AVEO PHARMACEUTICALS INC
Form 10-K
March 15, 2016

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

(Mark One)

x ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the fiscal year ended: December 31, 2015

Or

o 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)

Delaware	04-3581650
(State or Other Jurisdiction of Incorporation or Organization)	(I.R.S. Employer Identification No.)

One Broadway, 14th Floor

Cambridge, Massachusetts 02142

(Address of Principal Executive Offices) (zip code)

Registrant's telephone number, including area code: (617) 588-1960

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

Title of each class	Name of each exchange on which registered
Common Stock, $.001 par value	NASDAQ Global Select 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 o No x

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 o No x

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 x No o

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 x No o

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. o

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	o	Accelerated filer	x
Non-accelerated filer	o (Do not check if a smaller reporting company)	Smaller reporting company	o

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

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 Select Market at the close of business on June 30, 2015, was $93,586,098.

The number of shares outstanding of the registrant's Common Stock as of March 9, 2016: 58,181,715.

Documents incorporated by reference:

Portions of our definitive proxy statement for our 2016 annual meeting of stockholders are incorporated by reference into Part III of this Annual Report on Form 10-K.

AVEO PHARMACEUTICALS, INC.

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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 and our collaborators’ future discovery, development and commercialization efforts, plans, timelines and strategies, our collaborations, our future operating results, future prospects 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,” “target,” “will” and other words and terms of similar meaning. Yo 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, preclinical trials and clinical development activities, our dependence on our existing and future strategic partners, our ability to obtain any necessary financing to conduct our planned 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 and other risk factors. Please refer to the section entitled “Risk Factors” in Part I—Item 1A of this report for a description of these risks and uncertainties. Unless required by law, we do not undertake any obligation to publicly update any forward-looking statements.

PART I

ITEM 1. Business

Overview

We are a biopharmaceutical company dedicated to advancing a broad portfolio of targeted therapeutics for oncology and other areas of unmet medical need. Our proprietary platform has delivered unique insights into cancer and related diseases. Our strategy is to leverage these biomarker insights and partner resources to advance the development of our clinical pipeline. We are focused on developing our lead candidate tivozanib in North America as a treatment for renal cell carcinoma and other cancers. We have entered into partnerships to fund the further development of three of our four clinical stage assets, including AV-380, ficlatuzumab, and tivozanib in non-oncologic indications worldwide and oncology indications outside North America. We are also seeking a partnership for AV-203, our fourth development program. These programs and partnerships are described as follows:

- Tivozanib: Tivozanib is a potent, selective, long half-life vascular endothelial growth factor ("VEGF") tyrosine kinase inhibitor ("TKI") of VEGF receptors 1, 2 and 3. In 2006, we acquired the exclusive rights to develop and commercialize tivozanib in all countries outside of Asia under a license from Kyowa Hakko Kirin Co., Ltd. (formerly Kirin Brewery Co. Ltd.), or KHK. We have programs to evaluate tivozanib in several tumor types, including renal cell, colorectal and breast cancer. We are evaluating all options for funding the clinical and regulatory advancement of tivozanib in the programs discussed below, including through partnership with one or more third parties.

RCC First Line Phase 3 Trial (TIVO-1): We conducted a global phase 3 clinical trial comparing the efficacy and safety of tivozanib with Nexavar® (sorafenib), an approved therapy, for first-line treatment of renal cell carcinoma, or RCC. The trial met its primary endpoint for progression-free survival, or PFS, but showed a non-statistically significant trend favoring the sorafenib arm in overall survival, or OS. In June 2013, the U.S. Food and Drug Administration, or FDA, issued a complete response letter informing us that it would not approve tivozanib for the treatment of first line advanced RCC based on the study data from this trial, and recommended that we perform an additional study adequately sized to assure the FDA that there is no adverse effect on OS.

In January 2015, we announced our receipt of confirmation from the European Medicines Agency, or EMA, that tivozanib is eligible for submission of an application for a European Union Marketing Authorization under the Agency's centralized procedure for the treatment of RCC. Confirmation of eligibility for submission is not predictive of the EMA's approval of a Marketing Authorization Application, or MAA. Tivozanib has previously been granted orphan drug designation in Europe for the treatment of RCC. Our partner, EUSA Pharma (UK) Limited, or EUSA, submitted a MAA for tivozanib for the treatment of RCC to the EMA in February 2016 based on our existing dataset, which includes the results from the TIVO-1 study of tivozanib in the first-line treatment of RCC.

TIVO-1 Extension Study (One-way Crossover from Sorafenib to Tivozanib): We have completed a TIVO-1 extension study, known as Study 902, in which patients with advanced RCC received tivozanib as second-line treatment subsequent to disease progression on the sorafenib arm in the TIVO-1 first-line RCC trial. We presented the final results at the 2015 American Society of Clinical Oncology (ASCO) Annual Meeting on June 1, 2015. The final results show a median PFS of 11.0 months and median OS of 21.6 months, demonstrating the clinically meaningful efficacy of tivozanib in a VEGF treatment refractory population. We believe that the long OS derived from tivozanib following sorafenib in Study 902 contributed to the discordance in the results between the PFS benefit which significantly favored tivozanib and the OS which trended in favor of sorafenib in the TIVO-1 trial.

RCC Third Line Phase 3 Trial (TIVO-3): We are planning to conduct a phase 3 trial of tivozanib in the third-line treatment of patients with refractory RCC. The study will use PFS as the primary endpoint and OS as a secondary endpoint to support a request for regulatory approval of tivozanib as a third-line treatment and to address the overall survival concerns from TIVO-1 as a first-line treatment presented in the June 2013 complete response letter from the FDA. Our study design, which we have shared with the FDA, contemplates a randomized, controlled, multi-center, open-label phase 3 study of approximately 322 subjects randomized 1:1 to receive either tivozanib or sorafenib. Subjects enrolled in the study may include those who have received prior immunotherapy, including immune checkpoint (PD-1) inhibitors, reflecting a potentially evolving treatment landscape. The primary objective of the study would be to show improved PFS. Secondary endpoints would include OS and objective response rate, or ORR, as well as safety and pharmacokinetic endpoints.

RCC PD-1 Combination Trial: We are designing a phase 1 study of tivozanib combined with a PD-1 inhibitor for the treatment of patients with RCC. We are evaluating all options for funding, including partnerships, for the clinical and regulatory advancement of tivozanib in combination with PD-1 inhibitors in RCC.

CRC Phase 2 Results: In March 2015, we announced results from a predefined biomarker analysis of our BATON-CRC study, a randomized phase 2 clinical trial of modified FOLFOX6, a commonly used chemotherapy, combined with tivozanib or Avastin® (bevacizumab), which both target angiogenesis signaling pathways, in first line treatment of metastatic CRC. In this study, among prospectively defined biomarkers, patients with low (below the median,

representing 50% of the population) serum neuropilin-1, or NRP-1, a cell surface protein that modulates blood vessel development, showed an improved PFS versus patients with high serum NRP-1 in both treatment arms, supporting the value of serum NRP-1 as a potential prognostic marker for angiogenesis inhibitors. Further, in the subgroup with samples available at the interim analysis, patients identified using a research-use assay to have low serum NRP-1 demonstrated longer PFS when treated with tivozanib compared to bevacizumab, which suggests that first line colorectal cancer patients with low NRP-1 levels may benefit from treatment with tivozanib over bevacizumab, a standard of care in this disease. In April 2015, we presented the results from the phase 2 BATON-CRC study and the Company's ongoing assay development efforts to the FDA in connection with our evaluation of a proposed pivotal phase 3 trial of tivozanib in CRC. In response to questions we posed to the FDA regarding this proposed trial, the FDA suggested that we continue work on the development of our biomarker assay to address variability between assays presented. As such, we hope to identify a commercially viable assay, which may enable a prospectively defined, randomized Phase 2 or Phase 3 study.

Tivozanib Partnerships:

EUSA License Agreement: In December 2015, we entered into a license agreement with EUSA under which we granted EUSA the right to develop and commercialize tivozanib for all diseases and conditions in humans, excluding non-oncologic diseases or conditions of the eye, in Europe (excluding Russia, Ukraine and the Commonwealth of Independent States), Latin America (excluding Mexico), Africa, Australasia and New Zealand. EUSA submitted a MAA for tivozanib for the treatment of RCC with the EMA in February 2016.

Pharmstandard License Agreement: In August 2015, we entered into a license agreement under which we granted to a subsidiary of Pharmstandard OJSC, or Pharmstandard, the exclusive right to develop, manufacture and commercialize tivozanib in the territories of Russia, Ukraine and the Commonwealth of Independent States, or CIS, for all conditions excluding non-oncologic ocular conditions. Under this agreement, Pharmstandard is responsible for all activities and costs associated with the further development, regulatory filings, health services and commercialization of tivozanib in the specified territories. In December 2015, Pharmstandard submitted an application for marketing authorization for tivozanib based on TIVO-1 results in Russia that was accepted by the Ministry of Health in February 2016.

Ophthotech Option for Ocular Conditions (Non-Oncologic): In November 2014, we entered into a research and exclusive option agreement with Ophthotech Corporation, or Ophthotech, under which we granted Ophthotech an option to develop and commercialize tivozanib outside of Asia for the potential diagnosis, prevention and treatment of non-oncologic diseases or conditions of the eye in humans.

- Ficlatuzumab: Ficlatuzumab is a potent Hepatocyte Growth Factor, or HGF, inhibitory antibody. HGF is the sole known ligand of the c-Met receptor which is believed to trigger many activities that are involved in cancer development and metastasis. We have completed two phase 1 clinical studies of ficlatuzumab administered as a single agent and in combination with erlotinib, a TKI, of the epidermal growth factor receptor, or EGFR, and a phase 2 clinical study evaluating ficlatuzumab in combination with gefitinib, an EGFR TKI, in first line non-small cell lung cancer, or NSCLC. The phase 2 trial failed to demonstrate a statistically significant benefit in the intent-to-treat population. However, an exploratory analysis using a serum-based proteomic diagnostic test, known as VeriStrat®, identified a sub-population of patients who experienced a progression free survival and overall survival benefit from the addition of ficlatuzumab to gefitinib. VeriStrat is commercially available to help physicians guide treatment decisions for patients with second line advanced NSCLC. Data from the exploratory analyses with VeriStrat prompted the development of a separate investigational companion diagnostic test called BDX004. Based upon the exploratory analyses, BDX004 may be indicative of a predictive biomarker for the combination of ficlatuzumab and EGFR TKI over EGFR TKI alone in the first line EGFR mutation patients who have been previously identified to not respond well to the current standard of care.

In April 2014, we entered into a worldwide agreement with Biodesix, Inc., or Biodesix, to develop and commercialize ficlatuzumab with BDX004, a serum based diagnostic test which has been derived from the VeriStrat test, employing the same methodology and data processing algorithms as VeriStrat, for use in a confirmatory clinical trial. Pursuant to

the Biodesix agreement, in December 2014 we initiated a phase 2 confirmatory study of ficlatuzumab, which we refer to as the FOCAL study, in combination with erlotinib in first line advanced NSCLC patients who have an EGFR mutation and who are identified by the BDX004 test as being most likely to benefit from the addition of ficlatuzumab to the EGFR TKI. We began enrolling patients during the second half of 2015. Biodesix will fund up to $15 million of the cost of this study, as well as all of the costs associated with development and registration of BDX004, and any additional development, regulatory and commercial costs for ficlatuzumab will be shared equally. Under the Biodesix agreement, subject to regulatory approval, AVEO would lead worldwide commercialization of ficlatuzumab.

- AV-203: AV-203 is a potent anti-ErbB3 (also known as HER3) specific monoclonal antibody with high ErbB3 affinity. We have observed potent anti-tumor activity in mouse models. AV-203 selectively inhibits the activity of the ErbB3 receptor, and our preclinical studies suggest that neuregulin-1, or NRG1 (also known as heregulin), levels predict AV-203 anti-tumor activity in preclinical models. We have completed a phase 1 dose escalation study of AV-203, which

established a recommended phase 2 dose of AV-203 at 20mg/kg intravenously every 2 weeks, demonstrated good tolerability and promising early signs of activity, and reached the maximum planned dose of AV-203 monotherapy. No anti-drug antibodies were detected, and pharmacokinetic results indicated a dose-proportional increase in levels of AV-203.

The expansion cohort of this study among patients with a specific biomarker has been discontinued. We are seeking to pursue further clinical development of AV-203 with a strategic partner.

- AV-380: AV-380 is a potent humanized IgG1 inhibitory monoclonal antibody targeting growth differentiating factor-15, or GDF15, a divergent member of the TGF-ß family, for the potential treatment or prevention of cachexia. Cachexia is defined as a multi-factorial syndrome of involuntary weight loss characterized by an ongoing loss of skeletal muscle mass (with or without loss of fat mass) that cannot be fully reversed by conventional nutritional support and leads to progressive functional impairment. Cachexia is associated with various cancers as well as diseases outside of cancer including chronic kidney disease, congestive heart failure, and chronic obstructive pulmonary disease, or COPD. We believe that AV-380 represents a unique approach to treating cachexia because it addresses key underlying mechanisms of the syndrome and focuses on a significant area of patient need. It is estimated that approximately 30% of all cancer patients die due to cachexia and over half of cancer patients who die do so with cachexia present. (J Cachexia Sarcopenia Muscle 2010). In the United States alone, the estimated prevalence of cancer cachexia is over 400,000 patients, and the prevalence of cachexia due to cancer, COPD, congestive heart failure, frailty and end stage renal disease combined is estimated to total more than 5 million patients (Am J Clin Nutr 2006).

In September 2014, we presented the results from four preclinical studies of AV-380 in various in vivo cachexia models and in vitro assays at the 2nd Cancer Cachexia Conference held in Montreal Canada. Our research was also selected for presentation in an oral session at the conference. In April 2015, we also presented the results from a preclinical study of AV-380 in a cachectic human tumor xenograft model at the Annual Meeting of the American Association of Cancer Research. We have established preclinical proof of concept for GDF15 as a key driver of cachexia by demonstrating, in animal models, that the administration of GDF15 induces cachexia, and that inhibition of GDF15 reverses cachexia and provides a potential indication of an overall survival benefit.

In August 2015, we entered into a license agreement under which we granted Novartis International Pharmaceutical Ltd., or Novartis, the exclusive right to develop and commercialize AV-380 and related AVEO antibodies. Under this agreement, Novartis is responsible for all activities and costs associated with the further development, regulatory filing and commercialization of AV-380 worldwide.

In connection with the AV-380 program, we have in-licensed certain patents and patent applications from St. Vincent's Hospital in Sydney, Australia. We have demonstrated preclinical proof-of-concept for AV-380 in multiple cancer cachexia models and have completed cell line development.

Product Pipeline

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 utilized these novel models to identify and validate target genes that drive tumor growth, to identify drugs that can block the function of these targets, and to identify patients who are most likely to respond favorably to treatment with such drugs. Our cancer models, together with the various techniques we developed to use these models to aid in the discovery and development of new cancer drugs, were used to develop our product pipeline and are collectively referred to as our Human Response Platform.

Tivozanib: 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. The demonstrated clinical results for 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 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.

In 2012, we 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 of RCC. This phase 3 trial met its primary endpoint PFS but showed a non-statistically significant trend favoring the sorafenib arm in overall survival. Based on a review of our application for approval of the use of tivozanib for the treatment of first line advanced RCC, in June 2013, the U.S. Food and Drug Administration issued a complete response letter informing us that they would not approve tivozanib at this time based on these study data.

In August 2014, our collaboration and license agreement with Astellas terminated, at which time all rights for the development and commercialization of tivozanib reverted to AVEO. We had entered into the collaboration and license agreement with Astellas in February 2011, pursuant to which we and Astellas shared responsibility for tivozanib, including expenses for continued development and any future commercialization of tivozanib, in North America and Europe. Upon reversion back to AVEO of rights previously granted to Astellas, we reevaluated our tivozanib regulatory and development strategy, as well as partnering opportunities.

In January 2015, we announced our receipt of confirmation from the European Medicine Agency that tivozanib is eligible for submission of an application for a European Union Marketing Authorization under the Agency's centralized procedure for the treatment of RCC. Confirmation of eligibility for submission is not predictive of the European Medicines Agency's approval of a Marketing Authorization Application. Tivozanib has previously been granted orphan drug designation in Europe for the treatment of RCC. In December 2015, we entered into a license agreement with EUSA, under which we granted EUSA the right to develop and commercialize tivozanib for all diseases and conditions in humans, excluding non-oncologic diseases or conditions of the eye, in Europe (excluding Russia, Ukraine and the Commonwealth of Independent States), Latin America (excluding Mexico), Africa, Australasia and New Zealand. EUSA submitted a MAA for tivozanib for the treatment of RCC with the EMA in February 2016.

In August 2015, we entered into a license agreement under which we granted Pharmstandard the exclusive right to develop, manufacture and commercialize tivozanib in the territories of Russia, Ukraine and the Commonwealth of Independent States, or CIS, for all conditions excluding non-oncologic ocular conditions. Under this agreement, Pharmstandard is responsible for all activities and costs associated with the further development, regulatory filings, health services and commercialization of tivozanib in the specified territories. In December 2015, Pharmstandard submitted an application for marketing authorization for tivozanib based on TIVO-1 results in Russia that was accepted by the Ministry of Health in February 2016.

We also have evaluated tivozanib in additional clinical programs including our BATON (Biomarker Assessment of Tivozanib in ONcology) program, assessing biomarkers in solid tumors that may be predictive of clinical response to tivozanib in patients with metastatic colorectal cancer, and other clinical trials assessing locally recurrent or metastatic triple negative breast cancer.

The BATON-BC study in patients with breast cancer, led by AVEO, initiated patient enrollment in December 2012 in a randomized, double-blind, multi-center 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 more than one systemic therapy for advanced or metastatic breast cancer. On January 30, 2014, we announced that we and Astellas jointly decided to discontinue the BATON-BC clinical trial, due to insufficient enrollment.

