

Tivozanib is a potent, selective long half-life inhibitor of all three VEGF receptors that is designed to optimize VEGF blockade while minimizing off-target toxicities. VEGF stimulates the formation of new blood vessels, known as angiogenesis, which plays an important role in cancer progression and the spread of tumors within the body. Most tumors produce various forms of VEGF and other ligands which bind to the three VEGF receptors, each of which 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.

We believe that the efficacy and safety data for tivozanib reported from the TIVO-1 trial could position tivozanib as a first-line treatment for patients with advanced RCC. In the TIVO-1 trial, tivozanib demonstrated superior efficacy against an active comparator and a favorable safety profile, as evidenced by a lower rate of dose reductions and interruptions due to adverse events than the comparator. In addition, tivozanib is designed to be administered in a one-capsule, once-per-day dose on a schedule of three weeks continuous dosing followed by a one week rest period.

The demonstrated clinical results with tivozanib are supported by its core biochemical properties of potency, selectivity and long half-life inhibition of all three VEGF receptors. The potency of tivozanib across VEGF

Table of Contents

receptors 1, 2 and 3 provides a comprehensive blockade of the VEGF pathway. Its high level of selectivity for all three VEGF receptors is designed to minimize unintended side effects, such as fatigue, diarrhea and hand-foot syndrome, which are often associated with the currently approved therapies. Hypertension and dysphonia were the most commonly reported side effects in patients treated with tivozanib. The occurrence of hypertension and dysphonia are driven by inhibition of the VEGF pathway, and suggest that the pathway has been substantially inhibited by tivozanib. Both hypertension and dysphonia were manageable and reversible in clinical trials. In addition, because tivozanib has demonstrated a long half-life, meaning the time it takes for the concentration of a drug in circulation to be reduced by one-half, we believe it maintains a more consistent blockade of the relevant receptors and, accordingly, tivozanib is dosed on a one-capsule, once-per-day schedule.

We believe that tivozanib's favorable efficacy and safety profile, along with its potency, selectivity, and long half-life, may allow it to be successfully used as a monotherapy, and warrant further evaluation of tivozanib in combination with other anti-cancer therapies in multiple tumor types. These advantages, along with tivozanib's one capsule, once-per-day dosing regimen, may differentiate tivozanib from other VEGF receptor inhibitors that are currently marketed.

Tivozanib's development and planned development in various cancer tumor types are illustrated in the following chart:

Renal Cell Carcinoma

Based on the World Health Organization GLOBOCAN data (published in 2008), in the United States it is estimated that over 56,000 patients are diagnosed with RCC and that almost 14,000 die from the disease each year. In Europe it is estimated that over 73,000 patients are diagnosed with RCC and that over 31,000 die from the disease each year. According to the American Cancer Society, RCC accounts for approximately 90% of all kidney cancer. We estimate, based on publicly-available information for 2012, including quarterly and annual reports made available by companies that market drugs approved for RCC and secondary published sources, that the current worldwide RCC market is over \$2 billion, with agents targeting the VEGF pathway representing over 70% of sales. The market is expected to expand significantly over the next ten years, driven by an increased incidence of RCC, an increased use of frontline therapy as more tolerable agents are developed and an increased use of later-stage therapy as more treatment options become available.

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 (which account for 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 first-line treatment of advanced RCC is with one of the approved drugs that inhibit the VEGF pathway, most commonly the oral drugs Sutent, Nexavar and Votrient as

Table of Contents

well as the injectable product Avastin. Sutent, Nexavar, Votrient and Avastin (when administered in combination with alpha interferon) have all demonstrated improvements in PFS in clear cell RCC patients compared to placebo or interferon. Inlyta, an oral VEGF inhibitor, has also recently been approved for the treatment of RCC in the second-line setting, after failure of one prior systemic therapy. Torisel and Afinitor, drugs which target mTOR, have also been approved for the treatment of advanced RCC, although Afinitor has been approved in the second-line only.

Despite the efficacy of the approved oral VEGF pathway inhibitors, drugs such as Sutent, Nexavar and Votrient are also associated with significant side effects such as neutropenia, fatigue, diarrhea, hand-foot syndrome, mucositis, stomatitis and abnormalities in liver function. A significant number of patients in the pivotal phase 3 clinical trials for each of these drugs required a reduction, interruption or discontinuation of their therapy due to these side effects. In their respective pivotal phase 3 clinical trials, in which these drugs were tested against interferon alpha, in the case of Sutent, or placebo, the reported frequency of dose reductions of these drugs in patients with advanced RCC was 52% for Sutent, 13% for Nexavar and 36% for Votrient. The reported frequency of dose interruptions due to adverse events in the phase 3 clinical trials of these drugs in patients with advanced RCC was 54% for Sutent, 21% for Nexavar and 42% for Votrient.

We believe there is a need for an RCC therapy that demonstrates significant efficacy while providing 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.

TIVO-1 Study. Results from the TIVO-1 study, together with results from our completed phase 2 clinical trial, formed the basis for our NDA for the approval of tivozanib in the treatment of advanced RCC, which was accepted for filing by the FDA in the fourth quarter of 2012, and will form the basis for the anticipated submission of a marketing application to European regulatory agencies by our partner Astellas in the second half of 2013. According to the timelines established by PDUFA, we expect that the review of the NDA by the FDA will be complete by July 28, 2013.

The TIVO-1 study was conducted in patients with advanced clear cell RCC who had undergone a prior nephrectomy, and who were treatment-naïve or had received no more than one prior regimen of immunotherapy or chemotherapy and no prior VEGF or mTOR-targeted therapy. The TIVO-1 study enrolled 517 patients at 76 sites in 15 countries, including the United States, Canada, various countries in Europe, and South America as well as India. The TIVO-1 study was a global, phase 3, randomized clinical trial comparing the efficacy and safety of tivozanib with Nexavar for first-line treatment in RCC. The primary endpoint for the trial was PFS based on independent radiology review. Secondary endpoints included 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 provided information about symptoms and the impact of the cancer on a patient's daily life activities. Disease progression and tumor response rates were determined in accordance with standard Response Evaluation Criteria in Solid Tumors (version 1.0), or RECIST.

In the TIVO-1 study, patients were randomized in approximately equal numbers to treatment with tivozanib or Nexavar. Patients randomized to the tivozanib treatment arm received tivozanib on the same dose and schedule that was well tolerated in our phase 2 clinical trial of tivozanib. Patients randomized to the Nexavar treatment arm received the approved dose of Nexavar, which is 400 mg twice a day. Patients randomized to the tivozanib treatment arm who developed documented disease progression were discontinued from the clinical trial. Patients randomized to the Nexavar treatment arm who developed documented disease progression were discontinued from the clinical trial and were given the option to receive tivozanib by enrolling in a separate long-term treatment protocol. Of the 517 patients enrolled in TIVO-1, 260 were randomized to tivozanib and 257 were randomized to Nexavar. Of the 260 patients randomized to the tivozanib arm, 259 received treatment with tivozanib. In order to

Table of Contents

meet FDA standards for assessing results in phase 3 trials, all radiology scans were assessed by a single, centralized group of independent radiology reviewers in the United States who were blinded to the assigned treatment.

In the TIVO-1 study, tivozanib demonstrated a statistically significant improvement in PFS over Nexavar with a median PFS of 11.9 months for tivozanib compared to a median PFS of 9.1 months for Nexavar in the overall study population. Tivozanib also demonstrated a statistically significant improvement in PFS with a median PFS of 12.7 months compared to a median PFS of 9.1 months for Nexavar in the pre-specified subpopulation of patients who received no prior systemic anti-cancer therapy for metastatic disease a subpopulation that comprised approximately 70% of the total study population.

Overall survival was a secondary endpoint of the TIVO-1 study. The final overall survival, or OS, analysis, as specified by the TIVO-1 protocol, showed a median OS of 28.8 months (95% confidence interval, or CI: 22.5 NA) for the tivozanib arm versus a median OS of 29.3 months (95% CI: 29.3 NA) for the Nexavar arm. No statistical difference between the two arms (HR=1.245, p=0.105) was observed. Due to the fact that patients in the Nexavar arm who developed disease progression were given the option to receive tivozanib, a substantial difference in the use of subsequent therapies resulted. Of 189 patients who discontinued their initial therapy on the tivozanib arm, 36% received some form of subsequent therapy, including 10% who received subsequent anti-VEGF therapy. Of 226 patients who discontinued their initial therapy on the Nexavar arm, 74% received some form of subsequent therapy, including 70% who received subsequent anti-VEGF therapy (98% of whom received tivozanib). We believe that the different utilization of second line therapies in the two arms of the TIVO-1 study impacted the relative performance of the two arms in the OS endpoint.

Dose interruptions due to an adverse event occurred in 46 (18%) tivozanib-treated patients compared to 91 (35%) Nexavar-treated patients (p<0.001). Dose reductions due to an adverse event occurred in 30 (12%) tivozanib-treated patients compared to 110 (43%) Nexavar-treated patients (p<0.001). There were 11 (4%) tivozanib-treated patients who discontinued the study due to drug-related adverse events compared to 14 (5%) Nexavar-treated patients (p=0.683).

Table 1 lists treatment-emergent adverse events (defined as any adverse event which first occurs or increases in severity after the first dose of study drug, regardless of whether it is considered to be related to the use of the study drug) seen in ≥10% of patients in either treatment arm. It includes the percentage of patients experiencing an adverse event as well as the percentage of patients that experienced a Grade 3 (severe or medically significant, but not immediately life-threatening consequences) or Grade 4 (life-threatening consequences) adverse event.