The BATON-CRC study, led by Astellas, which enrolled a total of 265 patients randomized 2 to 1, was an open-label, phase 2 study with a primary endpoint evaluating the superiority of tivozanib in combination with modified FOLFOX6, a standard chemotherapy, compared to bevacizumab in combination with modified FOLFOX6 as first-line treatment in patients with advanced metastatic colorectal cancer. On December 13, 2013, we announced that the study was unlikely to meet the primary endpoint in the intent-to-treat population and on February 14, 2014, we announced that we and Astellas agreed to discontinue this study. The data from the preplanned interim analysis of this study was presented at the European Society for Medical Oncology, or ESMO, on September 29, 2014. The final data through February 28, 2014, including predefined biomarker data from the study, were presented at the American Association for Cancer Research, or AACR Tumor Angiogenesis and Vascular Normalization Conference in March 2015.

An objective of the BATON-CRC study was the assessment of prospectively defined biomarkers that may be predictive of response in selected patient subpopulations. Among these, patients with low (below the median, representing 50% of the patient population) neuropilin-1, or NRP-1, showed an improved PFS versus patients with

high NRP-1 in both treatment arms, supporting the value of NRP-1 as a potential prognostic marker for angiogenesis inhibitors. Further, patients with low serum NRP-1 demonstrated longer PFS when treated with tivozanib (17.9 months, n=52), compared to bevacizumab (11.2 months, n=28) (HR=0.380, p=0.0075). Patients with high NRP-1 had inferior PFS outcomes regardless of treatment assignment, with progression free survival of 7.3 months and 7.5 months for the tivozanib and bevacizumab arms, respectively. As soluble NRP-1 is known to bind to VEGF and is believed to inhibit VEGF binding to VEGF Receptor 2, we hypothesize that VEGF inhibitors may only be effective in patients with low serum NRP-1 levels, and that in patients with low serum NRP-1, a more complete blockade of VEGF pathway inhibition may be beneficial. Of note, exploratory biomarker analyses from two prior studies with tivozanib in RCC presented at the 17th Annual Symposium on Anti-Angiogenesis and Immune Therapies in February 2015 indicated that NRP-1 is a possible biomarker of tivozanib efficacy in patients with RCC. We hope to identify a commercially viable assay, which may enable a prospectively defined, randomized Phase 2 or Phase 3 study.

We are planning to conduct a phase 3 trial of tivozanib in the third-line treatment of patients with refractory RCC. The study will use PFS as the primary endpoint and OS as a secondary endpoint to support a request for regulatory approval of tivozanib as a third-line treatment and to address the overall survival concerns from TIVO-1 as a first line treatment presented in the June 2013 complete response letter from the FDA. Our study design, which we have shared with the FDA, contemplates a randomized, controlled, multi-center, open-

label phase 3 study of approximately 322 subjects randomized 1:1 to receive either tivozanib or sorafenib. Subjects enrolled in the study may include those who have received prior immunotherapy, including immune checkpoint (PD-1) inhibitors, reflecting a potentially evolving treatment landscape. The primary objective of the study would be to show improved PFS. Secondary endpoints would include OS and objective response rate, or ORR, as well as safety and pharmacokinetic endpoints. We are evaluating all options for funding, including partnerships, for the clinical and regulatory advancement of tivozanib in RCC as well as colorectal cancer, or CRC.

In November 2014, we entered into a Research and Exclusive Option Agreement with Ophthotech Corporation, pursuant to which we provided Ophthotech an exclusive option to enter into a definitive license agreement under which we would grant Ophthotech the right to develop and commercialize tivozanib outside of Asia for the potential diagnosis, prevention and treatment of non-oncologic diseases or conditions of the eye in humans. Pursuant to this option agreement, we granted to Ophthotech an exclusive, royalty free license or sublicense, as applicable, under our intellectual property rights solely to perform the research and development activities related to the use of tivozanib as set forth in the development plan during the option period described below. These activities include formulation work for ocular administration, preclinical research and the conduct of a phase 1/2a, proof of concept clinical trial of a product containing tivozanib in patients with wet age-related macular degeneration. Ophthotech may exercise its option at any time until the latest to occur of: (i) twelve (12) months after the achievement of a certain clinical efficacy milestones, (ii) ninety (90) days after the date Ophthotech is required to make certain clinical efficacy milestone payments, and (iii) thirty (30) days after AVEO and Ophthotech agree as to the definitive form of license agreement.

Ficlatuzumab: Hepatocyte Growth Factor (HGF) Inhibitory Antibody

Through the use of our Human Response Platform, our scientists 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 selectively target the HGF/c-Met pathway.

In September 2014, at the 2014 Congress of the European Society for Medical Oncology, or ESMO, we presented the results of our exploratory analysis using a serum-based molecular diagnostic test to identify a patient sub-population that experienced a progression free survival and overall survival benefit on the combination therapy in the ficlatuzumab phase 2 trial. The results suggest that VeriStrat, a serum protein test that is commercially available to help physicians guide treatment decisions for patients with NSCLC, may be selective of positive clinical response for ficlatuzumab plus gefitinib over gefitinib alone. For this retrospective exploratory analysis, 180 pre-treatment serum samples analyzed with VeriStrat and were assigned a label of either “VeriStrat Good” (VSG) or “VeriStrat Poor” (VSP) (VSG=145, VSP=35). While the study failed to demonstrate improved OS or PFS over gefitinib alone in the intent-to-treat population, the addition of ficlatuzumab to gefitinib provided significant clinical benefit to the VSP subgroup.

Based on this data, in April 2014, we entered into a worldwide agreement with Biodesix, Inc. to develop and commercialize HGF inhibitory antibody ficlatuzumab, with Biodesix’s proprietary companion diagnostic test, BDX004, a serum protein test derived from Veristrat. Pursuant to this agreement, we are conducting the FOCAL study, a phase 2, global, randomized, double-blind, placebo controlled clinical study, evaluating ficlatuzumab, our HGF inhibitory antibody, in combination with erlotinib (Tarceva®), an epidermal growth factor receptor tyrosine kinase inhibitor (EGFR TKI) in first line EGFR-mutated NSCLC patients. BDX004 will be used to select patients for entry into the trial.

AV-203: Anti-ErbB3 Antibody

Through the use of our Human Response Platform, we identified the importance of the ErbB3 receptor in tumor growth. ErbB3 belongs to a family of proteins that also includes epidermal growth factor receptor, or EGFR, and HER2, all of which have been implicated in promoting the growth of significant numbers of tumor types.

ErbB3 is believed to be an important receptor regulating cancer cell growth and survival, and high ErbB3 levels have been shown to correlate with poor prognoses in several tumor types. It has also been implicated in resistance to certain drugs which target EGFR in lung cancer and with resistance to radiotherapy. AV-203 inhibits the activity of the ErbB3 receptor and our preclinical studies suggest that neuregulin-1, or NRG1, levels predict AV-203 anti-tumor activity and we have filed a U.S. patent application relating to a method of predicting tumor response to ErbB3 inhibitors based on NRG1 levels.

In March 2014, we amended our option and license agreement with Biogen Idec GMbH Inc., or Biogen, regarding the development and commercialization of our ErbB3-targeted antibodies for the potential treatment and diagnosis of cancer and other diseases in humans. Pursuant to the amendment, Biogen agreed to terminate its rights and obligations under our agreement, including Biogen's option to (i) obtain a co-exclusive (with AVEO) license to develop and manufacture ErbB3 targeted antibodies and

(ii) obtain exclusive commercialization rights to ErbB3 products in countries in the world other than North America. Pursuant to the amendment, we are obligated to pay Biogen a specified percentage of milestone payments received by us from future partnerships after March 28, 2016 and single digit royalty payments on net sales related to the sale of ErbB3 products, up to cumulative maximum amount of $50 million. As a result, we retain worldwide rights to AV-203, a clinical stage ErbB3-targeted antibody and are obligated to in good faith use reasonable efforts to seek a collaboration partner for the purpose of funding further development and commercialization of ErbB3 targeted antibodies. We are currently exploring partnership opportunities to advance the clinical development of AV-203.

AV-380 Program in Cachexia

In 2012, we initiated a program focusing on cachexia, which we refer to as our AV-380 program. AV-380 is a potent humanized IgG1 inhibitory monoclonal antibody targeting growth differentiating factor-15, or GDF15, a divergent member of the TGF-ß family, for the potential treatment or prevention of cachexia. Cachexia is a serious and common complication of advanced cancer and a number of chronic diseases. It is defined as a multi-factorial syndrome of involuntary weight loss characterized by an ongoing loss of skeletal muscle mass (with or without loss of fat mass) that cannot be fully reversed by conventional nutritional support and leads to progressive functional impairment. The pathophysiology is characterized by a negative protein and energy balance driven by a variable combination of reduced food intake and abnormal metabolism. Other symptoms or conditions associated with cachexia include anemia, breathing difficulties, edema, insulin resistance, muscle weakness/asthenia, and fatigue.

In September 2014, we presented the results from four preclinical studies of AV-380 in various in vivo cachexia models and in vitro assays at the 2nd Cancer Cachexia Conference held in Montreal Canada. Our research was also selected for presentation in an oral session at the conference. We believe our research set forth our proof of concept for GDF15, by demonstrating that GDF15 is elevated in cachectic animal models and patients versus non-cachectic, administration of GDF15 induces cachexia and inhibition of GDF15 reverses cachexia.

In connection with the AV-380 program, we have in-licensed certain patents and patent applications from St. Vincent’s Hospital in Sydney, Australia. We have completed cell line development and manufacturing of the first cGMP batch of AV-380.

We believe that cachexia represents a significant area of patient need, particularly in cancer patients. Weight loss during cancer treatment is associated with more chemotherapy-related side effects, fewer completed cycles of chemotherapy, a reduction in response to therapy and decreased survival rates (J Gastroenterol 2013; Eur J Cancer 1998; Br J Cancer 2004). In a cohort of over 3,000 patients in the U.S. studied by the Eastern Cooperative Oncology Group, or ECOG, the prevalence of weight loss even before starting chemotherapy was observed to be substantial across several cancers: over 80% in pancreatic and gastric cancers and over 50% in prostate, colorectal and lung cancers (Am Med Journal 1980). It is estimated that more than 30% of all cancer patients die due to cachexia and over half of cancer patients who die do so with cachexia present. (J Cachexia Sarcopenia Muscle 2010). In the United States alone, the estimated prevalence of cancer cachexia is over 400,000 patients, and the prevalence of cachexia due to cancer, COPD, congestive heart failure, frailty and end stage renal disease combined is estimated to total more than 5 million patients (Am J Clin Nutr 2006).

In August 2015, we entered into a license agreement under which we granted Novartis International Pharmaceutical Ltd. the exclusive right to develop and commercialize AV-380 and related AVEO antibodies. Under this agreement, Novartis is responsible for all activities and costs associated with the further development, regulatory filing and commercialization of AV-380 worldwide. In connection with the license, Novartis has also acquired our inventory of AV-380 clinical quality drug substance.

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, but not limited to, Roche Laboratories, Inc., or Roche, Pfizer Inc., or Pfizer, Bayer HealthCare AG, or Bayer, Amgen, Inc., Eli Lilly and Company, or Lilly, GlaxoSmithKline plc, or GSK, GTx, Inc., Helsinn and XBiotech, Novartis, Bristol-Myers Squibb, Merck, Merrimack Pharmaceuticals, Inc., Arqule, Inc., Exelixis, Inc., Easai Co., Ltd. and AstraZeneca are pursuing the development or are currently marketing pharmaceuticals that target VEGF, HGF, ErbB3, and cachexia, 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 the lives of people with cancer 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.

Tivozanib Competition

There are currently ten FDA-approved drugs in oncology which target the VEGF receptors. Seven of the FDA-approved VEGF pathway inhibitors are oral small molecule receptor tyrosine kinase inhibitors, or TKIs. Nexavar (sorafenib) and Stivarga (regorafenib) are marketed by Bayer and Onyx, a subsidiary of Amgen, Sutent (sunitinib) and Inlyta (axitinib) are marketed by Pfizer, and Votrient (pazopanib) is marketed by Novartis. Most of these approved VEGFR TKIs are not specific to the VEGF 1, 2 and 3 receptors. Nexavar is approved for advanced RCC and unresectable hepatocellular cancer. Stivarga is approved for refractory metastatic colorectal cancer, or mCRC, and refractory gastrointestinal stromal tumors, or GIST. Sutent is approved for advanced RCC, GIST, 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. Caprelsa (vandetanib), marketed by AstraZeneca, and Cometriq (cabozantinib), marketed by Exelixis, are approved for medullary thyroid carcinoma.

Avastin (bevacizumab), marketed by Roche/Genentech, is an infused monoclonal antibody approved in combination with other anti-cancer agents for the treatment of mCRC, non-squamous non-small cell lung cancer, and metastatic RCC. It is also approved as a monotherapy for the treatment of glioblastoma in patients with progressive disease following prior therapy. Zaltrap (zif-aflibercept), marketed by Sanofi and Regeneron, is a VEGF-trap molecule that binds to multiple circulating VEGF factors, and is approved in combination with standard chemotherapy agents for treatment of second line metastatic CRC. Cyramza (ramucirumab), marketed by Lilly, is an antibody that binds to the VEGFR-2 receptor that is approved for the treatment of advanced gastric or gastro-esophageal junction adenocarcinoma and in combination with docetaxel for the treatment of NSCLC.

Many of the approved VEGF pathway inhibitor agents are in ongoing development in additional cancer indications including RCC. Additionally, we are aware of a number of companies that have ongoing programs to develop both small molecules and biologics that target the VEGF pathway.

In addition, the emergence of PD1/PDL1 inhibitor therapies present additional competition for tivozanib in advanced RCC. For example, Opdivo (nivolumab), marketed by Bristol-Myers Squibb, is an approved anti-PD1 for second line RCC. Additional clinical trials as mono and combination therapies of PD1/PDL1 with VEGF TKIs are in the pipeline targeting RCC.

Ficlatuzumab Competition

We believe the products that are considered competitive with ficlatuzumab include those agents targeting the HGF/c-Met pathway. The agents exclusively targeting this pathway consist of the only other HGF-targeted antibody, Amgen’s AMG-102 (rilotumumab), initiated in a phase 3 clinical trial (which has been discontinued), as well as Lilly’s c-Met receptor antibody LY-2875358, currently in multiple phase 2 trials. In addition, Roche has conducted multiple phase 3 trials for a c-Met receptor antibody onartuzumab (MetMAb/ 5D5 Fab). Roche announced that an independent data monitoring committee recommended that its phase 3 trial of onartuzumab in second and third line NSCLC be stopped due to lack of efficacy.

Other marketed or late clinical-stage drugs which target the HGF/c-Met pathway, though not exclusively, include Pfizer’s PF-2341066 (Xalkori, crizotinib), Exelixis Inc.’s XL-184 (Cometriq, cabozantinib), ArQule, Inc.’s/ Daiichi Sankyo, Inc.’s ARQ-197 (tivantanib), Mirati Therapeutics’ (formerly MethylGene) MGCD-265, Eisai Co. Ltd.’s E-7050 (golvatinib), Exelixis Inc.’s and GSK’s XL-880 (foretinib), Incyte Corp.’s and Novartis’s INCB-028060 and

Sanofi-Aventis's SAR-125844, EMD Serono's MSC2156119J, Amgen Astellas BioPharma's AMG 337, Lilly's merestinib (LY2801653), Les Laboratoires Servier SAS's S-49076, AstraZeneca and Hutchison MediPharma's savolitinib, Merck KGaA's tepotinib, AbbVie's ABT-700, Deciphera Pharma's altiratinib, Amgen's AMG-208, Betta Pharmaceutical's BPI-9016 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 are monoclonal antibodies that specifically target the ErbB3 receptor, including Merrimack Pharmaceuticals, Inc.'s MM-121, which is currently in phase 2 clinical development, and Daiichi Sankyo, Inc.'s and Amgen, Inc.'s patritumab (AMG-888), which recently entered phase 3 clinical development for non-small cell lung cancer. Other clinical-stage ErbB3-specific competitors include Roche's RG-7116, Novartis's elgemtumab, Regeneron's REGN1400, GSK's GSK-2849330, Kolltan's KTN-3379, Merus's MCLA-128, AstraZeneca's sapitinib, Koltan Pharma's KTN-3379 and Sihuan Pharma's pirotinib and sirotinib, . Clinical stage competitor's targeting ErbB3 in addition to other targets include Roche's MEHD7945A, and Merrimack Pharmaceuticals, Inc.'s MM-111 and MM-141.

AV-380 Program in Cachexia Competition

Only a limited number of agents have been approved for the treatment or prevention of cachexia caused by any disease. In the United States, Megace is the only approved agent for the treatment of cachexia (in patients with the diagnosis of AIDS). Megace and medroxyprogesterone are approved for cancer cachexia in Europe. Three agents have recently completed or are currently being studied in phase 3 trials. One agent, GTx, Inc.'s selective androgen receptor modulator, or SARM, called enobosarm (GT-024) recently completed two phase 3 trials for the prevention and treatment of muscle wasting in newly diagnosed locally advanced or metastatic non-small cell lung cancer patients. The trials suggested limited benefits in a larger patient population and the company has discontinued its commercialization efforts. Another agent that has recently completed phase 3 trials is Helsinn's anamorelin, for which Helsinn recently filed for EMA approval for treating locally advanced non-small cell lung cancer patients who have cachexia,. A third agent, XBiotech's xilonix (MABp1), is in a phase 3 trial for metastatic colorectal cancer patients who are cachectic and refractory to standard therapies and has shown encouraging overall survival results.

A number of agents with different mechanisms of action have completed or are currently being studied in phase 2 trials in cachexia or muscle wasting. Agents targeting the muscle regulatory molecule myostatin include Lilly's LY2495655, Regeneron's REGN-1033, and Atara Biosciences' PINTA 745, which was recently announced to have failed to demonstrate clinical proof of concept in its phase 2 study. Novartis is currently studying bimagrumab (BYM-338), an agent targeting the activin receptor. Drugs with other mechanisms currently in or recently completing phase 2 clinical trials include Alder Biosciences' clazakizumab (ALD-518, targeting IL-6), PsiOxus' MT-102 (dual acting catabolic/anabolic transforming agent), Acacia's APD-209 (progestin/β_2 antagonist) and Ohr Pharmaceuticals' OHR118 (cytoprotectant/immunomodulator). PsiOxus's espindolol has completed Phase-1 trials

Strategic Partnerships

We are party to the following collaboration and license agreements:

EUSA

In December 2015, we entered into a license agreement with EUSA under which we granted to EUSA the exclusive, sublicensable right to develop, manufacture and commercialize tivozanib in the territories of Europe (excluding Russia, Ukraine and the Commonwealth of Independent States), Latin America (excluding Mexico), Africa, Australasia and New Zealand for all diseases and conditions in humans, excluding non-oncologic diseases or conditions of the eye.

Under the license agreement, EUSA made a research and development funding payment to us of $2.5 million and is required to make a payment of $4.0 million upon the grant by the European Medicines Agency, or the EMA, of marketing approval for tivozanib for treatment of renal cell carcinoma. We are eligible to receive additional research funding from EUSA, including up to $20.0 million if EUSA elects to utilize data generated by our planned phase 3 study in third line renal cell carcinoma, and up to $2.0 million for a potential phase 1 combination study with a checkpoint inhibitor. We will be entitled to receive milestone payments of $2.0 million per country upon reimbursement approval for renal cell carcinoma in each of France, Germany, Italy, Spain and the United Kingdom, and an additional $2.0 million for the grant of marketing approval in three of the following five countries: Argentina, Australia, Brazil, South Africa and Venezuela. We will also be eligible to receive a payment of $2.0 million in connection with EUSA's filing with the EMA for marketing approval for tivozanib for the treatment of each of up to three additional indications and $5.0 million per indication in connection with the EMA's grant of marketing approval for each of up to three additional indications, as well as potentially up to $335.0 million upon EUSA's achievement of certain sales thresholds. We will also be eligible to receive tiered double digit royalties on net sales, if any, of licensed products in the licensed territories ranging from a low double digit up to mid-twenty percent depending on the level of annual net sales. A percentage of any milestone and royalty payments we receive are due to Kyowa Hakko Kirin Co., Ltd. (formerly Kirin Brewery Co., Ltd.), or KHK, as a sublicensing fee under the license agreement between us and

KHK dated as of December 21, 2006.

EUSA is obligated to use commercially reasonable efforts to develop and commercialize tivozanib throughout the licensed territories. With the exception of certain support to be provided by us prior to the grant of marketing approval by the EMA, EUSA has responsibility for all activities and costs associated with the further development, manufacture, regulatory filings and commercialization of tivozanib in the licensed territories. EUSA is obligated to use commercially reasonable efforts to file an application with the EMA for approval of marketing authorization for tivozanib for the treatment of renal cell carcinoma, which EUSA filed in February 2016.

The term of the license agreement commenced on the effective date and will continue on a product-by-product and country-by-country basis until the later to occur of (a) the expiration of the last valid patent claim for such product in such country, (b) the expiration of market or regulatory data exclusivity for such product in such country or (c) the 10th anniversary of the effective date. Either party may terminate the license agreement in the event of the bankruptcy of the other party or a material breach by the other party that remains uncured, following receipt of written notice of such breach, for a period of (a) thirty (30) days in the case of breach

for nonpayment of any amount due under the license agreement, and (b) ninety (90) days in the case of any other material breach. EUSA may terminate the license agreement at any time upon one hundred eighty (180) days' prior written notice. In addition, we may terminate the license agreement upon thirty (30) days' prior written notice if EUSA challenges any of the patent rights licensed under the license agreement.

Novartis

In August 2015, we entered into a license agreement with Novartis International Pharmaceutical Ltd., which we refer to as Novartis, under which we granted Novartis the exclusive right to develop and commercialize AV-380 and our related antibodies that bind to GDF-15 worldwide. Under this agreement, Novartis is responsible for all activities and costs associated with the further development, regulatory filing and commercialization of AV-380 worldwide.

Novartis made an upfront payment to us of $15.0 million during September 2015. We will also be eligible to receive (a) up to $53 million in potential clinical milestone payments and up to $105 million in potential regulatory milestone payments tied to the commencement of clinical trials and to regulatory approvals of products developed under the license agreement in the United States, the European Union and Japan; and (b) up to $150 million in potential sales based milestone payments based on annual net sales of such products. Upon commercialization, we are eligible to receive tiered royalties on net sales of approved products ranging from the high single digits to the low double digits. Novartis has responsibility under the license agreement for the development, manufacture and commercialization of the licensed antibodies and any resulting approved therapeutic products.

The term of the license agreement commenced in August 2015 and will continue on a country-by-country basis until the later to occur of the 10th anniversary of the first commercial sale of a product in such country or the expiration of the last valid patent claim for a product in that country. We or Novartis may terminate the license agreement in the event of a material breach by the other party that remains uncured for a period of sixty (60) days, which period may be extended an additional thirty (30) days under certain circumstances. Novartis may terminate the license agreement, either in its entirety or with respect to any individual products or countries, at any time upon sixty (60) days' prior written notice. In addition, we may terminate the license agreement upon thirty (30) days' prior written notice if Novartis challenges certain patents controlled by us related to our antibodies.

Novartis also exercised its right under the license agreement to acquire our inventory of clinical quality drug substance, reimbursing us for approximately $3.5 million for such existing inventory.

Pharmstandard Group

In August 2015, we entered into an exclusive license agreement with JSC "Pharmstandard-Ufimskiy Vitamin Plant", or Pharmstandard, a subsidiary of Pharmstandard OJSC, under which we granted Pharmstandard the exclusive right to develop, manufacture and commercialize tivozanib in the territories of Russia, Ukraine and the Commonwealth of Independent States for all conditions excluding non-oncologic ocular conditions.

Pharmstandard is obligated to use commercially reasonable efforts to develop and commercialize tivozanib throughout the licensed territories, and Pharmstandard has responsibility for all activities and costs associated with the further development, manufacture, regulatory filings and commercialization of tivozanib in the licensed territories. In December 2015, Pharmstandard filed an application for marketing authorization in Russia for tivozanib for the treatment of renal cell carcinoma.

Pharmstandard made an upfront payment to us of $1.0 million and will be obligated to pay an additional $0.5 million upon registration of the license agreement with a Russian regulatory agency. Pharmstandard submitted an application for marketing authorization in Russia during December 2015. We are also eligible to receive $7.5 million in connection with the first marketing authorization of tivozanib in Russia. If Russian regulatory authorities require additional studies to be conducted prior to approval, this amount would be reduced to $3.0 million. In addition, we are

eligible to receive $3.0 million for each additional approved indication of tivozanib, if Pharmstandard elects to seek any such approvals, as well as a high single-digit royalty on net sales in the sublicensed territories. A percentage of all upfront, milestone and royalty payments we receive under the agreement are due to KHK as a sublicensing fee under our license agreement with KHK.

The term of the license agreement commenced in August 2015 and will continue on a product-by-product and country-by-country basis until the later to occur of (a) the expiration of the last valid patent claim for such product in such country, (b) the expiration of the last marketing authorization for such product in such country or (c) the 10th anniversary of the first commercial sale of such product in such country. Either party may terminate the license agreement in the event of a material breach by the other party that remains uncured, following receipt of written notice of such breach, for a period of (a) thirty (30) days, in the case of breach for nonpayment of any amount due under the license agreement, and (b) ninety (90) days, in the case of any other material breach. After the first anniversary, Pharmstandard may terminate the license agreement at any time upon ninety (90) days' prior written notice. In

addition, we may terminate the license agreement upon thirty (30) days' prior written notice if Pharmstandard challenges certain patents controlled by us or our licensor, KHK, related to tivozanib.

Ophthotech Corporation

In November 2014 we entered into a Research and Exclusive Option Agreement, or Option Agreement, with Ophthotech Corporation pursuant to which we provided Ophthotech an exclusive option to enter into a definitive license agreement whereby we would grant Ophthotech the right to develop and commercialize our VEGF receptor tyrosine kinase inhibitor, tivozanib, outside of Asia for the potential diagnosis, prevention and treatment of non-oncologic diseases or conditions of the eye in humans.

Pursuant to this Option Agreement, we granted to Ophthotech an exclusive, royalty free license or sublicense, as applicable, under intellectual property rights controlled by us solely to perform the research and development activities related to the use of tivozanib for the specific purposes outlined in the agreement during the option period (as defined below). These activities include formulation work for ocular administration, preclinical research and the conduct of a phase 1/2a, proof of concept clinical trial of a product containing tivozanib in patients with wet age-related macular degeneration, or the POC Study.

Ophthotech paid us $500,000 in consideration for the grant of the option. Such amount is non-refundable and not creditable against any other amounts due under the agreement. We are obligated to make available to Ophthotech, at no cost to Ophthotech, certain quantities of tivozanib hydrochloride solely for conducting its option period research including manufacturing additional quantities of tivozanib in the event stability data indicates that the current supply will expire prior to the end of February 2017.

During the option period, if Ophthotech elects to continue the development of tivozanib for non-oncologic diseases of the eye, we are entitled to receive a one-time milestone payment of $2.0 million upon acceptance of the first Investigational New Drug application for the purpose of conducting a human clinical study of tivozanib in ocular diseases, which we refer to as the IND Submission Milestone Payment. We are also entitled to receive a one-time milestone payment of $6.0 million, which we refer to as the Clinical Efficacy Milestone Payment, on the earlier of (a) December 31, 2016 and (b) the later to occur of: (i) the achievement of a clinical milestone in the POC Study, or the Clinical Efficacy Milestone and (ii) the earlier of (A) the date twelve (12) months after our and Ophthotech's agreement as to the form and substance of the KHK Amendment (as defined below) or (B) the date ninety (90) days after the entry into the KHK Amendment, subject to our right to terminate the Option Agreement on 90 days' written notice (the date on which such payment is due, referred to as the Clinical Efficacy Milestone Payment Trigger Date).

Ophthotech may exercise the option at any time until the latest to occur of: (i) twelve (12) months after the achievement of the Clinical Efficacy Milestone, (ii) ninety (90) days after the Clinical Efficacy Milestone Payment Trigger Date, and (iii) thirty (30) days after we and Ophthotech agree as to the definitive form of license agreement, which we refer to as the Option Period.

During the Option Period, we will not grant a license to any third party that would preclude us from being able to grant to Ophthotech the rights and licenses that are contemplated by the definitive license agreement, and we will not engage in any research, development or commercialization of tivozanib in the field covered by the contemplated definitive license agreement, except as specified in the Option Agreement.

The terms of the Option Agreement are subject to our obligations to Kirin Brewery Co. Ltd. (now Kyowa Hakko Kirin), or KHK, under a license agreement entered into by us with KHK in 2006, pursuant to which we acquired exclusive rights to develop and commercialize tivozanib for all human diseases outside of Asia, referred to as the KHK License Agreement. A percentage of all payments received by us under the Option Agreement and any definitive license agreement must be paid to KHK. We are required to maintain the KHK Agreement in effect, and not enter into any amendment or termination thereof that would adversely affect our rights, during the option period.

During the option period, we and Ophthotech are obligated to negotiate in good faith the form and substance of a definitive license agreement, as well as the form and substance of an amendment to our license agreement with KHK (such amendment referred to as the KHK Amendment) to modify certain rights and obligations of the parties and sublicensees thereunder, particularly with respect to rights to improvements that are not specifically related to tivozanib, and regulatory affairs matters.

Upon exercise of the option, Ophthotech is required to pay us a one-time option exercise fee of $2.0 million in addition to the IND Submission Milestone Payment if such payment has not then been previously paid. If upon exercise of the option, the Clinical Efficacy Milestone Payment Trigger Date has not yet occurred, we shall be entitled to the Clinical Efficacy Milestone Payment at such time that the Clinical Efficacy Milestone Payment Date does occur if the license agreement remains in effect as of such date. The license agreement, if entered into upon Ophthotech's exercise of the Option, will provide for us to be entitled to receive (i) $10.0 million upon meeting certain efficacy and safety endpoints in phase 2 clinical trials that would enable the commencement of a phase 3 clinical trial, (ii) $20.0 million upon marketing approval in the United States, (iii) $20.0 million upon marketing approval in the UK,

Germany, Spain, Italy and France and (iv) up to $45.0 million in sales-based milestone payments. Ophthotech would also be required to pay tiered, double digit royalties, up to a mid-teen percentage, on net sales of tivozanib or products containing tivozanib.

Either party may terminate the Option Agreement in the event of an uncured material breach of the Option Agreement by the other party which remains uncured for a period of ninety (90) days (or thirty (30) days for a breach relating to non-payment), or upon bankruptcy or like proceedings relating to the other party. Ophthotech may terminate the Option Agreement at any time upon ninety (90) days' prior written notice to us. In addition, we may terminate the Option Agreement upon thirty (30) days' prior written notice to Ophthotech if Ophthotech challenges certain patents controlled by us related to tivozanib. Unless terminated as provided above, the Option Agreement will expire upon the expiration of the option or the entry into the definitive license agreement.

Biodesix

In April 2014, we entered into a worldwide agreement with Biodesix to develop and commercialize our HGF inhibitory antibody ficlatuzumab, with BDX004, a proprietary companion diagnostic test developed by Biodesix and based upon the exploratory analyses with VeriStrat®, a serum protein test that is commercially available to help physicians guide treatment decisions for patients with advanced NSCLC.

Under the agreement, we granted Biodesix perpetual, non-exclusive rights to certain intellectual property, including all clinical and biomarker data related to ficlatuzumab, to develop and commercialize BDX004. Biodesix granted us perpetual, non-exclusive rights to certain intellectual property, including diagnostic data related to BDX004, with respect to the development and commercialization of ficlatuzumab; each license includes the right to sublicense, subject to certain exceptions. Pursuant to a joint development plan, as monitored by a joint steering committee, we retain primary responsibility for clinical development of ficlatuzumab in a phase 2 proof of concept, or POC, clinical study of ficlatuzumab for non-small cell lung cancer, in which BDX004, a diagnostic test derived from VeriStrat will be used to select clinical trial subjects, referred to as the FOCAL study. The FOCAL study will be fully funded by Biodesix up to a maximum of $15 million, referred to as the Cap. Biodesix will also be responsible for all of the costs associated with development and registration of BDX004. After the Cap is reached, we and Biodesix will share equally in the costs of the FOCAL study, and we and Biodesix will each be responsible for 50% of development and regulatory costs associated with all future ficlatuzuamab clinical development trials agreed-upon by Biodesix and us, including all milestone payments and royalties payable to third parties, if any.

Pending marketing approval of ficlatuzumab and subject to a commercialization agreement to be entered into after receipt of results from the FOCAL study, each party would share equally in commercialization profits and losses, subject to our right to be the lead commercialization party.

Biodesix is solely responsible for the BDX004 development costs, as well as BDX004 sales and marketing costs. Subject to and following the approval of the BDX004 test as a companion diagnostic for ficlatuzumab, Biodesix has agreed to make the BDX004 test available and use commercially reasonable efforts to seek reimbursement in all geographies where ficlatuzumab is approved. We have agreed to reimburse Biodesix a pre-specified amount, under certain circumstances for VeriStrat tests performed.

Prior to the first commercial sale of ficlatuzumab and after the earlier of (i) the Cap being reached or (ii) the completion of the FOCAL study, each party has the right to elect to discontinue participating in further development or commercialization efforts with respect to ficlatuzumab, which is referred to as an Opt-Out. If either we or Biodesix elects to Opt-Out, with such party referred to as the Opting-Out Party, then the Opting-Out Party shall not be responsible for any future costs associated with developing and commercializing ficlatuzumab other than any ongoing clinical trials. After election of an Opt-Out, the non-opting out party shall have sole decision-making authority with respect to further development and commercialization of ficlatuzumab. Additionally, the Opting-Out Party shall be entitled to receive, if ficlatuzumab is successfully developed and commercialized, a royalty equal to 10% of net sales

of ficlatuzumab throughout the world, if any, subject to offsets under certain circumstances.

If Biodesix elects to Opt-Out, it will continue to be responsible for its development and commercialization obligations with respect to BDX004. If we elect to Opt-Out, we will continue to make the existing supply of ficlatuzumab available to Biodesix for the purposes of enabling Biodesix to complete the development of ficlatuzumab, and Biodesix will have the right to commercialize ficlatuzumab.

Prior to any Opt-Out, the parties shall share equally in any payments received from a third party licensee; provided, however, after any Opt-Out, the Opting-Out Party shall be entitled to receive only a reduced portion of such third party payments. The agreement will remain in effect until the expiration of all payment obligations between the parties related to development and commercialization of ficlatuzumab, unless earlier terminated.

St. Vincent's Hospital

In July 2012, we entered into a license agreement with St. Vincent's Hospital Sydney Limited, which we refer to as St. Vincent's, which was amended and restated in August 2015, under which we obtained an exclusive, worldwide license to research, develop, manufacture and commercialize products for therapeutic applications that benefit from inhibition or decreased expression or activity of MIC-1, which is also known as GDF15. We believe GDF15 is a novel target for cachexia and we are using this license in our AV-380 program for cachexia. Under the agreement, we have the right to grant sublicenses subject to certain restrictions. We have a right of first negotiation to obtain an exclusive license to certain improvements that St. Vincent's or third parties may make to licensed therapeutic products. Under the license agreement, St. Vincent's also granted us non-exclusive rights for certain related diagnostic products and research tools.