Table 1: Treatment Emergent Adverse Events (All Causality) Occurring in ≥10% of Patients in the Phase 3 Trial

Adverse Event Term	Tivozanib (n=259, %)		Nexavar (N=257, %)	
	Total	Grade 3 (4)	Total	Grade 3 (4)
Hypertension	44%	24% (2%)	34%	17% (<1%)
Diarrhea	22%	2% (0)	32%	6% (0)
Dysphonia	21%	0 (0)	5%	0 (0)
Fatigue	18%	5% (0)	16%	4% (0)
Weight Decreased	17%	<1% (0)	20%	3% (0)
Asthenia	15%	4% (<1%)	16%	3% (0)
Palmar-plantar erythrodysesthesia (hand-foot syndrome)	13%	2% (0)	54%	17% (0)
Back pain	14%	3% (0)	7%	2% (0)
Nausea	11%	<1% (0)	8%	<1% (0)
Dyspnea	10%	2% (0)	8%	2% (0)
Decreased appetite	10%	<1% (0)	9%	<1% (0)
Alopecia	2%	0 (0)	21%	0 (0)

Fatal adverse events were observed in both arms of the trial. Fatal events due to causes other than tumor progression were observed in nine patients in the tivozanib arm and nine patients in the Nexavar arm. In the

Table of Contents

tivozanib arm, two deaths were due to myocardial infarction, two were due to cardiac failure, and one each was due to hypertension, dyspnea, cerebrovascular accident, aortic aneurysm rupture and pulmonary embolism. In the Nexavar arm, three deaths were due to cerebrovascular accident, two were due to cardiac failure, and one each was due to coronary artery insufficiency, hemorrhage, pulmonary embolus, and acute respiratory distress syndrome.

Table 2 lists treatment-related adverse events (defined as any adverse event which first occurs or increases in severity after the first dose of a study drug and is considered by the study investigator to be related to the use of the study drug) seen in $\geq 5\%$ of patients in either treatment arm.

Table 2: Drug-related AEs $\geq 5\%$ in either group, n (%) of Patients in the Phase 3 Trial

Related Adverse Event Term	Tivozanib (N=259)	Nexavar (N=257)
Hypertension	109 (42.1)	79 (30.7)
Diarrhea	47 (18.1)	71 (27.6)
Dysphonia	47 (18.1)	11 (4.3)
Palmar-plantar erythrodyesthesia (hand-foot syndrome)	34 (13.1)	137 (53.3)
Alopecia	6 (2.3)	53 (20.6)

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. 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.

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 PFS from start of treatment and PFS after random assignment to tivozanib or placebo.

Based on final data from the tivozanib phase 2 clinical trial, the overall median PFS of patients in the phase 2 clinical trial was 11.7 months, as determined by independent radiologists. PFS 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, PFS was similar between those patients who were treatment naïve (14.3 months), and those who had received prior therapy with cytokines and/or chemotherapy (15.9 months). There were 51 patients who remained on tivozanib therapy for more than 2 years.

A significantly higher percentage of patients on tivozanib remained progression-free 12 weeks following random assignment as compared to placebo. As assessed by the study investigators, 57% of patients randomized to tivozanib were progression-free compared to 28% of patients randomized to placebo. This difference was statistically significant ($p=0.001$). The median PFS 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.

Full results of the phase 2 trial were published in the Journal of Clinical Oncology in May 2012.

TAURUS. We initiated the TAURUS patient preference study in the third quarter of 2012. TAURUS is a randomized (1:1), double-blind, crossover controlled, multi-center phase 2 study comparing tivozanib versus Sutent in approximately 160 patients with advanced RCC who have received no prior systemic therapy. The primary objective of the study is to compare patient preference after receiving both tivozanib and Sutent in sequence. Secondary objectives are to evaluate the incidence of treatment-emergent Grade 3/4 adverse events and serious adverse events; frequency of dose modifications; and quality of life in patients treated with tivozanib versus Sutent.

Table of Contents

BATON-RCC. In February 2011, we initiated a phase 2 clinical trial in the US and Canada, which we refer to as BATON-RCC, evaluating tivozanib in 105 patients with advanced RCC who had undergone a prior nephrectomy, and who were treatment-naïve or had received no more than one prior regimen of immunotherapy or chemotherapy, with no prior VEGF or mTOR -targeted therapy. In this phase 2 clinical trial, we are evaluating biomarkers and their correlation with clinical activity and/or tumor related toxicity and conducting an expanded assessment of safety and activity in this patient population. The last patient completed the treatment phase of this trial in August 2012, and data analysis is ongoing.

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 2013, it is estimated that more than 140,000 patients will be diagnosed with colorectal cancer, or CRC, and approximately 50,000 patients will die from this disease. Based on the World Health Organization GLOBOCAN data (published in 2008), in Europe it is estimated that approximately 333,000 patients are diagnosed with CRC and that nearly 149,000 die from the disease each year. Despite recent advances in chemotherapy, the American Cancer Society reports that only 12% of patients with metastatic colorectal cancer survive beyond 5 years. Therefore, there is a need for new and more effective treatments for colorectal cancer. Based on recent clinical trials, Avastin in combination with chemotherapy has become the standard of care for metastatic colorectal cancer. These studies have demonstrated that the VEGF pathway is important in colorectal cancer. We believe more potent inhibitors of the pathway, such as tivozanib, have the potential to improve therapy for this disease.

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

We are also interested in exploring the safety and activity of tivozanib in combination with an mTOR inhibitor in CRC. A phase 2 investigator sponsored clinical trial combining tivozanib and Afinitor commenced in February 2011 and enrolled 40 patients with refractory metastatic CRC. Final results from this phase 2 clinical trial, presented at the 2012 ASCO Gastrointestinal Cancers Symposium, showed that 50% of patients had stable disease as best response and median PFS was 3.0 months. A previous trial of single-agent Afinitor given weekly noted 25.3% of patients with stable disease as best response and median PFS of 1.7 months.

Breast Cancer

We believe that tivozanib can provide an improved therapy for women diagnosed with breast cancer. In 2013, it is estimated that over 230,000 women will be diagnosed with invasive breast cancer, and approximately 40,000 women will die from breast cancer, in the United States, according to the American Cancer Society. Based on the World Health Organization GLOBOCAN data (published in 2008), in Europe it is estimated that approximately 300,000 patients are diagnosed with breast cancer and that nearly 90,000 die from the disease each year. Currently available chemotherapy and hormonal therapies have significantly enhanced the survival of women diagnosed with breast cancer; metastatic breast cancer, however, remains an incurable disease. Although the FDA revoked its approval of Avastin for use with Taxol® (paclitaxel) in the treatment of metastatic breast cancer, Avastin is still approved in Europe for advanced breast cancer when used in combination with Taxol.

Table of Contents

In 2012, we initiated patient enrollment in a phase 2 clinical trial, called BATON-BC, evaluating the efficacy of tivozanib in combination with Taxol compared to placebo in combination with Taxol in patients with locally recurrent or metastatic triple negative breast cancer who have received no prior systemic therapy for advanced or metastatic breast cancer. Triple negative breast cancer refers to breast cancer tumors that do not express the estrogen receptor, progesterone receptor or the human epidermal growth factor receptor-2, and accounts for approximately 12-20% of breast cancers, according to a 2007 article by R. Dent et al, in *Clinical Cancer Research* and a 2006 article by L. Carey et al, in *The Journal of the American Medical Association*. There are currently no approved targeted therapies for triple negative breast cancer. BATON-BC is a double-blind, placebo-controlled, randomized (2:1 tivozanib/placebo), multicenter study that will enroll approximately 147 patients at 50 sites worldwide. The trial will compare PFS of triple negative breast cancer patients treated with tivozanib in combination with Taxol versus placebo in combination with Taxol. Secondary objectives include evaluation of objective response rate, overall survival and safety. Additional exploratory objectives include the evaluation of potential tumor biomarkers predictive of tumor sensitivity and/or resistance to tivozanib in combination with Taxol and effectiveness of tivozanib in combination with Taxol in defined intrinsic molecular breast cancer subtypes. Final data from a phase 1b clinical trial of tivozanib in combination with a standard dose of Taxol in patients with metastatic breast cancer, which reported data in June 2011, indicated that the combination was well-tolerated and resulted in an objective response rate of 38%, with 5 of the 13 patients evaluable for efficacy experiencing partial response and 7 of the 13 patients (54%) evaluable for efficacy, experiencing stable disease with five patients (31%) experiencing stable disease for at least 24 weeks.

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

Ficlatuzumab: Hepatocyte Growth Factor (HGF) Inhibitory Antibody

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

In September 2012, we presented results of the phase 2 portion of a phase 1b/2 clinical trial testing a combination of ficlatuzumab with Iressa, an epidermal growth factor receptor, or EGFR, tyrosine kinase inhibitor, randomized 1:1 versus Iressa alone in patients with newly diagnosed, treatment naïve non-small cell lung cancer, or NSCLC. Patients who demonstrated disease progression during treatment with Iressa alone had the opportunity to be treated with ficlatuzumab in combination with Iressa provided that safety was maintained and the patient continued to meet trial eligibility criteria. This 188-patient, randomized clinical trial, which is being conducted in Asia, is studying response rate and PFS in distinct patient subsets: those with activating EGFR mutations and those with wild-type EGFR. In addition, we are evaluating patient outcome based on c-Met levels expressed in their tumors. The primary endpoint of the study was overall response rate (ORR); secondary endpoints included PFS, OS and correlation of biomarkers with clinical activity. In the intent to treat (ITT)

Table of Contents

population, the addition of ficlatuzumab to Iressa did not result in statistically significant improved ORR or PFS in Asian treatment-naïve NSCLC patients. The preliminary OS hazard ratio in the ITT population for ficlatuzumab plus Iressa versus Iressa monotherapy was 0.84 (95% CI 0.52, 1.37). Final OS data will be presented once they are mature. The combination was well-tolerated, with no clinically meaningful differences in adverse event rates observed between the two arms. Given that our current priority is the anticipated registration and planned commercialization of tivozanib, we are focusing our efforts on further ficlatuzumab development through external collaborations.

In November 2011, we entered into an agreement with Boehringer Ingelheim International GmbH, or Boehringer Ingelheim, for large-scale process development and clinical manufacturing of ficlatuzumab. In connection with the agreement, Boehringer Ingelheim is producing ficlatuzumab at its biopharmaceutical sites in Fremont, CA (drug substance) and Beberach, Germany (drug product). We have retained all rights to the development and commercialization of ficlatuzumab.

AV-203: Anti-ErbB3 Antibody

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 of which have been implicated in promoting the growth of significant numbers of tumors, particularly in breast and lung 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 to treatment, 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.

In May 2012, we initiated a phase 1, multi-center, dose-escalation study of AV-203, a monoclonal antibody that selectively targets the ErbB3 receptor. This study will evaluate the safety, tolerability, dose-limiting toxicities, maximum tolerated dose and/or recommended phase 2 dose of AV-203 in subjects with metastatic or advanced solid tumors. Secondary endpoints in the study include characterizing the pharmacokinetic profile of AV-203 and anti-drug antibody levels, and evaluating the preliminary anti-tumor activity. A core component of the study will be the exploration of predictive biomarkers for AV-203 response identified using our Human Response Platform. Up to 30 patients are expected to enroll in the dose-escalation portion of the study, and up to 60 additional patients may be enrolled in the biomarker exploration component of the study.

In March 2009, we entered into an exclusive option and license agreement with Biogen Idec, under which we granted Biogen Idec an exclusive option to obtain rights to co-develop (with us) and commercialize our ErbB3-targeted antibodies for the potential treatment and diagnosis of cancer and other diseases outside of North America. 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 North America. We retain the exclusive right to commercialize ErbB3

Table of Contents

antibody products in North America. 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 North America.

Other Pipeline Programs

Using our Human Response Platform, we have identified a number of other promising targets that appear to be potent drivers of tumor growth. Genetic screens conducted using the Human Response Platform have demonstrated that activation of the Notch signaling pathway plays an important role in tumor formation and the maintenance of cancer stem cell populations in tumors. Our team has demonstrated inhibition of tumor growth with a Notch 1 antibody candidate in preclinical tumor models. Work in our Human Response Platform has also identified Fibroblast Growth Factor 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. In 2012, we also initiated a program focusing on cancer cachexia, a serious and common complication of advanced cancer and a number of chronic diseases. In connection with this program, we have in-licensed certain patents and patent applications from St. Vincent's Hospital in Sydney, Australia.

Our Human Response Platform

We were founded with the goal of developing a fundamentally new kind of pre-clinical 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 & Co., Inc., or Merck, OSI Pharmaceuticals, Inc., or OSI, Astellas 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. 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.

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 subject 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 subject animal contain the cancer-causing mutations. Third, because of the switch that we introduce into our models, we can activate the cancer-causing mutations after the subject animals are born, replicating what is seen in many human cancers. In many other models, these mutations are activated before the subject animals are born, and interfere with their normal embryonic development. Finally, because tumors in our model develop spontaneously after introduction

Table of Contents

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.

Because each of the tumors that develop 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 subtypes, 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.

For instance, 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 and a pending U.S. patent application on different biomarker tests, or similar tests, for identifying patients likely to be sensitive or resistant to treatment with tivozanib. We intend to use these candidate biomarker tests in clinical trials of tivozanib.

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

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

Competition

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

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

Table of Contents***Tivozanib Competition***

Angiogenesis inhibitors represent a rapidly growing drug category in oncology with 2012 sales estimated to be approximately \$8.0 billion worldwide, based on 2012 quarterly and annual reports made publicly available by companies marketing such drugs. There are currently nine FDA-approved drugs in oncology which target the angiogenesis pathway. Five of these are FDA-approved VEGF pathway inhibitors indicated for RCC.

Four of the FDA-approved VEGF receptor tyrosine kinase inhibitors, or TKIs are oral small molecules. Nexavar is marketed by Bayer and Onyx Pharmaceuticals, Inc., Sutent and Inlyta are marketed by Pfizer, and Votrient is marketed by GSK. Most of these approved VEGF TKIs are not specific to the VEGF receptors. Nexavar is approved for advanced RCC and unresectable hepatocellular cancer. Sutent is approved for advanced RCC, gastrointestinal stromal tumors, and progressive, well-differentiated pancreatic neuroendocrine tumors. Inlyta is approved for advanced RCC after failure of one prior systemic therapy. Votrient is approved for advanced RCC and advanced soft tissue sarcoma after prior chemotherapy.

Avastin, marketed by Roche, is an infused monoclonal antibody approved in combination with other anti-cancer agents for the treatment of metastatic colorectal cancer, non-squamous non-small cell lung cancer, and advanced RCC. It is also approved as a monotherapy for the treatment of glioblastoma in patients with progressive disease following prior therapy. Other approved agents for the treatment of RCC are Torisel, marketed by Pfizer, and Afinitor, marketed by Novartis Pharmaceuticals Corporation, or Novartis, both of which inhibit mTOR.

We are aware of a number of companies that have ongoing programs to develop both small molecules and biologics that target the VEGF pathway. Other VEGF pathway inhibitors that have launched or are in late-stage development in other cancer types include Amgen Inc. s and Takeda Pharmaceutical Company Limited s AMG706 (motesanib), AstraZeneca plc s AZD2171 (Recentin, cediranib) and AZD6474 (Calprelsa/Zactima, vandetanib), Bayer s BAY-73-4506 (Stivarga, regorafenib), Boehringer Ingelheim s BIBF-1120 (Vargatef, nintedanib), Bristol-Myers Squibb Company s BMS-582664 (brivanib alaninate), Eisai Co. Ltd. s E-7080 (lenvatinib mesylate), Exelixis Inc. s XL-184 (Cometriq, cabozantinib), ImClone LLC s IMC-1121b (ramucirumab), Kadmon Corporation, LLC s KD-019, Novartis s TKI-258 (dovitinib), Onco Therapy Science Inc. s OTS-102 (elpamotide), Pfizer and Taiho s SU-006668 (orantinib), Progen Pharmaceuticals Ltd. s PI-88 (muparfostat), and Regeneron Pharmaceuticals, Inc. s, or Regeneron s, and Sanofi-Aventis US LLC s ziv-aflibercept (Zaltrap).

Ficlatuzumab Competition

We believe the products in development targeting HGF consist of Amgen s AMG-102 (rilotumumab), currently in phase 3 clinical trials, and Galaxy Biotech, LLC s HuL2G7, which has completed a phase 1 clinical trial.

Other marketed or later-stage clinical-stage drugs which target the HGF/c-Met pathway include Roche s onartuzumab (MetMab/ 5D5 Fab), ArQule, Inc. s/ Daiichi Sankyo, Inc. s ARQ-197 (tivantanib), MethyIGene, Inc. s MGCD-265, Eisai Co. Ltd. s E-7050 (golvatinib), Exelixis Inc. s XL-184 (Cometriq, cabozantinib), Exelixis Inc. s and GSK s XL-880 (foretinib), Incyte Corp. s and Novartis s INCB-028060, Pfizer s PF-2341066 (Xalkori, crizotinib), Sanofi-Aventis s SAR-125844, Eli Lilly & Co. s LY-2875358, and Bristol-Myers Squibb Company s and Aslan Pharmaceuticals BMS-777607.

AV-203 Program Competition

We believe the most direct competitors to our AV-203 program that are in late stage development are monoclonal antibodies that specifically target the ErbB3 receptor, including Merrimack Pharmaceuticals, Inc. s and Sanofi-Aventis US LLC s MM-121, which is currently in phase 2 clinical development, and Daiichi Sankyo, Inc. s and Amgen, Inc. s U3-1287/ AMG-888, which is also in phase 2 clinical development. Other clinical-stage competitors include Roche s MEHD7945A and RG-7116, Merrimack Pharmaceuticals, Inc. s MM-111 and MM-141, Novartis s LJM716, Regeneron s REGN1400, and Enzon Pharmaceuticals and Santaris Pharmaceuticals s EZN-3920.

Table of Contents

Strategic Partnerships

We have entered into multiple strategic partnerships in which we have in-licensed rights to compounds and granted rights to tivozanib, our antibody candidates and certain aspects of our Human Response Platform. Many of 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.