Under the license agreement, we (or a sublicensee) are obligated to use diligent efforts to conduct research and clinical development and commercially launch at least one licensed therapeutic product, and to maximize profits from licensed therapeutic products for the benefit of us and St. Vincent's. Subject to certain conditions, we have also agreed to achieve specified research, development and regulatory milestones by specified dates. If we (or a sublicensee) do not achieve a given milestone by the agreed date, we have the option of paying the amount we would have been obligated to pay had we timely achieved the milestone, and, if we do so, St. Vincent's will not have the right to terminate the license agreement based on our failure to timely achieve such milestone.

We have also agreed that, for as long as there is a valid claim in the licensed patents, we will not, and we will ensure that our affiliates and our sublicensees do not, develop or commercialize any product, other than a licensed therapeutic product, for the treatment, prevention or prophylaxis of cachexia, decreased appetite or body weight, that binds to GDF15 or the GDF15 receptor and that is a GDF15 antagonist, and will not license or induce any other person to do the same.

In connection with entering into the original license agreement with St. Vincent's in July 2012, we paid St. Vincent's an upfront license fee of $0.7 million and a low five-figure amount to reimburse St. Vincent's for patent-related expenses it incurred with respect to a specified licensed patent. In connection with the amendment and restatement of the original license agreement in August 2015, we made an additional upfront payment of $1.5 million.

Under our license agreement with St. Vincent's, we may be required to:

- make milestone payments, up to an aggregate total of $18.9 million, upon achievement of specified development and regulatory milestones for the first three indications for licensed therapeutic products, some of which payments may be increased by a mid to high double-digit percentage rate for milestones payments made after we grant any sublicense under the license agreement, depending on the sublicensed territory or territories;
- pay tiered royalty payments equal to a low-single-digit percentage of any net sales we or our sublicensees make from licensed therapeutic products, an obligation we share with Novartis equally. The royalty rate escalates within the low-single-digit range during each calendar year based on increasing licensed therapeutic product sales during such calendar year. Our royalty payment obligations for a licensed therapeutic product in a particular country end on the later of 10 years after the date of first commercial sale of such licensed therapeutic product in such country or expiration of the last-to-expire valid claim of the licensed patents covering such licensed therapeutic product in such country, and are subject to offsets under certain circumstances; and
- reimburse St. Vincent's for some or all of the reasonable costs and expenses it incurs in patent management, filing, prosecuting and maintaining the licensed patents.

The license agreement will remain in effect until the later of 10 years after the date of first commercial sale of licensed therapeutic products in the last country in which a commercial sale is made, or expiration of the last-to-expire valid claim of the licensed patents, unless we elect, or St. Vincent's elects, to terminate the license agreement earlier.

St. Vincent's has the right to terminate the agreement due to any patent-related challenge by us, our affiliates or any sublicensee, or if we or our affiliates or any sublicensee cause or induce any other person to make a patent-related

challenge, and such challenge continues after a specified cure period.

We have the right to terminate the agreement on six months' notice if we terminate our GDF15 research and development programs as a result of the failure of a licensed therapeutic product in pre-clinical or clinical development, or if we form the reasonable view that further GDF15 research and development is not commercially viable, and we are not then in breach of any of our obligations under the agreement. If we form the reasonable view that further GDF15 research and development is not commercially viable and terminate the agreement before we start a phase 1 clinical trial on a licensed therapeutic product, we will be required to pay St. Vincent's a low-to-mid six-figure termination payment.

Any termination of the agreement, in whole or in part, will result in a loss of our rights to the relevant licensed patents and know-how. If St. Vincent's terminates the agreement in its entirety due to our breach, insolvency or a patent-related challenge, or we terminate the agreement due to a development failure or lack of commercial viability, as described above, St. Vincent's will have a non-exclusive license from us to certain intellectual property rights and know-how relating to the licensed therapeutic products, and we must transfer to St. Vincent's certain then-existing regulatory approvals and related documents for the licensed therapeutic products.

Astellas Pharma

In February 2011, we entered into a collaboration and license agreement with Astellas and certain of its indirect wholly-owned subsidiaries pursuant to which we and Astellas made plans to develop and seek to commercialize tivozanib for the treatment of a broad range of cancers. On February 12, 2014, Astellas exercised its right to terminate the agreement. The termination of the agreement became effective August 11, 2014, at which time tivozanib rights returned to us. In accordance with the collaboration and license agreement, we and Astellas agreed to equally share committed development costs, including the costs of completing certain tivozanib clinical development activities that were initiated as part of our partnership with Astellas. For additional information regarding the terms of this agreement, see "Part II, Item 7, Management's Discussion and Analysis of Financial Condition and Results of Operations Strategic Partnerships."

Biogen Idec

In March 2009, we entered into an exclusive option and license agreement with Biogen Idec International GmbH, or 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 were responsible for developing ErbB3 antibodies through completion of the first phase 2 clinical trial designed in a manner that, if successful, would generate data sufficient to support advancement to a phase 3 clinical trial. In March 2014, we amended our agreement with Biogen Idec, whereby Biogen Idec agreed to the termination of its rights and obligations under the agreement, including Biogen Idec's option to (i) obtain a co-exclusive (with us) license to develop and manufacture ErbB3 targeted antibodies and (ii) obtain exclusive commercialization rights to ErbB3 products in countries in the world other than North America. As a result, we retain worldwide rights to AV-203, a clinical stage ErbB3-targeted antibody. Pursuant to the amendment, we are obligated to in good faith use reasonable efforts to seek a collaboration partner for the purpose of funding further development and commercialization of ErbB3-targeted antibodies. Pursuant to the amendment, we are obligated to pay Biogen Idec a percentage of milestone payments received by us from future partnerships after March 28, 2016 and single digit royalty payments on net sales related to the sale of ErbB3 products, up to cumulative maximum amount of $50.0 million.

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 KHK 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. 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. The total remaining payments for clinical and regulatory milestones under our license agreement with KHK are $38.0 million, in the aggregate, provided that the associated clinical and regulatory milestones specific to licensed territories will be replaced by a specified percentage of any non-research and development amounts we receive from any third parties in the event we sublicense our rights under the agreement..

We also 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. We are also required to pay tiered royalty payments on net sales we make of tivozanib in our territory, which range from the low to mid-teens as a percentage of net sales. The royalty rate escalates within this range based on increasing tivozanib sales. Our royalty payment obligations in a particular country in our territory begin on the date of the first commercial sale of tivozanib in that country, and end on the later of 12 years after the date of first commercial sale of tivozanib in that country or the date of the last to expire of the patents covering tivozanib that have been issued in that country. In the event we sublicense the rights licensed to us under the license agreement with KHK, the associated clinical and regulatory milestones specific to licensed territories will be replaced by a specified percentage of any amounts we receive from any third party sublicensees. This provision does not apply to amounts we receive in respect of research and development funding or equity investments, subject to certain limitations.

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

Intellectual Property Rights

Patent Rights

We have built a strong intellectual property portfolio, and, whenever possible, we have multiple tiers of patent protection for our product candidates. With respect to tivozanib, we have exclusively licensed patents that cover the molecule and its therapeutic use (patent expiration 2022, with the possibility of patent term extension to 2027 in the United States and Europe), 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.

Tivozanib

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 one pending international PCT patent application relating to the use of Neuropilin-1, as a serum-based biomarker for identifying patients, including patients with colorectal cancer, likely to respond to treatment with tivozanib.

With respect to tivozanib related technologies, we have:

- U.S. patents: 2 issued; 1 pending; expirations ranging from 2029 to 2036
- Australian patents: none granted; 1 pending; expiration 2030
- International applications: 1 pending

Ficlatuzumab

With respect to our anti-HGF antibodies, including ficlatuzumab, we have eight U.S. patents covering our anti-HGF antibodies, nucleic acids and expression vectors encoding the antibodies, host cells, methods of making the antibodies, and methods of treatment using the antibodies. With respect to our anti-HGF antibody program we have:

- U.S. patents: 8 granted; expirations ranging from 2027 to 2028
- European patents: 1 granted; none pending; expirations 2027
- Japanese patents: 3 granted; 0 pending; expirations 2027

- Canadian patents: 0 granted; 1 pending; expirations 2027
- Australian patents: 1 granted; none pending; expiration 2027

AV-203

With respect to our anti-ErbB3 antibodies, including AV-203, we have two U.S. patents covering our anti-ErbB3 antibodies, nucleic acids and expression vectors encoding the antibodies, host cells, and methods of making the antibodies, a U.S. patent application relating to related embodiments, and a U.S. patent application relating to a method of predicting tumor response to our anti-ErbB3 antibody. With respect to our anti- ErbB3 antibody program we have:

- U.S. patents: 2 granted; 2 pending; expirations ranging from 2031 to 2032
- European patents: 1 granted; 1 pending; expirations ranging from 2031 to 2032
- Japanese patents: none granted; 2 pending; expirations ranging from 2031 to 2032
- Canadian patents: none granted; 2 pending; expirations ranging from 2031 to 2032
- Australian patents: none granted; 2 pending; expirations ranging from 2031 to 2032

Anti-GDF15 Antibodies

With respect to our anti-GDF15 antibodies, we have exclusively licensed certain patent rights from Saint Vincent's Hospital in the field of GDF15 inhibition for therapeutic, preventative and palliative applications, including increasing appetite and/or body weight in subjects where decreased appetite and/or body weight loss due to elevated expression or amounts of GDF15. A U.S. Patent covering method of increasing appetite and /or body weight administering an effective amount of an anti-GDF15 antibody is expected to expire in 2029, which includes approximately 4 years of patent term adjustment granted by the U.S. Patent and Trademark Office. We also have rights in a granted European patent in the field of GDF15 inhibition for decreased appetite and/or body weight due to elevated expression or amounts of GDF15 in patients with cancer, and are pursuing broader claims in a divisional patent application. The granted European patents will expire in 2025.

With respect to the licensed technologies, we have:

- U.S. patents: 2 issued; 1 pending; expirations ranging from 2025 to 2029
- European patents: 3 granted; 1 pending; expirations ranging from 2016 to 2052
- Japanese patents: 3 granted; 1 pending; expirations in 2025.
- Canadian patents: 1 granted; 1 pending; expiration 2016 to 2025
- Australian patents: 3 granted; none pending; expiration 2016 to 2028

Complementing these in-licensed patents relating to GDF15 inhibition is our own issued U.S. patent covering our inhibitory GDF15 antibodies, which is expected to expire in 2033. Additionally, we have a filed U.S. application and international patent applications that cover our GDF15 antibodies, nucleic acids and expression vectors encoding the antibodies, host cells, and methods of making the antibodies. These patents, if issued, would also be expected to expire in 2033. We have also filed three international patent applications covering the use of our inhibitory GDF15 antibodies in improving cardiac and renal function in patients with congestive heart failure and chronic kidney disease, respectively, as well as use in conjunction with chemotherapeutic agents to increase survival in a cancer cachexia patient. These patents, if issued would be expected to expire in 2035 and early 2036.

Other

In addition to patents relating to tivozanib and our ficlatuzumab, AV-203, and anti-GDF15 antibody programs, our patent portfolio contains a number of other patents and patent applications relevant to our business. We own a granted U.S. patent and issued foreign counterparts covering a method of making a chimeric mouse cancer model. We also own a granted U.S. patent and an issued foreign counterparts covering a method of producing primary tumor material via directed complementation. We also own a granted U.S. patent and pending U.S. patent application covering a mouse model that contains a human breast tumor. We own pending patent applications that cover 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.

Technology Platform

With respect to our technology platforms, we have:

- U.S. patents: 3 issued; 1 pending; expirations ranging from 2024 to 2026
  - European patents: 1 granted; expiration in 2024
  - Japanese patents: 1 granted; expiration in 2024
- Australian patents: 1 granted; 1 pending; expirations ranging from 2024 to 2032

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. 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. With regard to AV-203, we are aware of a third party United States patent that contains broad claims relating to anti-ErbB3 antibodies. In the event that an owner of one or more of these patents were to bring an infringement action against us, we may have to argue that our product, its manufacture or use does not infringe a valid claim of the patent in question. Furthermore, 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.

Over the years, we have attempted to identify potential third party intellectual property issues during the early stages of research of our research programs, in order to minimize the cost and disruption of resolving such issues. From time to time, we have found it necessary or prudent to obtain licenses from third party intellectual property holders. Where licenses are readily available at reasonable cost, such licenses are considered a normal cost of doing business. In other instances, however, we may have used the results of freedom-to-operate studies to guide our research away from areas where we believed we were 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.

In spite of our 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 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.

Manufacturing

We currently contract with third parties, to the extent we require, for the manufacture of our product candidates and intend to do so in the future for both clinical and potential commercial needs. 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 and planned clinical trials. In addition, we currently engage a separate contract manufacturer to manufacture, package, label and distribute clinical supplies of tivozanib on an as–needed basis.

We are responsible for all process development and all manufacturing of ficlatuzumab for future development and commercialization and have an agreement with Boehringer Ingelheim for large-scale process development and clinical manufacturing of ficlatuzumab. In connection with the agreement, Boehringer Ingelheim has produced ficlatuzumab at its biopharmaceutical sites in Fremont, California (drug substance) and Biberach, Germany (drug product).

To date, our third-party manufacturers have met our manufacturing requirements. We believe that there are alternate sources of supply that can satisfy our current clinical 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 and Product Approval

Government authorities in the United States, at the federal, state and local level, and in other countries and jurisdictions, including the European Union, extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, packaging, storage, recordkeeping, labeling, advertising, promotion, distribution, marketing, post-approval monitoring and reporting, and import and export of pharmaceutical products. The processes for obtaining regulatory approvals in the United States and in foreign countries and jurisdictions, along with subsequent compliance with applicable statutes and regulations and other regulatory authorities, require the expenditure of substantial time and financial resources.

Review and Approval of Drugs and Biologics in the United States

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 Public Health Service Act, or PHSA, FDCA and related regulations, and other federal, state and local statutes and regulations. An applicant seeking approval to market and distribute a new drug or biological product in the United States must typically undertake the following:

- completion of preclinical laboratory tests, animal studies and formulation studies in compliance with the FDA's good laboratory practice, or GLP, regulations;
- submission to the FDA of an IND, which must take effect before human clinical trials may begin;
- approval by an independent institutional review board, or IRB, representing each clinical site before each clinical trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with good clinical practices, or GCP, to establish the safety and efficacy of the proposed drug product for each indication;
- preparation and submission to the FDA of a new drug application, or NDA, for a drug candidate product and a biological licensing application, or BLA, for a biological product requesting marketing for one or more proposed indications;
- review by an FDA advisory committee, where appropriate or if applicable;
- satisfactory completion of one or more FDA inspections of the manufacturing facility or facilities at which the product, or components thereof, are produced to assess compliance with current Good Manufacturing Practices, or cGMP, requirements and to assure that the facilities, methods and controls are adequate to preserve the product's identity, strength, quality and purity;
- satisfactory completion of FDA audits of clinical trial sites to assure compliance with GCPs and the integrity of the clinical data;
- payment of user fees and securing FDA approval of the NDA or BLA; and
- compliance with any post-approval requirements, including the potential requirement to implement a Risk Evaluation and Mitigation Strategy, or REMS, and the potential requirement to conduct post-approval studies.

Preclinical Studies

Before an applicant begins testing a compound with potential therapeutic value in humans, the product candidate enters the preclinical testing stage. Preclinical studies include laboratory evaluation of the purity and stability of the manufactured substance or active pharmaceutical ingredient and the formulated product, as well as in vitro and animal studies to assess the safety and activity of the product candidate for initial testing in humans and to establish a rationale for therapeutic use. The conduct of preclinical studies is subject to federal regulations and requirements, including GLP regulations. The results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and plans for clinical studies, among other things, are submitted to the FDA as part of an IND. Some long-term preclinical testing, such as animal tests of reproductive adverse events and carcinogenicity, and long term toxicity studies, may continue after the IND is submitted.

The IND and IRB Processes

An IND is an exemption from the FDCA that allows an unapproved product candidate to be shipped in interstate commerce for use in an investigational clinical trial and a request for FDA authorization to administer an investigational drug to humans. Such authorization must be secured prior to interstate shipment and administration of any new drug or biologic that is not the subject of an approved NDA or BLA. In support of a request for an IND, applicants must submit a protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. In addition, the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and plans for clinical trials, among other things, are submitted to the FDA as part of an IND. The FDA requires a 30-day waiting period after the filing of each IND before clinical trials may begin. This waiting period is designed to allow the FDA to review the IND to determine whether human research subjects will be exposed to unreasonable health risks. At any time during this 30-day period, or thereafter, the FDA may raise concerns or questions about the conduct of the trials as outlined in the IND and impose a clinical hold or partial clinical hold. In this case, the IND sponsor and the FDA must resolve any outstanding concerns before clinical trials can begin.

In addition to the foregoing IND requirements, an IRB representing each institution participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that institution, and the IRB must conduct continuing review and reapprove the study at least annually. The IRB must review and approve, among other things, the study protocol and informed consent information to be provided to study subjects. An IRB must operate in compliance with FDA regulations. Information about certain clinical trials must be submitted within specific timeframes to the National Institutes of Health, or NIH, for public dissemination on its ClinicalTrials.gov website. An IRB can suspend or terminate approval of a clinical trial at its institution, or an institution it represents,

if the clinical trial is not being conducted in accordance with the IRB's requirements or if the product candidate has been associated with unexpected serious harm to patients.

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, an IRB or ethics committee, or by us for various reasons. Additionally, some trials are overseen by an independent group of qualified experts organized by the trial sponsor, known as a data safety monitoring board or committee. This group provides authorization for whether or not a trial may move forward at designated check points based on access that only the group maintains to available data from the study. Suspension or termination of development during any phase of clinical trials can occur if it is determined that the participants or patients are being exposed to an unacceptable health risk. Other reasons for suspension or termination may be made by us based on evolving business objectives and/or competitive climate.

Human Clinical Studies in Support of an NDA or BLA

Clinical trials involve the administration of the investigational product to human subjects under the supervision of qualified investigators in accordance with GCP requirements, which include, among other things, the requirement that all research subjects provide their informed consent in writing before their participation in any clinical trial. Clinical trials are conducted under written study protocols detailing, among other things, the inclusion and exclusion criteria, the objectives of the study, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated.

The clinical investigation of an investigational drug or biological product is generally divided into four phases. Although the phases are usually conducted sequentially, they may overlap or be combined. The four 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.
- Phase 4. Post-approval studies may be conducted after initial marketing approval. These studies are used to gain additional experience from the treatment of patients in the intended therapeutic indication.

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and more frequently if serious adverse events occur. In addition, IND safety reports must be submitted to the FDA for any of the following: serious and unexpected suspected adverse reactions; findings from other studies or animal or in vitro testing that suggest a significant risk in humans exposed to the drug; and any clinically important increase in the case of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. The FDA or the sponsor or the data monitoring committee may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk. The FDA will typically inspect one or more clinical sites to assure compliance with GCP and the integrity of the clinical data submitted.

Review of an NDA or BLA by the FDA

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 proposed 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 NDA and BLA are thus the vehicles through which applicants formally propose that the FDA approve a new product for marketing and sale in the United States for one or more indications. Every new product candidate must be the subject of an approved NDA or BLA before it may be commercialized in the United States. Under federal law, the submission of most NDAs and BLAs is subject to an application user fee, currently exceeding $2.3 million, and the sponsor of an approved NDA or BLA is also subject to annual product and establishment user fees, currently exceeding $114,000 per product and $585,000 per establishment. These fees are typically increased annually. Certain exceptions and waivers are available for some of these fees, such as an exception from the application fee for drugs with orphan designation and a waiver for certain small businesses, an exception from the establishment fee when the establishment does not engage in manufacturing the drug during a particular fiscal year, and an exception from the product fee for a drug that is the same as another drug approved under an abbreviated pathway.

Following submission of an NDA or BLA, the FDA conducts a preliminary review of the application generally within 60 calendar days of its receipt and strives to inform the sponsor by the 74th day after the FDA's receipt of the submission to determine whether the application is sufficiently complete to permit substantive review. The FDA may request additional information rather than accept the application for filing. In this event, the application must be resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review. The FDA has agreed to specified performance goals in the review process of NDAs and BLAs. Under that agreement, 90% of applications seeking approval of New Molecular Entities, or NMEs, are meant to be reviewed within ten months from the date on which FDA accepts the NDA for filing, and 90% of applications for NMEs that have been designated for "priority review" are meant to be reviewed within six months of the filing date. For applications seeking approval of products that are not NMEs, the ten-month and six-month review periods run from the date that FDA receives the application. The review process and the Prescription Drug User Fee Act goal date may be extended by the FDA for three additional months to consider new information or clarification provided by the applicant to address an outstanding deficiency identified by the FDA following the original submission.

Before approving an application, the FDA typically will inspect the facility or facilities where the product is or will be manufactured. These pre-approval inspections may cover all facilities associated with an NDA or BLA submission, including drug component manufacturing (e.g., active pharmaceutical ingredients), finished drug product manufacturing, and control testing laboratories. The FDA will not approve an application 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. In addition, as a condition of approval, the FDA may require an applicant to develop a REMS. REMS use risk minimization strategies beyond the professional labeling to ensure that the benefits of the product outweigh the potential risks. To determine whether a REMS is needed, the FDA will consider the size of the population likely to use the product, seriousness of the disease, expected benefit of the product, expected duration of treatment, seriousness of known or potential adverse events, and whether the product is a new molecular entity.

The FDA may refer an application for a novel product to an advisory committee or explain why such referral was not made. Typically, an advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates and provides 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.

The FDA's Decision on an NDA or BLA

On the basis of the FDA's evaluation of the application and accompanying information, including the results of the inspection of the manufacturing facilities, the FDA may issue an approval letter or a complete response letter. An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. A complete response letter generally outlines the deficiencies in the submission and may require substantial additional testing or information in order for the FDA

to reconsider the application. If and when those deficiencies have been addressed to the FDA's satisfaction in a resubmission of the NDA, the FDA will issue an approval letter. The FDA has committed to reviewing such resubmissions in two or six months depending on the type of information included. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

If the FDA approves a product, it may limit the approved indications for use for the product, require that contraindications, warnings or precautions be included in the product labeling, require that post-approval studies, including Phase 4 clinical trials, be conducted to further assess the drug's safety after approval, require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution restrictions or other risk management mechanisms, including REMS, which can materially affect the potential market and profitability of the product. The FDA may prevent or limit further marketing of a product based on the results of post-market studies or surveillance programs. After approval, many 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.

Fast Track, Breakthrough Therapy and Priority Review Designations

The FDA is authorized to designate certain products for expedited review if they are intended to address an unmet medical need in the treatment of a serious or life-threatening disease or condition. These programs are fast track designation, breakthrough therapy designation and priority review designation.

Specifically, the FDA may designate a product for fast track review if it is intended, whether alone or in combination with one or more other drugs, for the treatment of a serious or life-threatening disease or condition, and it demonstrates the potential to address unmet medical needs for such a disease or condition. For fast track products, sponsors may have greater interactions with the FDA and the FDA may initiate review of sections of a fast track product's NDA before the application is complete. This rolling review may be available if the FDA determines, after preliminary evaluation of clinical data submitted by the sponsor, that a fast track product may be effective. The sponsor must also provide, and the FDA must approve, a schedule for the submission of the remaining information and the sponsor must pay applicable user fees. However, the FDA's time period goal for reviewing a fast track application does not begin until the last section of the NDA is submitted. In addition, the fast track designation may be withdrawn by the FDA if the FDA believes that the designation is no longer supported by data emerging in the clinical trial process.

Second, in 2012, Congress enacted the Food and Drug Administration Safety and Improvement Act. This law established a new regulatory scheme allowing for expedited review of products designated as "breakthrough therapies." A product may be designated as a breakthrough therapy if it is intended, either alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The FDA may take certain actions with respect to breakthrough therapies, including holding meetings with the sponsor throughout the development process; providing timely advice to the product sponsor regarding development and approval; involving more senior staff in the review process; assigning a cross-disciplinary project lead for the review team; and taking other steps to design the clinical trials in an efficient manner.

Third, the FDA may designate a product for priority review if it is a drug that treats a serious condition and, if approved, would provide a significant improvement in safety or effectiveness. The FDA determines, on a case-by-case basis, whether the proposed drug represents a significant improvement when compared with other available therapies. Significant improvement may be illustrated by evidence of increased effectiveness in the treatment of a condition, elimination or substantial reduction of a treatment-limiting drug reaction, documented enhancement of patient compliance that may lead to improvement in serious outcomes, and evidence of safety and effectiveness in a new

subpopulation. A priority designation is intended to direct overall attention and resources to the evaluation of such applications, and to shorten the FDA's goal for taking action on a marketing application from ten months to six months.

Post-Approval Regulation

Drugs and biologics manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion and reporting of adverse experiences with the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims, are subject to prior FDA review and approval. There also are continuing, annual user fee requirements for any marketed products and the establishments at which such products are manufactured, as well as new application fees for supplemental applications with clinical data.

In addition, manufacturers and other entities involved in the manufacture and distribution of approved products are required to register their establishments with the FDA and state agencies, and are subject to periodic unannounced inspections by the FDA and these state agencies for compliance with cGMP requirements. Changes to the manufacturing process are strictly regulated and often

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 the sponsor and any third-party manufacturers that the sponsor may decide to use. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance.

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess new safety risks; or imposition of distribution or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, suspension of the approval, or complete withdrawal of the product from the market or product recalls;
- fines, warning letters or holds on post-approval clinical trials;
- refusal of the FDA to approve pending NDAs or supplements to approved NDAs, or suspension or revocation of product license approvals;
- product seizure or detention, or refusal to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. Products may be promoted only for the approved indications and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability.

In addition, the distribution of prescription pharmaceutical products is subject to the Prescription Drug Marketing Act, or PDMA, and its implementing regulations, as well as the Drug Supply Chain Security Act, or DSCA, which regulate the distribution and tracing of prescription drugs and prescription drug samples at the federal level, and set minimum standards for the regulation of drug distributors by the states. The PDMA, its implementing regulations and state laws limit the distribution of prescription pharmaceutical product samples, and the DSCA imposes requirements to ensure accountability in distribution and to identify and remove counterfeit and other illegitimate products from the market.

Generic Drugs

In 1984, with passage of the Hatch-Waxman Amendments to the FDCA, Congress established an abbreviated regulatory scheme authorizing the FDA to approve generic drugs that are shown to contain the same active ingredients as, and to be bioequivalent to, drugs previously approved by the FDA pursuant to NDAs. To obtain approval of a generic drug, an applicant must submit an abbreviated new drug application, or ANDA, to the agency. An ANDA is a comprehensive submission that contains, among other things, data and information pertaining to the active pharmaceutical ingredient, bioequivalence, drug product formulation, specifications and stability of the generic drug, as well as analytical methods, manufacturing process validation data and quality control procedures. ANDAs are "abbreviated" because they generally do not include preclinical and clinical data to demonstrate safety and effectiveness. Instead, in support of such applications, a generic manufacturer may rely on the preclinical and clinical testing previously conducted for a drug product previously approved under an NDA, known as the reference-listed drug, or RLD.

Specifically, in order for an ANDA to be approved, the FDA must find that the generic version is identical to the RLD with respect to the active ingredients, the route of administration, the dosage form, the strength of the drug and the conditions of use of the drug. At the same time, the FDA must also determine that the generic drug is "bioequivalent" to the innovator drug. Under the statute, a generic drug is bioequivalent to a RLD if "the rate and extent of absorption of

the drug do not show a significant difference from the rate and extent of absorption of the listed drug..." Upon approval of an ANDA, the FDA indicates whether the generic product is "therapeutically equivalent" to the RLD in its publication "Approved Drug Products with Therapeutic Equivalence Evaluations," also referred to as the "Orange Book." Physicians and pharmacists consider a therapeutic equivalent generic drug to be fully substitutable for the RLD. In addition, by operation of certain state laws and numerous health insurance programs, the FDA's designation of therapeutic equivalence often results in substitution of the generic drug without the knowledge or consent of either the prescribing physician or patient.

Under the Hatch-Waxman Amendments, the FDA may not approve an ANDA until any applicable period of non-patent exclusivity for the RLD has expired. The FDCA provides a period of five years of non-patent data exclusivity for a new drug containing a new chemical entity. For the purposes of this provision, a new chemical entity, or NCE, is a drug that contains no active

moiety that has previously been approved by the FDA in any other NDA. An active moiety is the molecule or ion responsible for the physiological or pharmacological action of the drug substance. In cases where such NCE exclusivity has been granted, an ANDA may not be filed with the FDA until the expiration of five years unless the submission is accompanied by a Paragraph IV certification, in which case the applicant may submit its application four years following the original product approval. The FDCA also provides for a period of three years of exclusivity if the NDA includes reports of one or more new clinical investigations, other than bioavailability or bioequivalence studies, that were conducted by or for the applicant and are essential to the approval of the application.

Biosimilars

The 2010 Patient Protection and Affordable Care Act, which was signed into law on March 23, 2010, included a subtitle called the Biologics Price Competition and Innovation Act of 2009 or BPCIA. That Act established a regulatory scheme authorizing the FDA to approve biosimilars and interchangeable biosimilars. To date, one biosimilar product has been approved by FDA for use in the United States. No interchangeable biosimilars, however, have been approved. The FDA has issued several guidance documents outlining an approach to review and approval of biosimilars. Additional guidance is expected to be finalized by FDA in the near term.

Under the Act, a manufacturer may submit an application for licensure of a biologic product that is "biosimilar to" or "interchangeable with" a previously approved biological product or "reference product." In order for the FDA to approve a biosimilar product, it must find that there are no clinically meaningful differences between the reference product and proposed biosimilar product in terms of safety, purity, and potency. For the FDA to approve a biosimilar product as interchangeable with a reference product, the agency must find that the biosimilar product can be expected to produce the same clinical results as the reference product, and (for products administered multiple times) that the biologic and the reference biologic may be switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biologic.

Under the BPCIA, an application for a biosimilar product may not be submitted to the FDA until four years following the date of approval of the reference product. The FDA may not approve a biosimilar product until 12 years from the date on which the reference product was approved. Even if a product is considered to be a reference product eligible for exclusivity, another company could market a competing version of that product if the FDA approves a full BLA for such product containing the sponsor's own preclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity and potency of their product. The BPCIA also created certain exclusivity periods for biosimilars approved as interchangeable products. At this juncture, it is unclear whether products deemed "interchangeable" by the FDA will, in fact, be readily substituted by pharmacies, which are governed by state pharmacy law.

Orphan Drug Designation and Exclusivity

Under the Orphan Drug Act, the FDA may designate a drug product as an "orphan drug" if it is intended to treat a rare disease or condition, generally meaning that it affects fewer than 200,000 individuals in the United States, or more in cases in which there is no reasonable expectation that the cost of developing and making a drug product available in the United States for treatment of the disease or condition will be recovered from sales of the product. A company must request orphan drug designation before submitting an NDA or BLA for the candidate product. If the request is granted, the FDA will disclose the identity of the therapeutic agent and its potential use. Orphan drug designation does not shorten the PDUFA goal dates for the regulatory review and approval process, although it does convey certain advantages such as tax benefits and exemption from the PDUFA application fee.

If a product with orphan designation receives the first FDA approval for the disease or condition for which it has such designation or for a select indication or use within the rare disease or condition for which it was designated, the product generally will receive orphan drug exclusivity. Orphan drug exclusivity means that the FDA may not approve another sponsor's marketing application for the same drug for the same indication for seven years, except in certain

limited circumstances. Orphan exclusivity does not block the approval of a different product for the same rare disease or condition, nor does it block the approval of the same product for different indications. If a drug or biologic designated as an orphan drug ultimately receives marketing approval for an indication broader than what was designated in its orphan drug application, it may not be entitled to exclusivity. Orphan exclusivity will not bar approval of another product under certain circumstances, including if a subsequent product with the same drug or biologic for the same indication is shown to be clinically superior to the approved product on the basis of greater efficacy or safety, or providing a major contribution to patient care, or if the company with orphan drug exclusivity is not able to meet market demand.

Pediatric Exclusivity

Pediatric exclusivity is another type of non-patent marketing exclusivity in the United States and, if granted, provides for the attachment of an additional six months of marketing protection to the term of any existing regulatory exclusivity, including the non-patent and orphan exclusivity. This six-month exclusivity may be granted if an NDA or BLA sponsor submits pediatric data that fairly respond to a written request from the FDA for such data. The data do not need to show the product to be effective in the

pediatric population studied; rather, if the clinical trial is deemed to fairly respond to the FDA's request, the additional protection is granted. If reports of requested pediatric studies are submitted to and accepted by the FDA within the statutory time limits, whatever statutory or regulatory periods of exclusivity or patent protection cover the product are extended by six months. This is not a patent term extension, but it effectively extends the regulatory period during which the FDA cannot approve another application.

Review and Approval of Drug Products in the European Union

In order to market any product outside of the United States, a company must also comply with numerous and varying regulatory requirements of other countries and jurisdictions regarding quality, safety and efficacy and governing, among other things, clinical trials, marketing authorization, commercial sales and distribution of drug products. Whether or not it obtains FDA approval for a product, the company would need to obtain the necessary approvals by the comparable foreign regulatory authorities before it can commence clinical trials or marketing of the product in those countries or jurisdictions. The approval process ultimately varies between countries and jurisdictions and can involve additional product testing and additional administrative review periods. The time required to obtain approval in other countries and jurisdictions might differ from and be longer than that required to obtain FDA approval. Regulatory approval in one country or jurisdiction does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country or jurisdiction may negatively impact the regulatory process in others.

Clinical Trial Approval in the EU

Pursuant to the currently applicable Clinical Trials Directive 2001/20/EC and the Directive 2005/28/EC on Good Clinical Practice, or GCP, an applicant must obtain approval from the competent national authority of the EU Member State in which the clinical trial is to be conducted. If the clinical trial is conducted in different EU Member States, the competent authorities in each of these EU Member States must provide their approval for the conduct of the clinical trial. Furthermore, the applicant may only start a clinical trial at a specific study site after the competent ethics committee has issued a favorable opinion.

In April 2014, the EU adopted a new Clinical Trials Regulation (EU) No 536/2014, which is set to replace the current Clinical Trials Directive 2001/20/EC. The new Clinical Trials Regulation will be directly applicable to and binding in all 28 EU Member States without the need for any national implementing legislation. The new Clinical Trials Regulation (EU) No 536/2014 will become applicable no earlier than 28 May 2016. It will overhaul the current system of approvals for clinical trials in the EU. Specifically, the new legislation aims at simplifying and streamlining the approval of clinical trials in the EU. Under the new coordinated procedure for the approval of clinical trials, the sponsor of a clinical trial will be required to submit a single application for approval of a clinical trial to a reporting EU Member State (RMS) through an EU Portal. The submission procedure will be the same irrespective of whether the clinical trial is to be conducted in a single EU Member State or in more than one EU Member State. The Clinical Trials Regulation also aims to streamline and simplify the rules on safety reporting for clinical trials.

Marketing Authorization

In the EU, marketing authorizations for medicinal products may be obtained through several different procedures founded on the same basic regulatory process.