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, with the right to grant sublicenses subject to certain restrictions, to research, develop, manufacture and commercialize tivozanib, pharmaceutical compositions thereof and associated biomarkers. Our exclusive license covers all territories in the world, except for Asia. KHK has retained rights to tivozanib in Asia. Under the license agreement, we obtained exclusive rights in our territory under certain KHK patents, patent applications and know-how related to tivozanib, to research, develop, make, have made, use, import, offer for sale, and sell tivozanib for the diagnosis, prevention and treatment of any and all human diseases and conditions. 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. 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 conduct certain clinical trials of, seek marketing approval for or commercialize any other cancer product that also works by inhibiting the activity of the VEGF receptor.

Upon entering into the license agreement with KHK, we made a one-time cash payment in the amount of \$5.0 million. In March 2010, we made a \$10.0 million milestone payment to KHK in connection with the dosing of the first patient in our phase 3 clinical trial of tivozanib. We made a \$22.5 million payment to KHK during the year ended December 31, 2011 related to the up-front license payment received under the collaboration and license agreement with Astellas which we entered into in February 2011. In December 2012, we made a \$12.0 million milestone payment to KHK in connection with the acceptance by the FDA of our NDA filing for tivozanib.

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

make future milestone payments upon the achievement of specified regulatory milestones in the United States, including a possible milestone payment of \$18.0 million to KHK in connection with the FDA granting marketing approval in the United States;

pay tiered royalty payments on net sales we make of tivozanib in our territory ranging from the low to mid-teens as a percentage of our net sales of tivozanib. The royalty rate escalates within this range during each calendar year based on increasing tivozanib sales during such calendar year. 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, end on the later of 12 years after the date of first commercial sale of tivozanib in that country or expiration of the last-to-expire valid claim of the licensed patents covering tivozanib in that country, and are subject to offsets under certain circumstances; and

pay 30% of certain amounts we receive under our collaboration and license agreement with Astellas, which we describe below, in connection with Astellas' development and commercialization activities outside of North America and Asia related to tivozanib (including a potential \$4.5 million milestone payable to KHK in connection with the acceptance by the EMA of the filing of a Marketing Authorization Application and \$9.0 million to KHK in connection with the EMA granting marketing approval in Europe), other than amounts we receive in respect of research and development funding or equity investments, subject to certain limitations.

Table of Contents

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, or KHK elects, 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

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 seek to 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 North America and Europe under the joint development plan and joint commercialization plan, respectively. Throughout the rest of the world (which excludes North America, Europe and Asia) which we refer to as the royalty territory, Astellas has an exclusive, royalty-bearing license to develop and commercialize tivozanib. Our plan to commercialize tivozanib in collaboration with Astellas, as described herein, is subject to our and Astellas' receipt of necessary regulatory approvals from the 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 NDA in the United States, and Astellas will hold all marketing authorizations in the rest of the world, other than Asia.

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

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

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

Table of Contents

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' 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, Canada and Mexico, 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. We and Astellas may commercialize products (other than tivozanib) in the royalty territory, on a country-by-country basis, after expiration of the applicable royalty term, and in North America and Europe after expiration of all valid claims under the licensed patents.

In connection with the agreement, we received an initial cash payment of \$125 million, comprised of a \$75 million license fee and \$50 million in research and development funding, both of which are non-creditable and non-refundable against any amounts due under the collaboration agreement. We retained net proceeds of approximately \$97.6 million of the initial cash payment from Astellas, after payments to KHK and strategic, legal and financial advisors. In December 2012, we received a \$15.0 million milestone payment from Astellas in connection with the acceptance by the FDA of our NDA filing for tivozanib. We are also eligible to receive an aggregate of approximately \$1.3 billion in potential future milestone payments, comprised of (i) up to \$85 million in substantive milestone payments upon achievement of specified clinical and development milestone events, (ii) up to \$475 million in substantive milestone payments upon achievement of specified regulatory milestone events, including up to \$75 million in milestone payments in connection with specified regulatory filings, and receipt of marketing approvals, for tivozanib to treat RCC in the United States and Europe, and (iii) up to approximately \$780 million in milestone payments upon the achievement of specified commercial sales events.

Significant potential near-term regulatory milestones include marketing approval by the FDA in the United States (\$30 million) and acceptance by the EMA of the first filing of a Marketing Authorization Application (\$15 million). We are also eligible to receive a \$30 million milestone payment upon marketing approval by the EMA. In addition, if tivozanib is successfully developed and launched in the royalty territory, Astellas will be required to pay to us tiered, double digit royalties on net sales of tivozanib in the royalty territory, if any, subject to offsets under certain circumstances. We are required to pay KHK low to mid-teen royalties on our net sales in North America, and 30% of certain amounts we may receive from Astellas in connection with Astellas' development and commercialization activities in Europe and the royalty territory, including up-front license fees, milestone payments and royalties.

Unless terminated earlier in accordance with its terms, the collaboration agreement with Astellas expires (a) with respect to the royalty territory, on a country-by-country basis, upon the latest to occur of: (i) the expiration of the last-to-expire valid claim of an AVEO patent or joint patent covering the composition of tivozanib, (ii) the expiration of the last-to-expire valid claim of an AVEO patent or joint patent covering the use of tivozanib, but only for so long as no generic competition exists in such country, and (iii) twelve years from first commercial sale of tivozanib in such country, and (b) with respect to North America and Europe as a whole, upon the expiration of all payment obligations between the parties related to development and commercialization of tivozanib in North America and Europe. 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

Table of Contents

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

Biogen Idec

In March 2009, we entered into an exclusive option and license agreement with Biogen Idec regarding the development and commercialization of our discovery-stage ErbB3-targeted antibodies for the potential treatment and diagnosis of cancer and other diseases in humans outside of North America. 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. Until a specified time 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 North America. We retain the exclusive right to commercialize ErbB3 antibody products in North America. In this description, the countries in the world other than North America are referred to as Biogen Idec's territory, and North America is referred to as our territory. If Biogen Idec exercises its exclusive option to ErbB3 antibody products, Biogen Idec will grant us (a) 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 North America.

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 North America. 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. If either party wishes to develop a ErbB3 antibody product for a new indication under the agreement, and the other party does not also wish to develop that product for such indication, the party that desires to conduct development activities regarding the new indication has the right to independently, and at its sole cost, develop and manufacture the new ErbB3 antibody product for such indication for commercialization solely in its territory, and the other party may elect, under specified circumstances, to pay to obtain rights to relevant clinical data to pursue regulatory approval for such indication in its territory.

Table of Contents

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 North America. 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 North America 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 North America, and we are required to use commercially reasonable efforts to do so in countries in our territory where marketing approval has been obtained. Biogen Idec has the sole right, at its sole expense (including manufacturing costs) to commercialize ErbB3 antibody products in its territory, and is required to use commercially reasonable efforts to do so in countries in its territory where marketing approval has been obtained.

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

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

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

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

Table of Contents

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 increased 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 our territory. If all or substantially all of our assets are acquired by, or we merge with or become controlled by, another entity, and the other entity is independently developing or commercializing a product containing an ErbB3 antibody, 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 neither party's activities will be subject to the oversight of the joint committee. If Biogen Idec elects to maintain the agreement and the other party fails to divest the ErbB3 product within a specified time period, Biogen Idec will have the right to assume the key development, manufacturing, budgeting and governance rights, responsibilities, and obligations under the agreement that had previously been our rights and obligations.

OSI Pharmaceuticals

In September 2007, we entered into a collaboration and license agreement with OSI. This strategic partnership is primarily focused on the identification and validation of genes and targets involved in the processes of epithelial-mesenchymal transition or mesenchymal-epithelial transition, in cancer. The research program portion of our strategic partnership with OSI, which concluded in June 2011, focused on the development of proprietary target-driven tumor models for use in target validation, drug screening and biomarker identification to support OSI's drug discovery and development activities. In connection with the terms of our agreement, OSI elected to obtain exclusive rights, with the right to grant sublicenses, under certain aspects of our intellectual property, to research, develop, make, sell and import drug products and associated diagnostics 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, OSI, in November 2010, exercised an option to license certain elements of our proprietary

Table of Contents

technology platform, including components of the Human Response Platform for the identification/characterization of novel epithelial-mesenchymal transition agents and proprietary patient selection biomarkers, in support of OSI's clinical development programs. We received \$12.5 million upon delivery of the notice of option exercise, and we received the remaining \$12.5 million in July 2011 in connection with the successful transfer of the applicable technology. In March 2011, we earned \$1.5 million related to deliverables and research milestones under the agreement. In May 2012, we earned a patent-related milestone payment of \$250,000 upon filing of a patent application by OSI, and we also earned a clinical and development milestone payment of \$750,000 for commencement by OSI of GLP toxicology studies.

Under the July 2009 expanded agreement, if all applicable milestones are achieved, all remaining payments for the successful achievement of discovery, development and commercialization milestones under the agreement could total, in the aggregate, over \$46 million, comprised of approximately (i) \$8.4 million in substantive milestone payments upon achievement of specified clinical and development milestone events, (ii) \$20.7 million in substantive milestone payments upon achievement of specified regulatory milestone events, and (iii) \$17.5 million in substantive milestone payments upon the achievement of specified sales events. In addition, we are eligible to receive up to \$24.0 million in biomarker-related milestones. Upon commercialization of products which were part of the research program under the agreement, we are eligible to receive tiered royalty payments on sales of products by OSI, its affiliates and sublicensees.