The centralized procedure provides for the grant of a single marketing authorization that is valid for all EU Member States. The centralized procedure is compulsory for medicinal products produced by certain biotechnological processes, products designated as orphan medicinal products, and products with a new active substance indicated for the treatment of certain diseases,. It is optional for those products that are highly innovative or for which a centralized process is in the interest of patients. Under the centralized procedure in the EU, the maximum timeframe for the evaluation of a MAA 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 Committee for Medicinal Products for Human use, or CHMP. Accelerated evaluation may be granted by the CHMP in exceptional cases. These are defined as circumstances in which a medicinal product is expected to be of a “major public health interest.” Three cumulative criteria must be fulfilled in such circumstances: the seriousness of the disease, such as severely 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 these circumstances, the EMA ensures that the opinion of the CHMP is given within 150 days.

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.

The decentralized procedure provides for approval by one or more other concerned EU Member States of an assessment of an application for marketing authorization conducted by one EU Member State, known as the reference EU Member State. In accordance with this procedure, an applicant submits an application for marketing authorization to the reference EU Member State and the concerned EU Member States. This application is identical to the application that would be submitted to the EMA for authorization through the centralized procedure. The reference EU Member State prepares a draft assessment and drafts of the related materials within 120 days after receipt of a valid application. The resulting assessment report is submitted to the concerned EU Member States which, within 90 days of receipt, must decide whether to approve the assessment report and related materials. If a concerned EU Member State cannot approve the assessment report and related materials due to concerns relating to a potential serious risk to public health, disputed elements may be referred to the European Commission, whose decision is binding on all EU Member States. In accordance with the mutual recognition procedure, the sponsor applies for national marketing authorization in one EU Member State. Upon receipt of this authorization the sponsor can then seek the recognition of this authorization by other EU Member States. Authorization in accordance with either of these procedures will result in authorization of the medicinal product only in the reference EU Member State and in the other concerned EU Member States..

A marketing authorization may be granted only to an applicant established in the EU. Regulation No. 1901/2006 provides that, prior to obtaining a marketing authorization in the EU, an applicant must demonstrate compliance with all measures included in a Pediatric Investigation Plan, or PIP, approved by the Pediatric Committee of the EMA, covering all subsets of the pediatric population, unless the EMA has granted a product-specific waiver, class waiver, or a deferral for one or more of the measures included in the PIP.

Orphan Drug Designation and Exclusivity in the EU

Regulation (EC) No 141/2000 and Regulation (EC) No. 847/2000 provide that a product can be designated as an orphan medicinal product by the European Commission if its sponsor can establish that the product is intended for the diagnosis, prevention or treatment of: (1) a life-threatening or chronically debilitating condition affecting not more than five in ten thousand persons in the EU when the application is made, or (2) a life-threatening, seriously debilitating or serious and chronic condition in the EU and that without incentives the medicinal product is unlikely to be developed. For either of these conditions, the applicant must demonstrate that there exists no satisfactory method of diagnosis, prevention or treatment of the condition in question that has been authorized in the EU or, if such method exists, the medicinal product will be of significant benefit to those affected by that condition.

Once authorized, orphan medicinal products are entitled to ten years of market exclusivity in all EU Member States and, in addition, a range of other benefits during the development and regulatory review process, including scientific assistance for study protocols, authorization through the centralized marketing authorization procedure covering all member countries and a reduction or elimination of registration and marketing authorization fees. However, marketing authorization may be granted to a similar medicinal product with the same orphan indication during the ten year period with the consent of the marketing authorization holder for the original orphan medicinal product or if the manufacturer of the original orphan medicinal product is unable to supply sufficient quantities. Marketing authorization may also be granted to a similar medicinal product with the same orphan indication if the product is safer, more effective or otherwise clinically superior to the original orphan medicinal product. The period of market exclusivity may, in addition, be reduced to six years if it can be demonstrated on the basis of available evidence that the original orphan medicinal product is sufficiently profitable not to justify maintenance of market exclusivity.

Pharmaceutical Coverage, Pricing and Reimbursement

In the United States and markets in other countries, patients who are prescribed treatments for their conditions and providers performing the prescribed services generally rely on third-party payors to reimburse all or part of the associated healthcare costs. Significant uncertainty exists as to the coverage and reimbursement status of products approved by the FDA and other government authorities. Thus, even if a product candidate is approved, sales of the

product will depend, in part, on the extent to which third-party payors, including government health programs in the United States such as Medicare and Medicaid, commercial health insurers and managed care organizations, provide coverage, and establish adequate reimbursement levels for, the product. The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the product once coverage is approved. Third-party payors are increasingly challenging the prices charged, examining the medical necessity, and reviewing the cost-effectiveness of medical products and services and imposing controls to manage costs. Third-party payors may limit coverage to specific products on an approved list, also known as a formulary, which might not include all of the approved products for a particular indication.

In order to secure coverage and reimbursement for any product that might be approved for sale, a company may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of the product, in addition to the costs required to obtain FDA or other comparable marketing approvals. Nonetheless, product candidates may not be considered medically necessary or cost effective. A decision by a third-party payor not to cover a product candidate could reduce physician utilization once the product is approved and have a material adverse effect on sales, results of operations and financial condition.

Additionally, a payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. Further, one payor's determination to provide coverage for a drug product does not assure that other payors will also provide coverage and reimbursement for the product, and the level of coverage and reimbursement can differ significantly from payor to payor.

The containment of healthcare costs also has become a priority of federal, state and foreign governments and the prices of drugs have been a focus in this effort. Governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit a company's revenue generated from the sale of any approved products. 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 a company or its collaborators receive marketing approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

Outside the United States, ensuring adequate coverage and payment for a product also involves challenges. Pricing of prescription pharmaceuticals is subject to governmental control in many countries. Pricing negotiations with governmental authorities can extend well beyond the receipt of regulatory marketing approval for a product and may require a clinical trial that compares the cost effectiveness of a product to other available therapies. The conduct of such a clinical trial could be expensive and result in delays in commercialization.

In the European Union, pricing and reimbursement schemes vary widely from country to country. Some countries provide that products may be marketed only after a reimbursement price has been agreed. Some countries may require the completion of additional studies that compare the cost-effectiveness of a particular drug candidate to currently available therapies or so called health technology assessments, in order to obtain reimbursement or pricing approval. For example, the European Union provides options for its member states to restrict the range of products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. European Union member states may approve a specific price for a product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the product on the market. Other member states allow companies to fix their own prices for products, but monitor and control prescription volumes and issue guidance to physicians to limit prescriptions. Recently, many countries in the European Union have increased the amount of discounts required on pharmaceuticals and these efforts could continue as countries attempt to manage healthcare expenditures, especially in light of the severe fiscal and debt crises experienced by many countries in the European Union. The downward pressure on health care costs in general, particularly prescription drugs, has become intense. As a result, increasingly high barriers are being erected to the entry of new products. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various European Union member states, and parallel trade, i.e., arbitrage between low-priced and high-priced member states, can further reduce prices. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any products, if approved in those countries.

Healthcare Law and Regulation

Healthcare providers and third-party payors play a primary role in the recommendation and prescription of drug products that are granted marketing approval. Arrangements with providers, consultants, third-party payors and customers are subject to broadly applicable fraud and abuse, anti-kickback, false claims laws, reporting of payments to physicians and teaching physicians and patient privacy laws and regulations and other healthcare laws and regulations that may constrain business and/or financial arrangements. Restrictions under applicable federal and state healthcare laws and regulations, include the following:

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the federal Anti-Kickback Statute, which prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, paying, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made, in whole or in part, under a federal healthcare program such as Medicare and Medicaid;

- the federal civil and criminal false claims laws, including the civil False Claims Act, and civil monetary penalties laws, which prohibit individuals or entities from, among other things, knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false, fictitious or fraudulent or knowingly making, using or causing to made or used a false record or statement to avoid, decrease or conceal an obligation to pay money to the federal government.
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created additional federal criminal laws that prohibit, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, and their respective implementing regulations, including the Final Omnibus Rule published in January 2013, which impose obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;
- the federal false statements statute, which prohibits knowingly and willfully falsifying, concealing ·or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services;
- the federal transparency requirements known as the federal Physician Payments Sunshine Act, under the Patient Protection and Affordable Care Act, as amended by the Health Care Education Reconciliation Act, or the Affordable Care Act, which requires certain manufacturers of drugs, devices, biologics and medical supplies to report annually to the Centers for Medicare & Medicaid Services, or CMS, within the United States Department of Health and Human Services, information related to payments and other transfers of value made by that entity to physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members; and
- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, which may apply to healthcare items or services that are reimbursed by non-governmental third-party payors, including private insurers.

Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring drug manufacturers to report information related to payments to physicians and other health care providers or marketing expenditures. State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Healthcare Reform

A primary trend in the United States healthcare industry and elsewhere is cost containment. There have been a number of federal and state proposals during the last few years regarding the pricing of pharmaceutical and biopharmaceutical products, limiting coverage and reimbursement for drugs and other medical products, government control and other changes to the healthcare system in the United States.

By way of example, the United States and state governments continue to propose and pass legislation designed to reduce the cost of healthcare. In March 2010, the United States Congress enacted the Affordable Care Act, which, among other things, includes changes to the coverage and payment for products under government health care programs. Among the provisions of the Affordable Care Act of importance to potential drug candidates are:

- an annual, nondeductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government healthcare programs, although this fee would not apply to sales of certain products approved exclusively for orphan indications;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to certain individuals with income at or below 133% of the federal poverty level, thereby potentially increasing a manufacturer's Medicaid rebate liability;
- expanded manufacturers' rebate liability under the Medicaid Drug Rebate Program by increasing the minimum rebate for both branded and generic drugs and revising the definition of "average manufacturer price," or AMP, for calculating and reporting Medicaid drug rebates on outpatient prescription drug prices and extending rebate liability to prescriptions for individuals enrolled in Medicare Advantage plans;
- addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected;
- expanded the types of entities eligible for the 340B drug discount program;
- established the Medicare Part D coverage gap discount program by requiring manufacturers to provide a 50% point-of-sale-discount off the negotiated price of applicable brand drugs to eligible beneficiaries during their

coverage gap period as a condition for the manufacturers' outpatient drugs to be covered under Medicare Part D;

- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research;
- the Independent Payment Advisory Board, or IPAB, which has authority to recommend certain changes to the Medicare program to reduce expenditures by the program that could result in reduced payments for prescription drugs. However, the

IPAB implementation has been not been clearly defined. PPACA provided that under certain circumstances, IPAB recommendations will become law unless Congress enacts legislation that will achieve the same or greater Medicare cost savings; and

- established the Center for Medicare and Medicaid Innovation within CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending. Funding has been allocated to support the mission of the Center for Medicare and Medicaid Innovation from 2011 to 2019.

Other legislative changes have been proposed and adopted in the United States since the Affordable Care Act was enacted. For example, in August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2012 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions of Medicare payments to providers of up to 2% per fiscal year, which went into effect in April 2013 and will remain in effect through 2024 unless additional Congressional action is taken. In January 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, further reduced Medicare payments to several providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

Employees

As of December 31, 2015, we had 19 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.

Research and Development Costs

Our research and development costs were $12.9 million, $38.3 million, and $68.5 million for the years ended December 31, 2015, 2014 and 2013, respectively. 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 alternative future use.

Segment and Geographic Information

We view our operations and manage our business in one operating segment. As of December 31, 2015, we operate only in the United States.

Executive Officers

The following table lists the positions, names and ages of our executive officers as of February 29, 2016:

Executive Officers

Michael P. Bailey	50	Chief Executive Officer, President and Director
Keith S. Ehrlich	65	Chief Financial Officer
Michael N. Needle	56	Chief Medical Officer

Michael P. Bailey was appointed President and Chief Executive Officer and a member of our Board of Directors effective January 6, 2015. Mr. Bailey joined our company in September 2010 as our Chief Commercial Officer and

was named our Chief Business Officer in June 2013. Prior to joining our company, Mr. Bailey served as Senior Vice President, Business Development and Chief Commercial Officer at Synta Pharmaceuticals, Inc., a biopharmaceutical company focused on research, development and commercialization of oncology medicines, from 2008 to September 2010. From 1999 to 2008, Mr. Bailey worked at ImClone Systems Incorporated, a biopharmaceutical company focused on the development and commercialization of treatments for cancer patients. During his nine-year tenure at ImClone, he was responsible for commercial aspects of the planning and launch of ERBITUX® (cetuximab) across multiple oncology indications, as well as new product planning for the ImClone development portfolio, which included CYRAMZA® (ramucirumab) and necitumumab. In addition, Mr. Bailey was a key member of the strategic leadership committees for ImClone and its North American and worldwide partnerships and led 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., a biotechnology company, 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 Mendoza College of Business at University of Notre Dame.

Keith S. Ehrlich, C.P.A. was appointed Chief Financial Officer in April 2015. Mr. Ehrlich has acted as a financial consultant to the Company from February 2015 to April 2015. Prior to joining our company, he worked with Synta. Mr. Ehrlich served as Synta's vice president of finance and administration from March 2004 until February 2015, and as its Chief Financial Officer from October 2006 to December 2014. Prior to Synta, Mr. Ehrlich served in various senior finance roles, including Chief Financial Officer of Argentys Corporation, Dyax Corp. and OraVax, Inc. Mr. Ehrlich also previously served as a director of finance at Vertex Pharmaceuticals, Inc. and as a senior audit manager with PricewaterhouseCoopers, LLP. Mr. Ehrlich received his B.A. in Biology from Drew University and his M.B.A. in Finance and Accounting from Rutgers University.

Michael N. Needle, MD was appointed Chief Medical Officer in January 2015. Dr. Needle has more than 15 years of pharmaceutical industry experience in drug development and regulatory affairs. This includes central roles in the development of oncology and hematology drugs, including Erbitux® (cetuximab), Revlimid® (lenalidomide) and Pomalyst® (pomolidimide). He most recently served as Chief Medical Officer for Array BioPharma Inc., a biopharmaceutical company, from April 2013 to September 2014. Prior to Array, Dr. Needle was Chief Medical Officer of the Multiple Myeloma Research Foundation and Consortium (MMRF), a research organization, from April 2012 to April 2013. Prior to MMRF, he held multiple Vice President level positions at Celgene Corporation, a biotechnology company, in Clinical Research and Development in Oncology, Strategic Medical Business Development, and Pediatric Strategy from March 2004 to April 2010. Dr. Needle also served as the Vice President of Clinical Affairs at ImClone from April 2000 to February 2004. Dr. Needle received his fellowship in Pediatric Hematology/Oncology at the Children's Hospital Medical Center, the Fred Hutchinson Cancer Research Center of the University of Washington in Seattle and the University of Texas M.D. Anderson Cancer Center in Houston. Dr. Needle has held faculty positions at the University of Pennsylvania and Columbia University. Dr. Needle graduated from Binghamton University with a Bachelor of Arts in Physics and received his medical degree from SUNY Downstate Medical Center, in Brooklyn, New York.

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 1 Broadway, 14th Floor, Cambridge, Massachusetts, 02142, and our telephone number is (617) 588-1960. 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 also make available, free of charge on our website, the reports filed with the SEC by our executive officers, directors and 10% stockholders pursuant to Section 16 under 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, or, in the case of Section 16 reports, as soon as reasonably practicable after copies of those filings are provided to us by the filing persons. 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 "For Investors" and "For Media," as a source of information about us.

We have adopted a code of business conduct and ethics, which applies to all of our officers, directors and employees, as well as charters for our audit committee, our compensation committee and our nominating and governance committee, and corporate governance guidelines. We have posted copies of our code of business conduct and ethics

and corporate governance guidelines, as well as each of our committee charters, on the Corporate Governance page of the Investors section of our website, which you can access free of charge.

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

Item 1A. Risk Factors

Our business is subject to numerous risks. We caution you that the following important factors, among others, could cause our actual results to differ materially from those expressed in forward-looking statements made by us or on our behalf in this Annual Report on Form 10-K and other filings with the SEC, press releases, communications with investors and oral statements. Any or all of our forward-looking statements in this Annual Report on Form 10-K and in any other public statements we make may turn out to be wrong. They can be affected by inaccurate assumptions we might make or by known or unknown risks and uncertainties. Many factors

mentioned in the discussion below will be important in determining future results. Consequently, no forward-looking statement can be guaranteed. Actual future results may differ materially from those anticipated in 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. You are advised, however, to consult any further disclosure we make in our reports filed with the SEC.

Risks Related to Our Financial Position and Need for Additional Capital

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

We have incurred net losses of $15.0 million, $52.7 million and $107.0 million for the fiscal years ended December 31, 2015, 2014 and 2013, respectively. As of December 31, 2015, we had an accumulated deficit of $495.0 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. 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 seek to develop our product candidates.

If we do not successfully develop and obtain regulatory approval for our existing and future pipeline of product candidates and effectively manufacture, market and sell any product candidates that are approved, we may never generate product sales. 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.

Our business is in early stage of development, which may make it difficult for you to evaluate the success of our business to date and to assess our future viability.

All of our product candidates are in early stages of development. We have not yet demonstrated our ability to obtain marketing approvals, manufacture a commercial scale medicine, or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful commercialization. Typically, it takes about 10 to 15 years to develop one new medicine from the time it is discovered to when it is available for treating patients. Preclinical studies and clinical trials may involve 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. Consequently, any predictions you make about our future success or viability may not be as accurate as they could be if we had a longer operating history.

In addition, as an early stage business, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors. To be profitable, we will need to transition from a company with a research and development focus to a company capable of supporting commercial activities. We may not be successful in such a transition.