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

The collaboration and license agreement will remain in effect until the expiration of both OSI's royalty obligations to us, and our royalty obligations to OSI, in each case determined on a product-by-product and country-by-country basis. 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 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, 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. OSI may elect to terminate the agreement with respect to a particular collaboration target and all its associated products, in which event OSI's license to such target and products terminates and reverts to us, subject to our continued milestone and royalty payment obligations to OSI. 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.

Intellectual Property Rights

Patent Rights

We have been building and will continue to build a strong intellectual property portfolio. We strive for multi-tiered patent protection, where possible. 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

Table of Contents

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. With respect to tivozanib, we have:

U.S. patents: 3 issued; none pending; expirations ranging from 2018 to 2023

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

Canadian patents: 1 granted; none pending; expiration 2022

Australian patents: 1 granted; none pending; expiration 2022

Complementing these in-licensed patents relating to tivozanib are two of our own issued U.S. patents that cover different biomarker tests for identifying human patients likely to respond to treatment with tivozanib, and an issued U.S. patent on a method of using tivozanib in combination with temsirolimus. With respect to tivozanib related technologies, we have:

U.S. patents: 3 issued; 3 pending; expirations ranging from 2029 to 2033

European patents: none granted; 3 pending; expirations ranging from 2029 to 2030

Canadian patents: none granted; 3 pending; expirations ranging from 2029 to 2030

Australian patents: none granted; 2 pending; expirations ranging from 2029 to 2030

We own issued U.S. patents containing composition-of-matter claims that cover our HGF antibodies, including ficlatuzumab, and our FGFR3 antibodies. In addition, we own pending patent applications covering our HGF antibodies, ErbB3 antibodies, FGFR2 antibodies, RON antibodies, GDF15 antibodies, Notch3 antibodies, and methods of making and using those antibodies. We are prepared to file patent applications on other antibodies in our antibody product pipeline soon after the experimental data necessary for an application becomes available. In addition, we own a pending patent application on use of a predictive biomarker for identifying patients likely to respond to one of our antibodies. We also own a granted U.S. patent and pending foreign counterpart patent applications covering a method of identifying cancer tissue likely to be sensitive or resistant to treatment with an inhibitor of Notch receptor activation. With respect to our antibody product pipeline, we have:

U.S. patents: 8 issued; 8 pending; expirations ranging from 2027 to 2033

European patents: 2 granted; 4 pending; expirations ranging from 2027 to 2031

Canadian patents: none granted; 6 pending; expirations ranging from 2027 to 2031

Australian patents: 2 granted; 4 pending; expirations ranging from 2027 to 2031

Edgar Filing: AVEO PHARMACEUTICALS INC - Form 10-K

International applications: 1 pending

In addition to patents relating to tivozanib, ficlatuzumab and other therapeutic antibodies in our product pipeline, our patent portfolio contains a number of other patents and patent applications relevant to our business. We own a granted U.S. patent and pending foreign counterpart applications covering a method of making a chimeric mouse cancer model. We also own a granted U.S. patent and pending foreign counterpart patent applications covering a method of producing primary tumor material via directed complementation. We also own pending U.S. and foreign patent applications covering a mouse model that contains a human breast tumor. We own a pending patent application that covers a general method for identifying new, multi-gene biomarkers for predicting response to an anti-cancer drug of interest, as well as specific multi-gene biomarkers identified by using the same method. With respect to our technology platforms, we have:

U.S. patents: 3 issued; 3 pending; expirations ranging from 2024 to 2033

European patents: 2 granted; 2 pending; expirations ranging from 2024 to 2026

Table of Contents

Canadian patents: none granted; 1 pending; expiration 2026

Australian patents: 3 granted; none pending; expirations ranging from 2024 to 2026

International applications: 1 pending

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

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

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

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 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

Table of Contents

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, patent litigation may be 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 effect 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 making any payments to us.

Trade Secrets

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.

Trademarks

We seek trademark protection in the U.S. and foreign jurisdictions where available and when appropriate. We have filed to register several trademarks intended for potential use in the marketing of tivozanib. We own a U.S. trademark that we use in connection with our research and development (Human Response Platform). We also own a U.S. trademark (The Human Response) and a U.S. trademark application (AVEO Oncology The Human Response) that we use in connection with our business, in general.

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

Table of Contents

treatment of choice for patients with advanced RCC. In order to achieve this goal, we entered into a strategic partnership with Astellas in connection with which we and Astellas will seek to develop and commercialize tivozanib in North America and Europe.

In anticipation of approval, we are focusing on certain key objectives including further refining our understanding of the RCC marketplace and market opportunity for tivozanib, optimizing our brand platform and positioning for launch, ensuring launch readiness by expanding our sales infrastructure and finalizing distribution capabilities and patient access offerings. 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. As the lead commercialization party for tivozanib in North America, we will have lead responsibility for formulating the commercialization strategy for North America, with each of us and Astellas responsible for conducting fifty percent (50%) of the sales efforts and medical affairs activities in North America. We recently appointed a Vice President of Sales as part of our ongoing efforts to continue to build our commercial team in a responsible, timely manner.

The commercial infrastructure for specialty oncology products typically consists of a targeted, field-based specialty sales force that calls on a focused group of physicians. This sales force would be supported by sales management and sales training, as well as internal and outsourced commercial groups including sales and commercial operations, marketing, market research, reimbursement services and distribution. Additional capabilities important to the oncology marketplace include the management of key accounts such as managed care organizations, group-purchasing organizations, specialty pharmacies, oncology group networks, and government accounts, all responsibilities and costs which we would share with our partner, Astellas. To develop the appropriate commercial infrastructure in the US, we are investing significant amounts of financial and management resources, prior to any confirmation that tivozanib will be approved. In Europe, although Astellas would be the lead commercialization party, we are obligated to provide up to 50% of the medical science liaisons in the major European countries as well as assist Astellas with the formulation of the European commercial strategy for tivozanib, including the strategic plan and allocation of resources.

Manufacturing

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

One of our contract manufacturers has manufactured what we believe to be sufficient quantities of tivozanib's drug substance to support our 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. The manufacturer of the drug substance for tivozanib has manufactured batches of the drug substance that will serve as the validation batches that will be reviewed by the FDA in connection with its review of the NDA for tivozanib and as the supply of tivozanib for commercial launch. If our third party manufacturers are unable to supply drug substance and/or drug product on a commercial basis, and we fail to establish commercially reasonable terms for commercial supply with alternative vendors, we may be delayed in successfully producing and marketing 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. In November 2011, we entered into an agreement with Boehringer Ingelheim for large-scale process development and clinical manufacturing of ficlatuzumab. In connection with the agreement, Boehringer Ingelheim is producing ficlatuzumab at its biopharmaceutical sites in Fremont, CA (drug substance) and

Table of Contents

Biberach, Germany (drug product). We are in the process of demonstrating the comparability of the ficlatuzumab drug product manufactured at Boehringer Ingelheim to the ficlatuzumab drug product we purchased from Merck.

In August 2010, we entered into an agreement with Laureate Pharma, Inc., or Laureate, for the clinical manufacture of AV-203 drug substance. Laureate has produced two batches of AV-203 drug substance for clinical trials at its site in Princeton, NJ. AV-203 drug product is produced at Microtest Laboratories, Inc. in Agawam, Massachusetts.

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.

Government Regulation

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

United States Government Regulation

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

The Investigational New Drug Process

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

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

The central focus of the initial IND submission is on the general investigational plan and the protocol(s) for human studies. The IND also includes results of animal studies or other human studies, as appropriate, as well as manufacturing information, analytical data and any available clinical data or literature to support the use of the investigational new drug or biological product. An IND must become effective before human clinical trials may

Table of Contents

begin. An IND will automatically become effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions related to the proposed clinical trials as outlined in the IND. In such a case, the IND may be placed on clinical hold and the IND sponsor and the FDA must resolve any outstanding concerns or questions before clinical trials can begin. Accordingly, submission of an IND may or may not result in the FDA allowing clinical trials to commence.

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

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

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

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

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

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

Table of Contents

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 that 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.

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.

Edgar Filing: AVEO PHARMACEUTICALS INC - Form 10-K

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.

Table of Contents

After the NDA or BLA 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 that 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 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.

Table of Contents

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

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

Europe / Rest of World Government Regulation

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

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

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 documentation requirements.

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

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

Table of Contents

Compliance

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

Available Special Regulatory Procedures

Formal Meetings

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

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

Advice from either the FDA or EMA is typically provided based on questions concerning, for example, quality (chemistry, manufacturing and controls testing), nonclinical testing and clinical studies, and pharmacovigilance plans and risk-management programs. Advice is not legally binding with regard to any future marketing authorization application of the product concerned. To obtain binding commitments from the FDA on the design and size of clinical trials intended to form the primary basis of an effectiveness claim, Special Protocol Assessment procedures are available. Where the FDA agrees to a Special Protocol Assessment, or SPA, the agreement may not be changed by either the sponsor or the FDA except if the sponsor and the FDA agree to a change, or a senior FDA official determines that a substantial scientific issue essential to determining the safety or effectiveness of the product was identified after the testing began. An SPA is not binding if new circumstances arise, and there is no guarantee that a study will ultimately be adequate to support an approval even if the study is conducted according to the terms of an SPA.