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

We will require substantial funds to continue our development programs and to fulfill our planned operating goals. In particular, our currently planned operating and capital requirements include the need for substantial working capital to support our development activities for tivozanib. For example, we estimate that the remaining uncommitted costs for a Phase 3 trial for RCC such as the one contemplated by us could be in the range of $34-36 million in the aggregate through 2018. We are also designing a phase 1 study of tivozanib combined with a PD-1 inhibitor for the treatment of patients with RCC. Moreover, we have future payment obligations and cost-sharing arrangements under certain of our

collaboration and license agreements. For example, under our agreements with KHK and St. Vincent's, we are required to make certain clinical and regulatory milestone payments, have royalty obligations with respect to product sales and are required to pay a specified percentage of sublicense revenue in certain instances. Moreover, under our agreement with Biodesix, we are obligated to share any costs for the phase 2 FOCAL study that exceed $15 million. Accordingly, we will need substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed or on attractive terms, or if we are unable to procure partnership arrangements to advance our programs, we would be forced to delay, reduce or eliminate our research and development programs and any future commercialization efforts.

We believe that our cash resources would allow us to fund our current operations into the fourth quarter of 2017. This estimate does not include our payment of potential licensing milestones or the uncommitted costs of conducting any contemplated clinical trials and assumes no milestone payments from our partners, no additional funding from new partnership agreements, no equity financings, no debt financings, no accelerated repayment thereof and no further sales of equity under our ATM. This estimate also does not include any amount we may agree to pay in excess of the estimated settlement liability that we have established for accounting purposes with respect to a potential settlement of claims with the SEC, as described below under the heading "Legal Proceedings" in Part I—Item 3 of this Form 10-K.

However, because of the numerous risks and uncertainties associated with the development and commercialization of pharmaceutical products, we are unable to estimate the exact amounts of our working capital requirements and the period in which we will have working capital to fund our operations. Accordingly, the timing and nature of activities contemplated for 2016 and thereafter will be conducted subject to the availability of sufficient financial resources.

Our future capital requirements depend on many factors, including:

- our ability to establish and maintain strategic partnerships, licensing or other arrangements and the financial terms of such agreements;
- the number and characteristics of the product candidates we pursue;
- the scope, progress, results and costs of 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 costs involved in preparing, filing, prosecuting, maintaining, defending and enforcing patent claims, including litigation costs and the outcome of such litigation;
- the absence of any breach, acceleration event or event of default under our loan agreement with Hercules or under any other agreements with third parties;
- the outcome of legal actions against us, including the current lawsuits and SEC proceedings described under “Part I, Item 3—Legal Proceedings,” including whether we enter into a settlement with the SEC within the estimated settlement liability we have established for accounting purposes;
- the cost of commercialization activities if any of our product candidates are approved for sale, including marketing, sales and distribution costs;
- the cost of manufacturing our product candidates and any products we successfully commercialize; and
- the timing, receipt and amount of sales of, or royalties on, our future products, if any.

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

We may seek to sell additional equity or debt securities or obtain additional credit facilities. The sale of additional equity or convertible debt securities may result in additional dilution to our stockholders. If we raise additional funds through the issuance of debt securities or preferred stock or through additional credit facilities, these securities and/or the loans under credit facilities could provide for rights senior to those of our common stock and could contain covenants that would restrict our operations. We may require additional capital beyond our currently forecasted amounts. Additional funds may not be available when we need them, on terms that are acceptable to us, or at all.

We also expect to seek additional funds through arrangements with collaborators, licensees or other third parties. These arrangements would generally require us to relinquish or encumber rights to some of our technologies or drug candidates, and we may not be able to enter into such arrangements on acceptable terms, if at all.

We anticipate that we will require additional funding. If we are unable to obtain such additional funding on a timely basis, whether through payments under existing or future collaborations or license agreement or sales of debt or equity, we may be required to delay, limit, reduce or terminate our clinical trials or development activities for one or more of our product candidates.

We may not be successful in establishing and maintaining strategic partnerships to further the development of each of our therapeutic programs. A failure to obtain such partnerships in the near future will have a material adverse effect on our operations and business.

We currently are exploring partnership opportunities to fund the further development of a majority of our development programs, including our lead program for tivozanib as well as AV-203. Accordingly, our success will depend in significant part on our ability to attract and maintain strategic partners and strategic relationships with major biotechnology or pharmaceutical companies to support the development and commercialization of these product

candidates. In these partnerships, we would expect our strategic partner to provide substantial funding, as well as significant capabilities in research, development, marketing and sales

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 development pipeline may be deemed insufficient, our product candidates and

programs may be deemed to be at too early of a stage of development for collaborative effort 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 have an adverse effect on our business or our operating plan, including delaying the development and commercialization of our product candidates.

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

- we will have limited resources with which to continue to operate our business and we may not be able to successfully complete any other strategic transactions;
- the development of certain of our product candidates may be terminated or delayed; and
- our cash expenditures related to development of our product candidates would increase significantly and we do not have the cash resources to develop our product candidates on our own.

Risks Related to our Litigation and SEC Investigation

We and certain of our former officers and present and former directors have been named as defendants in multiple lawsuits that could result in substantial costs and divert management's attention.

We, and certain of our former officers and directors, were named as defendants in a consolidated class action lawsuit initiated in 2013 that generally alleges that we and those individuals violated federal securities laws by making allegedly false and/or misleading statements concerning the development of our drug tivozanib and its prospects for FDA approval. The lawsuit seeks unspecified damages, interest, attorneys' fees, and other costs. The consolidated amended complaint was dismissed without prejudice on March 20, 2015, and the lead plaintiffs then filed a second amended complaint bringing similar allegations. This second amended complaint was dismissed with prejudice on November 18, 2015. The lead plaintiffs have appealed the court's decision to the United States Court of Appeals for the First Circuit. Another plaintiff has also filed a derivative complaint, allegedly on our behalf, naming us as a nominal defendant and also naming as defendants present and former members of our board of directors, alleging breach of fiduciary duty and abuse of control on the part of those directors with respect to the same statements at issue in the securities litigation. The derivative complaint seeks, among other relief, unspecified damages, costs and expenses, including attorneys' fees, an order requiring us to implement certain corporate governance reforms, restitution from the defendants and such other relief as the court might find just and proper. The derivative complaint was dismissed with prejudice on March 18, 2015. The plaintiff has appealed the court's decision to the United States Court of Appeals for the First Circuit.

We intend to continue to deny these allegations and to engage in a vigorous defense of these lawsuits. However, we are unable to predict the outcome of these matters at this time. Moreover, any conclusion of these matters in a manner adverse to us could have a material adverse effect on our financial condition and business. For example, we could incur substantial costs not covered by our liability insurance, suffer a significant adverse impact on our reputation and divert management's attention and resources from other priorities, including the execution of business plans and strategies that are important to our ability to grow our business, any of which could have a material adverse effect on our business. In addition, any of these matters could require payments that are not covered by, or exceed the limits of, our available liability insurance, which could have a material adverse effect on our operating results or financial condition.

We are in settlement discussions with the SEC. If such discussions do not result in a settlement, the SEC may pursue claims against us.

The SEC Staff has invited us, and three of our former officers, to discuss the settlement of potential claims that the SEC Staff may recommend that the Commission bring, asserting that we violated federal securities laws by omitting to disclose the recommendation of the staff of the U.S. Food and Drug Administration, on May 11, 2012, that we conduct an additional clinical trial with respect to Tivozanib. See "Part I, Item 3 – Legal Proceedings" for a further discussion of these claims. We have continued such discussions with the SEC Staff. If settlement discussions conclude without a settlement that is mutually acceptable to the SEC and us, the SEC may pursue claims against us. There can be no assurance that we will be able to resolve any potential claim of the Commission. The terms of any settlement with the Commission, the filing of any claims by the Commission, or the outcome of any claims that the Commission may bring against us, could have a material adverse impact on our business, cash position and prospects, and could significantly harm our reputation. Moreover, these ongoing matters with the Commission may adversely affect our ability to raise additional needed capital to fund our business, could divert our management's attention and resources from other priorities, including the execution of business plans and strategies that are important to our ability to grow our business, and may adversely

affect the trading price of our common stock. If the Commission makes claims against our former officers, they may seek advancement of legal expenses or indemnification for any losses, either of which could be material to the extent not covered by our director and officer liability insurance.

Risks Related to Development and Commercialization of Our Drug Candidates

In the near term, we are dependent on the success of tivozanib. If we are unable to initiate or complete the clinical development of, obtain marketing approval for or successfully commercialize tivozanib, either alone or with our collaborators, or if we experience significant delays in doing so, our business could be substantially harmed.

We currently have no products approved for sale and are investing a significant portion of our efforts and financial resources in the development of tivozanib. Our prospects are substantially dependent on our ability, or that of our collaborators, to develop, obtain marketing approval for and successfully commercialize tivozanib in one or more disease indications.

The success of tivozanib will depend on several factors, including the following:

- initiation and successful enrollment and completion of clinical trials;
- a safety, tolerability and efficacy profile that is satisfactory to the U.S. Food and Drug Administration, or FDA, or any comparable foreign regulatory authority for marketing approval;
- timely receipt of marketing approvals from applicable regulatory authorities;
- the performance of our collaborators;
- the extent of any required post marketing approval commitments to applicable regulatory authorities;
- establishment of supply arrangements with third party raw materials suppliers and manufacturers including with respect to the supply of active pharmaceutical ingredient for tivozanib;
- establishment of arrangements with third party manufacturers to obtain finished drug product that is appropriately packaged for sale;
- adequate ongoing availability of raw materials and drug product for clinical development and any commercial sales;
- obtaining and maintaining patent, trade secret protection and regulatory exclusivity, both in the United States and internationally, including our ability to maintain our license agreement with Kyowa Hakko Kirin Co., Ltd.;
- protection of our rights in our intellectual property portfolio;
- successful launch of commercial sales following any marketing approval;
- a continued acceptable safety profile following any marketing approval;
- commercial acceptance by patients, the medical community and third party payors;
- successful identification of biomarkers for patient selection; and
- our ability to compete with other therapies.

Many of these factors are beyond our control, including clinical development, the regulatory submission process, potential threats to our intellectual property rights and the manufacturing, marketing and sales efforts of our collaborators. If we are unable to develop, receive marketing approval for and successfully commercialize tivozanib on our own or with our collaborators, or experience delays as a result of any of these factors or otherwise, our business could be substantially harmed.

If clinical trials of any product candidates that we, or any collaborators, may develop fail to satisfactorily demonstrate safety and efficacy to the FDA and other regulators, we, or any collaborators, may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of these product candidates.

We, and any collaborators, are not permitted to commercialize, market, promote or sell any product candidate in the United States without obtaining marketing approval from the FDA. Foreign regulatory authorities, such as the European Medicines Agency, or the EMA, impose similar requirements. We, and any collaborators, must complete extensive preclinical development and clinical trials to demonstrate the safety and efficacy of our product candidates in humans before we will be able to obtain these approvals.

Clinical testing is expensive, is difficult to design and implement, can take many years to complete and is inherently uncertain as to outcome. We cannot guarantee that any clinical trials will be conducted as planned or completed on schedule, if at all. The clinical

development of our product candidates is susceptible to the risk of failure inherent at any stage of product development, including failure to demonstrate efficacy in a clinical trial or across a broad population of patients, the occurrence of adverse events that are severe or medically or commercially unacceptable, failure to comply with protocols or applicable regulatory requirements and determination by the FDA or any comparable foreign regulatory authority that a product candidate may not continue development or is not approvable. It is possible that even if one or more of our product candidates has a beneficial effect, that effect will not be detected during clinical evaluation as a result of one or more of a variety of factors, including the size, duration, design, measurements, conduct or analysis of our clinical trials. Conversely, as a result of the same factors, our clinical trials may indicate an apparent positive effect of a product candidate that is greater than the actual positive effect, if any. Similarly, in our clinical trials we may fail to detect toxicity of or intolerability caused by our product candidates, or mistakenly believe that our product candidates are toxic or not well tolerated when that is not in fact the case.

Any inability to successfully complete preclinical and clinical development could result in additional costs to us, or any collaborators, and impair our ability to generate revenues from product sales, regulatory and commercialization milestones and royalties. Moreover, if we, or any collaborators, are required to conduct additional clinical trials or other testing of our product candidates beyond the trials and testing that we or they contemplate, if we, or they, are unable to successfully complete clinical trials of our product candidates or other testing, or the results of these trials or tests are unfavorable, uncertain or are only modestly favorable, or there are unacceptable safety concerns associated with our product candidates, we, or any collaborators, may:

- incur additional unplanned costs;
- be delayed in obtaining marketing approval for our product candidates;
- not obtain marketing approval at all;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- obtain approval with labeling that includes significant use or distribution restrictions or significant safety warnings, including boxed warnings;
- be subject to additional post marketing testing or other requirements; or
- be required to remove the product from the market after obtaining marketing approval.

Our failure to successfully initiate and complete clinical trials of our product candidates and to demonstrate the efficacy and safety necessary to obtain regulatory approval to market any of our product candidates would significantly harm our business.

Adverse events or undesirable side effects caused by, or other unexpected properties of, tivozanib or any future product candidates that we develop may be identified during development and could delay or prevent their marketing approval or limit their use.

Adverse events or undesirable side effects caused by, or other unexpected properties of, tivozanib or any future product candidates that we may develop could cause us, any collaborators, an institutional review board or regulatory authorities to interrupt, delay or halt clinical trials of one or more of our product candidates and could result in a more restrictive label or the delay or denial of marketing approval by the FDA or comparable foreign regulatory authorities. If any of our product candidates is associated with adverse events or undesirable side effects or has properties that are unexpected, we, or any collaborators, may need to abandon development or limit development of that product candidate to certain uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk benefit perspective. Many compounds that initially showed promise in clinical or earlier stage testing have later been found to cause undesirable or unexpected side effects that prevented further development of the compound.

If we, or any collaborators, experience any of a number of possible unforeseen events in connection with clinical trials of our current or any future product candidates that we, or any collaborators, may develop, potential clinical development, marketing approval or commercialization of our product candidates could be delayed or prevented.

We, or any collaborators, may experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent clinical development, marketing approval or commercialization of our current product candidates or any future product candidates that we, or any collaborators, may develop, including:

- regulators or institutional review boards may not authorize us, any collaborators or our or their investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- we, or any collaborators, may have delays in reaching or fail to reach agreement on acceptable clinical trial contracts or clinical trial protocols with prospective trial sites;
- clinical trials of our product candidates may produce unfavorable or inconclusive results;

- we, or any collaborators, may decide, or regulators may require us or them, to conduct additional clinical trials or abandon product development programs;
- the number of patients required for clinical trials of our product candidates may be larger than we, or any collaborators, anticipate, patient enrollment in these clinical trials may be slower than we, or any collaborators, anticipate or participants may drop out of these clinical trials at a higher rate than we, or any collaborators, anticipate;
- the cost of planned clinical trials of our product candidates may be greater than we anticipate;
- our third party contractors or those of any collaborators, including those manufacturing our product candidates or components or ingredients thereof or conducting clinical trials on our behalf or on behalf of any collaborators, may fail to comply with regulatory requirements or meet their contractual obligations to us or any collaborators in a timely manner or at all;
- patients that enroll in a clinical trial may misrepresent their eligibility to do so or may otherwise not comply with the clinical trial protocol, resulting in the need to drop the patients from the clinical trial, increase the needed enrollment size for the clinical trial or extend the clinical trial's duration;
- we, or any collaborators, may have to delay, suspend or terminate clinical trials of our product candidates for various reasons, including a finding that the participants are being exposed to unacceptable health risks, undesirable side effects or other unexpected characteristics of the product candidate;
- regulators or institutional review boards may require that we, or any collaborators, or our or their investigators suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements or their standards of conduct, a finding that the participants are being exposed to unacceptable health risks, undesirable side effects or other unexpected characteristics of the product candidate or findings of undesirable effects caused by a chemically or mechanistically similar product or product candidate;
- the FDA or comparable foreign regulatory authorities may disagree with our, or any collaborators', clinical trial designs or our or their interpretation of data from preclinical studies and clinical trials;
- the FDA or comparable foreign regulatory authorities may fail to approve or subsequently find fault with the manufacturing processes or facilities of third party manufacturers with which we, or any collaborators, enter into agreements for clinical and commercial supplies;
- the supply or quality of raw materials or manufactured product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient, inadequate or not available at an acceptable cost, or we may experience interruptions in supply; and
- the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient to obtain marketing approval.

Product development costs for us, or any collaborators, will increase if we, or they, experience delays in testing or pursuing marketing approvals and we, or they, may be required to obtain additional funds to complete clinical trials and prepare for possible commercialization. We do not know whether any trials will begin as planned, will need to be restructured, or will be completed on schedule or at all. Significant clinical trial delays also could shorten any periods during which we, or any collaborators, may have the exclusive right to commercialize our product candidates or allow our competitors, or the competitors of any collaborators, to bring products to market before we, or any collaborators, do and impair our ability, or the ability of any collaborators, to successfully commercialize our product candidates and may harm our business and results of operations. In addition, many of the factors that lead to clinical trial delays may ultimately lead to the denial of marketing approval of any of our product candidates.

If we, or any collaborators, experience delays or difficulties in the enrollment of patients in clinical trials, our or their receipt of necessary regulatory approvals could be delayed or prevented.

We, or any collaborators, may not be able to initiate or continue clinical trials for our current product candidates or any future product candidates that we, or any collaborators, may develop if we, or they, are unable to locate and enroll a sufficient number of eligible patients to participate in clinical trials. Patient enrollment is a significant factor in the timing of clinical trials, and is affected by many factors, including:

- the size and nature of the patient population;

- the severity of the disease under investigation;
- the availability of approved therapeutics for the relevant disease;
- the proximity of patients to clinical sites;

- the eligibility criteria for the trial;
- the design of the clinical trial;
- efforts to facilitate timely enrollment;
- competing clinical trials; and
- clinicians' and patients' perceptions as to the potential advantages and risks of the drug being studied in relation to other available therapies, including any new drugs that may be approved for the indications we are investigating.