Orphan Drug Designation

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

Table of Contents

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

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

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

Pediatric Development

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

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

Table of Contents

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 phase 3 clinical trials, an NDA or BLA will either receive priority or standard review from the FDA. 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. Under PDUFA V, effective October 1, 2012, where an application receives priority review, the target date for FDA action will be 8 months from submission in the case of an application for a new chemical entity and 6 months from submission in the case of products that do not contain a new chemical entity. Where an application receives standard review, the target date for FDA action will be 12 months from submission in the case of an application for a new chemical entity and 10 months from submission in the case of products that do not contain a new chemical entity.

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

Pharmaceutical Coverage, Pricing and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any drug products for which we obtain regulatory approval. In the United States and markets in other countries, sales of any products for which we receive regulatory approval for commercial sale will depend in part on the availability of reimbursement from third party payors. Third party payors include government health administrative authorities,

Table of Contents

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

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

In 2010, Congress enacted sweeping healthcare reform legislation. This legislation is changing the way that healthcare is financed by both governmental and private insurers and significantly affects the pharmaceutical industry. Among the provisions of the legislation are provisions governing enrollment in federal healthcare programs, increases in the rebates pharmaceutical manufacturers must pay to state Medicaid programs, a new requirement that manufacturers pay states rebates on prescription drugs dispensed to Medicaid managed care enrollees, a revised definition of average manufacturer price, 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 payments and other transfers of value to healthcare providers and to the distribution of product samples to healthcare providers. In addition, the federal government has been given additional enforcement authority.

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

Different pricing and reimbursement schemes exist in other countries. In the European Union, governments influence the price of pharmaceutical products through their pricing and reimbursement rules and control of national healthcare systems that fund a large part of the cost of those products to consumers. Some jurisdictions operate positive and negative list systems under which products may only be marketed once a reimbursement price has been agreed. To obtain reimbursement or pricing approval, some of these countries may require the completion of clinical trials that compare the cost-effectiveness of a particular product candidate to currently available therapies. Other member states allow companies to fix their own prices for medicines, but monitor and control company profits.

The downward pressure on healthcare costs in general, particularly prescription drugs, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products. In addition, in some countries, cross-border imports from low-priced markets exert a commercial pressure on pricing within a country. The healthcare reform legislation, and the 2009 economic stimulus legislation, contained significant amounts of funding for comparative effectiveness research, which may lead to an increase in the dissemination of information comparing the effectiveness of drugs or other healthcare treatment options, which may negatively impact coverage and pricing decisions for our products.

Table of Contents

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

Biosimilars

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

Other Healthcare Laws and Compliance Requirements

In the United States, our activities are potentially subject to regulation by various federal, state and local authorities in addition to the FDA, including the Centers for Medicare and Medicaid Services, other divisions of the U.S. Department of Health and Human Services (e.g., the Office of Inspector General), the Department of Veterans Affairs, the U.S. Department of Justice and individual U.S. Attorney offices within the Department of Justice, and state and local governments. For example, sales, marketing and scientific/educational grant programs must comply with the anti-fraud and abuse provisions of the Social Security Act, the False Claims Act, the privacy provisions of the Health Insurance Portability and Accountability Act, or HIPAA, and similar state laws, each as amended. Pricing and rebate programs must comply with the requirements of the Medicaid Rebate Program, established by the Omnibus Budget Reconciliation Act of 1990, and with 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 the U.S. Department of Veterans Affairs and the 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 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 in place legislation requiring pharmaceutical companies to establish marketing compliance programs, file periodic reports with the state, make periodic public disclosures on sales, marketing, pricing, and other activities, and/or register their sales representatives, and to prohibit certain other sales and marketing practices.

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

Table of Contents

Our business activities outside the United States are subject to regulation under the U.S. Foreign Corrupt Practices Act, which generally prohibits U.S. companies and their intermediaries from making payments to foreign government officials for the purpose of obtaining or retaining business or securing any other improper advantage.

Employees

As of December 31, 2012, we had 219 employees worldwide. None of our employees is represented by a labor union or is covered by a collective bargaining agreement. We consider our relationship with our employees to be good.

Legal Proceedings

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

Research and Development Costs

Our research and development costs were \$91.4 million in 2012, \$101.7 million in 2011, and \$86.3 million in 2010. These costs consist of the cost of our own independent research and development efforts and the costs associated with collaborative research and development and in-licensing arrangements. Research and development costs, including upfront fees and milestones paid to collaboration partners, are expensed as incurred if the underlying products have not received regulatory approval and have no future alternative use.

Segment and Geographic Information

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

Executive Officers

The following table lists the positions, names and ages of our executive officers as of March 1, 2013:

Executive Officers

Tuan Ha-Ngoc	60	Chief Executive Officer, President and Director
David Johnston	57	Chief Financial Officer
Elan Ezickson	49	Executive Vice President, Chief Operating Officer
William Slichenmyer	55	Chief Medical Officer
Michael P. Bailey	47	Chief Commercial Officer
Jeno Gyuris	53	Chief Scientific Officer
Mary Ellen Jones	60	Senior Vice President, Human Resources
Joseph Vittiglio	41	Senior Vice President, General Counsel

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 boards of a number of academic and nonprofit organizations, including the Harvard School of Dental Medicine, the Tufts School of Medicine, and the MIT Koch Institute of Integrative Cancer Research. Mr. Ha-Ngoc served on the Board of Directors of ArQule, Inc.,

Table of Contents

from 2002 until 2006, and Human Genome Sciences, Inc. (now part of GlaxoSmithKline) from 2006 until 2012. 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 has served as our Executive Vice President, Chief Operating Officer since February 2012. Mr. Ezickson joined our company in April 2003 and served as our Chief Business Officer until July 2010 and our Executive Vice President, Chief Business Officer from July 2010 to February 2012. From 1994 to 2003, he worked at Biogen in roles that included President of Biogen Canada, Program Executive and Associate General Counsel. Mr. Ezickson holds a B.A. in Political Science from Yale University and a J.D. from the Columbia University School of Law.

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

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

Mary Ellen (Nell) Jones has served as our Senior Vice President, Human Resources since August 2011 and brings more than 30 years of human resources (HR) and operations experience to the company. Ms. Jones has been a successful HR leader in multiple industries, and is experienced in establishing HR services for high growth companies with domestic and international locations. Prior to joining AVEO, Ms. Jones served as senior vice president of HR at Verenum. Prior to Verenum, Ms. Jones was an HR executive at several other energy, research and technology companies in addition to several years of HR consulting services to client companies in

Table of Contents

a variety of industries. Ms. Jones has extensive experience in recruiting and retention, compensation, management coaching and organizational effectiveness and development. She received a B.A. degree from the College of the Holy Cross. She is a former member of the Board of Trustees of the College of the Holy Cross and a current member of its Board of Advisors.

Joseph Vittiglio was named Senior Vice President, General Counsel effective January 24, 2013. Mr. Vittiglio joined AVEO in October 2007 and served as our Corporate Counsel until January 2010, as our Vice President, Corporate Counsel from January 2010 until January 2012 and our Vice President, Chief Corporate Counsel from January 2012 to January 2013. Mr. Vittiglio has over 15 years of experience in corporate and securities law, with a particular focus in the biotech and pharmaceutical industries. Prior to joining AVEO, Mr. Vittiglio was the director of corporate legal affairs of Oscient Pharmaceuticals from 2005 through 2007. From 1998 through 2005, Mr. Vittiglio was an attorney at the Boston law firm of Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C., where his practice focused principally in the life science and technology industries, working on collaborative arrangements, corporate partnering, registered public securities offerings, mergers and acquisitions and venture financings. Mr. Vittiglio serves on the Board of Directors of two nonprofit organizations, the Casa Monte Cassino in Boston and Lynnfield Youth Soccer. Mr. Vittiglio holds a degree in International Relations from Tufts University and graduated from Northeastern University School of Law in 1996.

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.aveooncology.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.

Table of Contents

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 this Annual Report on Form 10-K and other filings with the SEC, press releases, communications with investors and oral statements. Actual future results may differ materially from those anticipated in our forward-looking statements. We undertake no obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise.

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

We are dependent on the success of our lead drug candidate, tivozanib, for which a New Drug Application was recently accepted for filing by the U.S. Food and Drug Administration.

To date, we have invested a significant portion of our efforts and financial resources in the research and development of tivozanib. We have announced data from our phase 3 registration clinical trial for tivozanib for the treatment of first-line advanced renal cell carcinoma, or RCC, referred to as TIVO-1, and are conducting additional clinical trials in RCC and other disease indications, many of which focus on tivozanib in combination with other known anti-cancer agents. On November 27, 2012, the U.S. Food and Drug Administration, or FDA, accepted for filing our New Drug Application, or NDA, seeking marketing approval of tivozanib for the treatment of advanced RCC. We expect that our partner, Astellas, will submit a Marketing Authorization Application, or MAA, with the European Medicines Agency, or EMA, in the second half of 2013.

Our near-term prospects, including our ability to finance our company and to generate revenues, will depend heavily on the successful development and commercialization of tivozanib. All of our other potential product candidates are in earlier stages of research and development. In October 2012, we announced a strategic restructuring whereby we plan to explore further development of ficlatuzumab and certain discovery assets through external collaborations and focus utilization of our Human Response Platform and discovery capabilities primarily on supporting the clinical development of tivozanib, as well as certain other novel antibody programs.

The clinical and commercial success of tivozanib will depend on a number of factors, including the following:

our ability to demonstrate to the satisfaction of the FDA, or equivalent foreign regulatory agencies, tivozanib's safety, efficacy and clinically meaningful benefit through completed, ongoing and any future clinical and non-clinical trials, including without limitation, the TIVO-1 study;

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

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

the prevalence and severity of adverse side effects;

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

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

the ability of our third-party manufacturers to manufacture clinical trial and commercial supplies of tivozanib and to develop, validate and maintain commercially viable manufacturing processes that are compliant with current good manufacturing practices, or

cGMP;

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;

Table of Contents

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;

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

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

a continued acceptable safety profile of the product following approval.

Many of these factors are beyond our control. Accordingly, we cannot assure you that we, or our strategic partner, will ever be able to obtain regulatory approval for, successfully commercialize, or generate revenues through the sale of tivozanib. If we, or our strategic partner, are not successful in commercializing tivozanib, or are significantly delayed in doing so, our business will be materially harmed and the price of our common stock could substantially decline.

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

We have reported data from our phase 3 clinical trial in which tivozanib demonstrated statistically significant superiority over Nexavar in the primary endpoint of progression-free survival, or PFS, in patients with RCC. In November 2012, the FDA accepted for filing the NDA seeking marketing approval of tivozanib for the treatment of advanced RCC. 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 PFS as compared to patients treated with Nexavar, but also that the improvement in PFS 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 PFS 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 PFS.

Overall survival is a key secondary endpoint in our phase 3 clinical trial. In our discussions with the FDA prior to commencement of the TIVO-1 clinical trial, the FDA indicated that we would not be required to show a statistically significant improvement in overall survival in patients treated with tivozanib in order to obtain approval by the FDA. An analysis of overall survival in TIVO-1 found that there is a trend (which is not statistically significant) toward better overall survival in patients randomized to Nexavar, most of whom received tivozanib as second line therapy due to the one-way crossover design of TIVO-1. The FDA has expressed concern regarding the overall survival trend in the TIVO-1 trial and has said that these findings will be a subject of review during the NDA process.

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. If the FDA or EMA determines that our phase 3 clinical trial results are not statistically significant, do not demonstrate a clinically meaningful benefit and an acceptable safety profile, do not reflect an acceptable risk-benefit profile for any reason, including due to the trend in overall survival we observed in TIVO-1 or for other reasons or if the FDA or EMA requires us to conduct additional 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.

Table of Contents

If we do not obtain regulatory approval for our product candidates, our business will be adversely affected.

Any 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 and a high risk of failure. Moreover, positive data from preclinical studies and clinical trials of our product candidates may not be predictive of results in ongoing or subsequent preclinical studies and clinical trials. A failure of one or more preclinical studies or clinical trials can occur at any stage of testing. There can be no assurance that we will demonstrate the required safety and efficacy to advance our research and development programs and/or obtain regulatory approvals for any of our product candidates. If any of our product candidates are not shown to be safe and effective in humans through clinical trials, we and/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.

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, post approval requirements 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 post approval 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;

fines, 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.

Table of Contents

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 including tivozanib. 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 third-party manufacturers for the manufacture of our product candidates for preclinical and clinical testing purposes and intend to continue to do so in the future, including for commercial purposes. If our third party manufacturers are unable to supply drug substance and/or drug product on a commercial basis, we may not be able to successfully produce and market tivozanib or could be delayed in doing so. 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. The manufacturer of the drug substance for tivozanib has manufactured batches of the drug substance that will serve as the validation batches that will be reviewed by the FDA in connection with its review of the NDA for tivozanib and as the supply of tivozanib for commercial launch. If there is any delay or problem with the manufacture of these batches of drug substance or if there is a delay in producing finished product from these batches, the approval of tivozanib may be delayed or the launch of tivozanib may be adversely affected.

We also expect to rely upon third parties to produce materials required for the clinical and commercial production of any other product candidates, including AV-203, our phase 1 candidate, or ficlatuzumab, our phase 2 candidate. If we are unable to arrange for third-party manufacturing sources, or to do so on commercially reasonable terms, we may not be able to complete development of such other product candidates or market them.

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

We rely on our manufacturers to purchase from third-party suppliers the materials necessary to produce our product candidates for our clinical studies and anticipated commercial activities. 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 this capital equipment or 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 this capital equipment or these raw materials by our manufacturers. Moreover, we currently do not have any agreements for the commercial production of these raw materials. 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

Table of Contents

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.

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.

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, suspended or terminated 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, including without limitation, a failure to meet study objectives or obtain the requisite level of statistical significance imposed by the FDA or other regulatory agencies;

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

Table of Contents

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

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

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

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

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

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, an element of our strategy is to discover, develop and commercialize novel antibody-based products. We are seeking to do so through our internal research programs and intend to explore strategic partnerships for such development. 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.

Table of Contents

Risks Related to Our Financial Position and Capital Requirements

We anticipate that we will continue to incur significant operating costs for the foreseeable future. It is uncertain if we will ever attain profitability in the future, which would depress the market price of our common stock.

We have incurred net losses in all prior reporting periods, other than for the year ended December 31, 2011, including a net loss of \$114.4 million during the year ended December 31, 2012. As of December 31, 2012, we had an accumulated deficit of \$320.3 million. To date, we have not commercialized any products or generated any revenues from the sale of products, and absent the realization of sufficient revenues from product sales, we may never attain profitability in the future. 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 development and commercialization activities, including planned development activities and commercialization of our lead product candidate, tivozanib, and the continued clinical development of our phase 1 product candidate, AV-203.

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

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

Since our inception, most of our resources have been dedicated to the discovery, preclinical and clinical development of our product candidates. In particular, we are currently conducting multiple clinical trials of our product candidates, each of which will require substantial funds to complete. We believe that we will continue to expend substantial resources for the foreseeable future developing tivozanib and certain other existing antibody programs. These expenditures will include costs associated with research and development, 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, cash equivalents, and marketable securities, including cash received from our public offering of common stock completed in January 2013, committed research and development funding, anticipated product revenue from tivozanib, as well as milestone payments that we expect to receive under our existing strategic partnership and licensing agreements, including milestone payments upon FDA approval of our NDA for tivozanib and upon the regulatory filing with the EMA for tivozanib, will allow us to fund our operating plan into the second quarter of 2014. However, the milestone payments we expect to receive are subject to uncertainties as we may be unable to obtain approval from the FDA or EMA of our regulatory filings within the time periods that we anticipate and we may ultimately be unable to obtain regulatory approval of, or commercialize, tivozanib for use in the treatment of advanced RCC or any other indication. In addition, our operating plan may change as a result of many factors currently unknown to us. 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 capital requirements depend on many factors, including:

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

Table of Contents

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 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.

Furthermore, in October 2012, we announced a strategic restructuring, with a corresponding reduction in the scope of certain of our research and development activities and associated resources. We may not be able to successfully implement this restructuring strategy and we may not realize the planned cost savings benefits of our restructuring, which would also impact our future capital requirements.

We anticipate seeking additional funds in the near term, through public or private equity or debt financings or other sources, such as strategic partnerships. 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, and the terms of additional capital may impose restrictions on 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. Even if we believe we have sufficient funds for our current or future operating plans, we may seek additional capital due to favorable market conditions or strategic considerations. 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.

A substantial portion of our future revenues may be dependent upon our strategic partnerships.

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 product candidates. We currently expect that a substantial portion of our future revenues may be

Edgar Filing: AVEO PHARMACEUTICALS INC - Form 10-K

dependent upon our strategic partnership with Astellas. Under this strategic partnership, Astellas has significant development and commercialization responsibilities with respect to tivozanib. If any of our 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

Table of Contents

commitments under these agreements with us, our future revenues could be negatively impacted and the development and commercialization of product candidates could be interrupted. In addition, if some or any of the development, regulatory and commercial milestones are not achieved or if certain net sales thresholds are not achieved, as set forth in the respective agreements, we will not fully realize the expected economic benefits of the agreements. Further, the achievement of certain of the milestones under our partnership agreements will depend on factors that are outside of our control and most are not expected to be achieved for several years, if at all. Any failure to successfully maintain our strategic partnership agreements could materially and adversely affect our ability to generate revenues.

For a discussion of additional risks that we face with respect to our strategic partnership agreements, see **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 below.

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

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

the status of our preclinical and clinical development programs;

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

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

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

the implementation of restructuring and cost-savings strategies;

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

compliance with regulatory requirements.

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

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

As widely reported, global credit and financial markets have been experiencing extreme disruptions over the past several years, including severely diminished liquidity and credit availability, declines in consumer confidence, declines in economic growth, increases in unemployment rates, and uncertainty about economic stability. There can be no assurance that further deterioration in credit and financial markets and confidence in economic conditions will not occur. Our general business strategy may be adversely affected by the current adverse economic conditions and volatile business environment and continued unpredictable and unstable market conditions. If the current equity and credit markets deteriorate further, or do not improve, it may make any necessary debt or equity financing more difficult, more costly, and more dilutive. Failure to secure any necessary financing in a timely manner and on favorable terms could have a material adverse effect on our growth strategy, financial performance and stock price and could require us to delay or abandon clinical development plans. In

Table of Contents

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, 2012, we had \$160.6 million of cash, cash equivalents and marketable securities consisting of money market funds, municipal bonds, asset-backed securities, asset-backed commercial paper, and corporate debt securities, including commercial paper. As of the date of this report, we are not aware of any downgrades, material losses, or other significant deterioration in the fair value of our cash equivalents or marketable securities. However, no assurance can be given that further deterioration in conditions of the global credit and financial markets would not negatively impact our current portfolio of cash equivalents or marketable securities or our ability to meet our financing objectives. Further dislocations in the credit market may adversely impact the value and/or liquidity of cash equivalents or marketable securities owned by us.

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

Risks Related to Our Business and Industry

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

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

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

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

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

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

obtain favorable reimbursement, formulary and guideline status;

obtain required regulatory approvals; and

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

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

against our current and future competitors, our business will not grow and our financial condition and operations will suffer.

Table of Contents

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

We set goals, and make public statements regarding our expectations, for the timing of certain accomplishments, such as the commencement and completion of preclinical studies, initiation and completion of clinical trials, filing and anticipated regulatory approval of our product candidates and other developments and milestones under our research and development programs. The actual timing of these events can vary significantly due to a number of factors, including, without limitation, delays or failures in our and our current and potential future collaborators' preclinical studies or clinical trials, the amount of time, effort and resources committed to our programs by us and our current and potential future collaborators and the uncertainties inherent in the regulatory approval process. As a result, there can be no assurance that our or our current and potential future collaborators' preclinical studies and clinical trials will advance or be completed in the time frames we expect or announce, that we or our current and potential future collaborators will make regulatory submissions or receive regulatory approvals as planned or that we or our current and potential future collaborators will be able to adhere to our current schedule for the achievement of key milestones under any of our programs. If we or any collaborators fail to achieve one or more of these milestones as planned, our business could be materially adversely affected and the price of our common stock could decline.

Because we have limited experience in developing and commercializing pharmaceutical products, there is a limited amount of information about us upon which you can evaluate our business and prospects.

Although certain of our individual employees may have extensive experience in developing and commercializing pharmaceutical products, as an organization we have limited experience in developing and commercializing pharmaceutical products and have not yet demonstrated an ability to successfully overcome many of the risks and uncertainties frequently encountered by companies in new and rapidly evolving fields, particularly in the biopharmaceutical area. For example, to execute our business plan, we will need to successfully:

execute product development activities;

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

build and maintain a strong intellectual property portfolio;

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

obtain reimbursement and gain market acceptance for our products;

develop and maintain successful strategic relationships and partnerships; and

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

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

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

Our success depends in part on our continued ability to attract, retain and motivate highly qualified management, clinical and scientific personnel. We are highly dependent upon our senior management, as well as others on our management team. The loss of services of any of these individuals or one or more of our other members of management could delay or prevent the successful development of our product pipeline, completion of our planned clinical trials or the commercialization of our product candidates. We do not carry key person

Table of Contents

insurance covering any members of our senior management. Our employment arrangements with all of these individuals are at will, meaning they or we can terminate their service at any time.

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 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 and commercialization, 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.

Table of Contents

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

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

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

injury to our reputation;

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 \$20 million in the aggregate. Although we maintain such insurance, any claim that may be brought against us could result in a court judgment or settlement in an amount that is not covered, in whole or in part, by our insurance or that is in excess of the limits of our insurance coverage. Our insurance policies also have various exclusions, and we may be subject to a product liability claim for which we have no coverage. We will have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient capital to pay such amounts.

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

Edgar Filing: AVEO PHARMACEUTICALS INC - Form 10-K

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.

Table of Contents

Risks Related to Commercialization of Our Product Candidates

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

Although certain of our individual employees may have extensive commercialization experience, as an organization we have limited sales, marketing, reimbursement and distribution experience. As we continue 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 commercial sale. 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, among physicians, patients, healthcare payors and, in the cancer market, acceptance by the major operators of cancer clinics.

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

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

the clinical indications for which the drug is approved;

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

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

the potential and perceived advantages over alternative treatments, including, with respect to tivozanib, advantages over Nexavar, Sutent, Inlyta, Votrient, Avastin 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.

Table of Contents

Reimbursement may be limited or unavailable in certain market segments for our product candidates, which could make it difficult for us to sell any approved 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 healthcare reform measures. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which drugs they will pay for and establish reimbursement levels. Reimbursement by a third-party payor may depend upon a number of factors, including the third-party payor's determination that use of a product is:

a covered benefit under its health plan;

safe, effective and medically necessary;

appropriate for the specific patient;

cost-effective; and

neither experimental nor investigational.

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

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

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

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

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

Table of Contents

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

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

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

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

Risks Related to Our Dependence on Third Parties

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

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

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

Table of Contents

We have entered into an exclusive option and license agreement with Biogen Idec regarding the development and commercialization of our ErbB3-targeted antibodies, including AV-203, for the potential treatment and diagnosis of cancer and other diseases outside of the United States, Canada and Mexico.

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

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 its 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 and Astellas must agree on all development and commercialization plans and strategies for North America and Europe before initiating such activities. If we cannot agree with Astellas with respect to specific development or commercialization initiatives, the program may be delayed or unsuccessful.

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

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

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

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

Our strategic partners may enter into one or more transactions with third parties, including a merger, consolidation, reorganization, sale of a substantial amount of its assets, sale of a substantial amount of its stock or change in control, which could divert the attention of a strategic partner's management and

Table of Contents

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

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

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

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

In addition to our current strategic partnerships, a part of our strategy is to enter into additional strategic partnerships in the future, including alliances with major biotechnology or pharmaceutical companies. For example, we recently announced that in connection with a strategic restructuring of our business, we plan to explore further development of ficlatuzumab and certain discovery assets through external collaborations. 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 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;

Table of Contents

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 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

Table of Contents

in our antibody product pipeline is uncertain. It is possible that the U.S. Patent and Trademark Office will not allow broad antibody claims that cover closely related antibodies as well as the specific antibody. Upon receipt of FDA approval, competitors would be free to market antibodies almost identical to ours, thereby decreasing our market share.

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

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

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

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

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

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

Table of Contents

regard to ficlatuzumab, we are aware of two separate families of United States patents, United States patent applications and foreign counterparts, with each of the two families being owned by a different third-party, that contain broad claims related to anti-HGF antibodies having certain binding properties and their use. We are also aware of a United States patent that contains claims related to a method of treating a tumor by administering an agent that blocks the ability of HGF to promote angiogenesis in the tumor. With regard to AV-203, we are aware of a third-party United States patent that contains broad claims relating to anti-ErbB3 antibodies. Based on our analyses, if any of the above third-party patents were asserted against us, we do not believe our proposed products or activities would be found to infringe any valid claim of these patents. If we were to challenge the validity of any issued United States patent in court, we would need to overcome a statutory presumption of validity that attaches to every United States patent. This means that in order to prevail, we would have to present clear and convincing evidence as to the invalidity of the patent's claims. There is no assurance that a court would find in our favor on questions of infringement or validity.

In order to avoid or settle potential claims with respect to any of the patent rights described above or any other patent rights of third parties, we may choose or be required to seek a license from a third-party and be required to pay license fees or royalties or both. These licenses may not be available on acceptable terms, or at all. Even if we or our strategic partners were able to obtain a license, the rights may be non-exclusive, 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.

Table of Contents

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

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

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

We are a party to several license agreements under which certain aspects of our business depend on patents and/or patent applications owned by other companies or institutions. In particular, we hold exclusive licenses from Kyowa Hakko Kirin for tivozanib. 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. 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

Table of Contents

required to sign a confidentiality agreement upon joining our company. We take steps to protect our proprietary information, and we seek to carefully draft our confidentiality agreements to protect our proprietary interests. Nevertheless, there can be no guarantee that an employee or an outside party will not make an unauthorized disclosure of our proprietary confidential information. This might happen intentionally or inadvertently. It is possible that a competitor will make use of such information, and that our competitive position will be compromised, in spite of any legal action we might take against persons making such unauthorized disclosures.

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

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

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

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

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

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

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

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

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

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.

Table of Contents

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

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

Risks Related to Ownership of Our Common Stock

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

The market price of our common stock has been, and is likely to continue to be, highly volatile and 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 Pfizer's Sutent and Inlyta, Onyx's Nexavar, GSK's Votrient, Roche's Avastin and the timing of these introductions or announcements;

actual or anticipated results from and any delays in our clinical trials;

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 of material developments in our business, financial condition and/or operations;

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;

Edgar Filing: AVEO PHARMACEUTICALS INC - Form 10-K

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.

Table of Contents

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, 2012, our executive officers, directors, entities affiliated with such executive officers and directors, and certain other significant stockholders, owned approximately 46% of our common stock, including shares subject to outstanding options and warrants that are exercisable within 60 days after December 31, 2012. 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 market price 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 market 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.

Table of Contents

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

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

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

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

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

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

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

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

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

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

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

Table of Contents

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

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

ITEM 1B. Unresolved Staff Comments

None

ITEM 2. Properties

We sublease our principal facilities, which consist of approximately 126,065 square feet of office, research and laboratory space located at 650 East Kendall Street, Cambridge, Massachusetts, which sublease expires in December 2024; approximately 55,200 square feet of research and office space located at 75 Sidney Street, Cambridge, Massachusetts, which sublease expires in February 2014; and approximately 25,714 square feet of office space located at 12 Emily Street, Cambridge, Massachusetts, under subleases expiring in February 2014 and May 2015. We believe that our existing facilities are sufficient for our current needs for the foreseeable future.

ITEM 3. Legal Proceedings

None.

ITEM 4. Mine Safety Disclosures

Not applicable.

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

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

	High	Low
2011		
First Quarter	\$ 16.00	\$ 13.05
Second Quarter	\$ 21.00	\$ 13.00
Third Quarter		