Our inability, or the inability of any collaborators, to enroll a sufficient number of patients for our, or their, clinical trials could result in significant delays or may require us or them to abandon one or more clinical trials altogether. Enrollment delays in our, or their, clinical trials may result in increased development costs for our product candidates, delay or halt the development of and approval processes for our product candidates and jeopardize our, or any collaborators', ability to commence sales of and generate revenues from our product candidates, which could cause the value of our company to decline and limit our ability to obtain additional financing, if needed.

Results of early clinical trials may not be predictive of results of future late stage clinical trials.

The outcome of early clinical trials may not be predictive of the success of later clinical trials, and interim results of clinical trials do not necessarily predict success in future clinical trials. Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late stage clinical trials after achieving positive results in earlier development, and we have and could, in the future, face similar setbacks. For example, in June 2013, the FDA issued a response letter informing us that it would not approve tivozanib for the treatment of first line advanced renal cell carcinoma based on the study data from our initial Phase 3 trial, and recommended that we perform an additional study that is adequately sized to assure the FDA that there is no adverse effect on overall survival. The design of a clinical trial can determine whether its results will support approval of a product and flaws in the design of a clinical trial may not become apparent until the clinical trial is well advanced. We have limited experience in designing clinical trials and may be unable to design and execute a clinical trial to support marketing approval. In addition, preclinical and clinical data are often susceptible to varying interpretations and analyses. Many companies that believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval for the product candidates. Even if we, or any collaborators, believe that the results of clinical trials for our product candidates warrant marketing approval, the FDA or comparable foreign regulatory authorities may disagree and may not grant marketing approval of our product candidates.

In some instances, there can be significant variability in safety or efficacy results between different clinical trials of the same product candidate due to numerous factors, including changes in trial procedures set forth in protocols, differences in the size and type of the patient populations, changes in and adherence to the dosing regimen and other clinical trial protocols and the rate of dropout among clinical trial participants. If we fail to receive positive results in clinical trials of our product candidates, the development timeline and regulatory approval and commercialization prospects for our most advanced product candidates, and, correspondingly, our business and financial prospects would be negatively impacted.

We have never obtained marketing approval for a product candidate and we may be unable to obtain, or may be delayed in obtaining, marketing approval for our current product candidates or any future product candidates that we, or any collaborators, may develop.

We have never obtained marketing approval for a product candidate. It is possible that the FDA may refuse to accept for substantive review any new drug applications, or NDAs, that we submit for our product candidates or may conclude after review of our data that our application is insufficient to obtain marketing approval of our product candidate. If the FDA does not accept or approve NDAs for any of our product candidates, it may require that we conduct additional clinical trials, preclinical studies or manufacturing validation studies and submit that data before it will reconsider our applications. Depending on the extent of these or any other FDA required trials or studies, approval of any NDA or application that we submit may be delayed by several years, or may require us to expend more resources than we have available. It is also possible that additional trials or studies, if performed and completed, may

not be considered sufficient by the FDA to approve our NDAs. Any delay in obtaining, or an inability to obtain, marketing approvals would prevent us from commercializing our product candidates or any companion diagnostics, generating revenues and achieving and sustaining profitability. If any of these outcomes occurs, we may be forced to abandon our development efforts for our product candidates, which could significantly harm our business.

Even if any product candidates that we, or any collaborators, may develop receive marketing approval, we or others may later discover that the product is less effective than previously believed or causes undesirable side effects that were not previously identified, which could compromise our ability, or that of any collaborators, to market the product.

Clinical trials of any product candidates that we, or any collaborators, may develop will be conducted in carefully defined subsets of patients who have agreed to enter into clinical trials. Consequently, it is possible that our clinical trials, or those of any collaborator, may indicate an apparent positive effect of a product candidate that is greater than the actual positive effect, if any, or alternatively fail to identify undesirable side effects. If, following approval of a product candidate, we, or others, discover that the product is less effective than previously believed or causes undesirable side effects that were not previously identified, any of the following adverse events could occur:

- regulatory authorities may withdraw their approval of the product or seize the product;
- we, or any collaborators, may be required to recall the product, change the way the product is administered or conduct additional clinical trials;
- additional restrictions may be imposed on the marketing of, or the manufacturing processes for, the particular product;
- we may be subject to fines, injunctions or the imposition of civil or criminal penalties;
- regulatory authorities may require the addition of labeling statements, such as a “black box” warning or a contraindication;
- we, or any collaborators, may be required to create a Medication Guide outlining the risks of the previously unidentified side effects for distribution to patients;
- we, or any collaborators, could be sued and held liable for harm caused to patients;
- the product may become less competitive; and
- our reputation may suffer.

Any of these events could harm our business and operations, and could negatively impact our stock price.

Even if our current product candidates, or any future product candidates that we, or any collaborators, may develop receives marketing approval, it may fail to achieve the degree of market acceptance by physicians, patients, third party payors and others in the medical community necessary for commercial success, in which case we may not generate significant revenues or become profitable.

We have never commercialized a product, and even if one of our product candidates is approved by the appropriate regulatory authorities for marketing and sale, it may nonetheless fail to gain sufficient market acceptance by physicians, patients, third party payors and others in the medical community. Physicians are often reluctant to switch their patients from existing therapies even when new and potentially more effective or convenient treatments enter the market. Further, patients often acclimate to the therapy that they are currently taking and do not want to switch unless their physicians recommend switching products or they are required to switch therapies due to lack of reimbursement for existing therapies.

Efforts to educate the medical community and third party payors on the benefits of our product candidates may require significant resources and may not be successful. If any of our product candidates is approved but does not achieve an adequate level of market acceptance, we may not generate significant revenues and we may not become profitable. The degree of market acceptance of our product candidates, if approved for commercial sale, will depend on a number of factors, including:

- the efficacy and safety of the product;
- the potential advantages of the product compared to competitive therapies;
- the prevalence and severity of any side effects;
- whether the product is designated under physician treatment guidelines as a first , second or third line therapy;

- our ability, or the ability of any collaborators, to offer the product for sale at competitive prices;
- the product's convenience and ease of administration compared to alternative treatments;
- the willingness of the target patient population to try, and of physicians to prescribe, the product;
- limitations or warnings, including distribution or use restrictions, contained in the product's approved labeling;
- the strength of sales, marketing and distribution support;

- changes in the standard of care for the targeted indications for the product; and
- availability and amount of coverage and reimbursement from government payors, managed care plans and other third party payors.

If we are unable to establish sales, marketing and distribution capabilities or enter into sales, marketing and distribution arrangements with third parties, we may not be successful in commercializing any product candidates if approved.

We do not have a sales, marketing or distribution infrastructure and have no experience in the sale, marketing or distribution of pharmaceutical products. To achieve commercial success for any approved product, we must either develop a sales and marketing organization or outsource these functions to third parties. We plan to build focused capabilities to commercialize development programs for certain indications where we believe that the medical specialists for the indications are sufficiently concentrated to allow us to effectively promote the product with a targeted sales team. The development of sales, marketing and distribution capabilities will require substantial resources, will be time consuming and could delay any product launch. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing and distribution capabilities is delayed or does not occur for any reason, we could have prematurely or unnecessarily incurred these commercialization costs. This may be costly, and our investment could be lost if we cannot retain or reposition our sales and marketing personnel. In addition, we may not be able to hire or retain a sales force in the United States that is sufficient in size or has adequate expertise in the medical markets that we plan to target. If we are unable to establish or retain a sales force and marketing and distribution capabilities, our operating results may be adversely affected. If a potential partner has development or commercialization expertise that we believe is particularly relevant to one of our products, then we may seek to collaborate with that potential partner even if we believe we could otherwise develop and commercialize the product independently.

In certain indications, we seek to enter into collaborations that we believe may contribute to our ability to advance development and ultimately commercialize our product candidates. We also seek to enter into collaborations where we believe that realizing the full commercial value of our development programs will require access to broader geographic markets or the pursuit of broader patient populations or indications. As a result of entering into arrangements with third parties to perform sales, marketing and distribution services, our product revenues or the profitability of these product revenues may be lower, perhaps substantially lower, than if we were to directly market and sell products in those markets. Furthermore, we may be unsuccessful in entering into the necessary arrangements with third parties or may be unable to do so on terms that are favorable to us. In addition, we may have little or no control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our products effectively.

If we do not establish sales, marketing and distribution capabilities, either on our own or in collaboration with third parties, we will not be successful in commercializing any of our product candidates that receive marketing approval.

If we are unable to successfully develop companion diagnostics for certain of our therapeutic product candidates, or experience significant delays in doing so, we may not realize the full commercial potential of these therapeutics.

A component of our business strategy may be to develop, in collaboration with a third party, companion diagnostics for some of our therapeutic product candidates. There has been limited success to date industry-wide in developing companion diagnostics. To be successful, our collaborator will need to address a number of scientific, technical, regulatory and logistical challenges. We have limited experience in the development of diagnostics and may not be successful in developing appropriate diagnostics to pair with any

of our therapeutic product candidates that receive marketing approval. The FDA and similar regulatory authorities outside the United States are generally expected to regulate companion diagnostics as medical devices. In each case,

companion diagnostics require separate regulatory approval prior to commercialization. For example, BDX004, our companion diagnostic test for ficlatuzumab in our FOCAL study, requires separate approval by the FDA, for which we must rely on Biodesix to obtain. In addition, we require a commercializable companion diagnostic assay to identify patients with low NRP-1 in order to proceed with the development of tivozanib in CRC. We have presented the results from the phase 2 BATON-CRC study and the Company's ongoing assay development efforts to the FDA in connection with our evaluation of a proposed pivotal Phase 3 trial of tivozanib in CRC. In response to questions we posed to the FDA regarding this proposed trial, the FDA suggested that we continue work on the development of our biomarker assay to address variability between assays presented, and that, at present, "insufficient data exists to determine the appropriateness of this [NRP-1 low] subgroup" for the proposed Phase 3 study. As such, we hope to identify a commercially viable assay, which will enable a prospectively defined, randomized Phase 2 study. Given our limited experience in developing diagnostics, we expect to rely in part on third parties for their design, development and manufacture. If we, or any third parties that we engage to assist us, are unable to successfully develop companion diagnostics for our therapeutic product candidates, or experience delays in doing so, the development of our therapeutic product candidates may be adversely affected, our therapeutic product candidates may not receive marketing approval and we may not realize the full commercial potential of any therapeutics that receive marketing approval. As a result, our business would be harmed, possibly materially.

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 will compete with existing, market-leading products.

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 cachexia. In addition, many of these competitors have significantly greater commercial infrastructures than we have. We will not be able to compete successfully unless we effectively:

- design and develop products that are superior to other products in the market in terms of, among other things, both safety and efficacy;
- obtain patent and/or other proprietary protection for our processes and product candidates;
- obtain required regulatory approvals;
- obtain favorable reimbursement, formulary and guideline status; 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 obtain approval, 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.

Even if we, or any collaborators, are able to commercialize any product candidate that we, or they, develop, the product may become subject to unfavorable pricing regulations, third party payor reimbursement practices or healthcare reform initiatives, any of which could harm our business.

The commercial success of our product candidates will depend substantially, both domestically and abroad, on the extent to which the costs of our product candidates will be paid by third party payors, including government health care programs and private health insurers. If coverage is not available, or reimbursement is limited, we, or any collaborators, may not be able to successfully commercialize our product candidates. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us, or any collaborators, to establish or maintain pricing sufficient to realize a sufficient return on our or their investments. In the United States, no uniform policy of coverage and reimbursement for products exists among third party payors and coverage and reimbursement levels for products can differ significantly from payor to payor. As a result, the coverage determination process is often a time consuming and costly process that may require us to provide scientific and clinical support for the use of our products to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance.

There is significant uncertainty related to third party payor coverage and reimbursement of newly approved drugs. Marketing approvals, pricing and reimbursement for new drug products vary widely from country to country. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we, or any collaborators, might obtain marketing approval for a product in a particular country, but then be subject to price regulations that delay commercial launch of the product, possibly for lengthy time periods, which may negatively impact the revenues we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability or the ability of any collaborators to recoup our or their investment in one or more

product candidates, even if our product candidates obtain marketing approval.

Patients who are provided medical treatment for their conditions generally rely on third party payors to reimburse all or part of the costs associated with their treatment. Therefore, our ability, and the ability of any collaborators, to commercialize successfully any of our product candidates will depend in part on the extent to which coverage and adequate reimbursement for these products and related treatments will be available from third party payors. Third party payors decide which medications they will cover and establish reimbursement levels. The healthcare industry is acutely focused on cost containment, both in the United States and elsewhere. Government authorities and other third party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications, which could affect our ability or that of any collaborators to sell our product candidates

profitably. These payors may not view our products, if any, as cost effective, and coverage and reimbursement may not be available to our customers, or those of any collaborators, or may not be sufficient to allow our products, if any, to be marketed on a competitive basis. Cost control initiatives could cause us, or any collaborators, to decrease the price we, or they, might establish for products, which could result in lower than anticipated product revenues. If the prices for our products, if any, decrease or if governmental and other third party payors do not provide coverage or adequate reimbursement, our prospects for revenue and profitability will suffer.

There may also be delays in obtaining coverage and reimbursement for newly approved drugs, and coverage may be more limited than the indications for which the drug is approved by the FDA or comparable foreign regulatory authorities. Moreover, eligibility for reimbursement does not imply that any drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution. Reimbursement rates may vary, by way of example, according to the use of the product and the clinical setting in which it is used. Reimbursement rates may also be based on reimbursement levels already set for lower cost drugs or may be incorporated into existing payments for other services.

In addition, increasingly, third party payors are requiring higher levels of evidence of the benefits and clinical outcomes of new technologies and are challenging the prices charged. Further, the net reimbursement for drug products may be subject to additional reductions if there are changes to laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. An inability to promptly obtain coverage and adequate payment rates from both government funded and private payors for any of our product candidates for which we, or any collaborator, obtain marketing approval could significantly harm our operating results, our ability to raise capital needed to commercialize products and our overall financial condition.

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, product 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.

Risks Related to Our Dependence on Third Parties

We rely on third parties, such as clinical research organizations, or CROs, to conduct 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, in consultation with our collaborators, where applicable, design the clinical trials for our product candidates, but we have relied, and will 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 plan to continue to rely on these third parties to conduct our ongoing any future 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.

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

We do not possess all of the capabilities to fully commercialize any of our product candidates on our own. 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. 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 as needed, including any failure

to deliver sufficient quantities of product candidates in a timely manner, could lead to a delay in, or failure to obtain, regulatory approval of any of our product candidates. In addition, such failure could be the basis for action by the FDA to withdraw approvals for product candidates previously granted to us and for other regulatory action, including recall or seizure, fines, imposition of operating restrictions, total or partial suspension of production or injunctions.

We rely on our manufacturers to purchase from third-party suppliers the materials necessary to produce our product candidates for our clinical studies. There are a small number of suppliers for certain capital equipment and raw materials that we use to manufacture our product candidates. 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 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 in the event that one or more of our product candidates gains marketing approval, third parties with whom we currently work will need to increase their scale of production or we will need to secure alternate suppliers.

If any of our current or future 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.

As part of our business strategy, we plan to enter into additional strategic partnerships in the future. If any current or future strategic partners do not devote sufficient time and resources to its arrangements with us, we may not realize the potential commercial benefits of the arrangement, and our results of operations may be adversely affected. In addition, if any strategic partner were to breach or terminate its arrangements with us, 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 its own, and we may find it difficult to attract a new alliance partner for such product candidate. For example, Biodesix can opt-out of its agreement with us after the completion of the proof of concept trial prior to the first commercial sale of ficlatuzumab, at which point Biodesix would not be responsible for any future costs associated with developing and commercializing ficlatuzumab other than any ongoing clinical studies.

Much of the potential revenue from any strategic partnership we may enter into in the future will likely consist of contingent payments, such as royalties payable on sales of any successfully developed drugs. Any such contingent revenue will depend upon our, and our strategic partners', ability to successfully develop, introduce, market and sell new drugs. In some cases, we will not be involved in these processes, and we will depend entirely on our strategic partners. Any of our future strategic partners may fail to develop or effectively commercialize these drugs because it:

- decides not to devote the necessary resources because of internal constraints, such as limited personnel with the requisite scientific expertise, limited cash resources or specialized equipment limitations, or the belief that other product candidates may have a higher likelihood of obtaining regulatory approval or may potentially generate a greater return on investment;
- does not have sufficient resources necessary to carry the product candidate through clinical development, regulatory approval and commercialization; or
- cannot 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.

Risks Related to Our Intellectual Property Rights

We could be unsuccessful in obtaining adequate patent protection for one or more of our product candidates, which could result in competition and a decrease in the potential market share for our product candidates.

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

Issued patents covering one or more of our products could be found invalid or unenforceable if challenged in patent office proceedings, or 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 one or more statutory requirements for patentability, including, for example, lack of novelty, obviousness, lack of written description or non-enablement. In addition, patent validity challenges may, under certain circumstances, be based upon non-statutory obviousness-type double patenting, which, if successful, could result in a finding that the claims are invalid for obviousness-type double patenting or the loss of patent term, including a patent term adjustment granted by the United States Patent and Trademark Officer, if a terminal disclaimer is filed to obviate a finding of obviousness-type double patenting. 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. Additionally, third parties are able to challenge the validity of issued patents through administrative proceedings in the patent offices of certain countries, including the United States Patent and Trademark Office and the European Patent Office. 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. 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.

With regard to AV-203, we are aware of a third-party United States patent that contains broad claims relating to anti-ErbB3 antibodies. Additionally, we are aware of a United States patent application and foreign counterparts that contains claims to the use of a companion diagnostic in conjunction with AV-203. 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 an 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 our partnerships 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.

An intellectual property litigation could lead to unfavorable publicity that could harm our reputation and cause 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. In such event, the market price of our common stock may decline.

AV-380 and tivozanib are protected by patents exclusively licensed from other companies or institutions. If the licensors terminate the licenses or fail to maintain or enforce the underlying patents, our competitive position would be harmed and our partnerships could be terminated.

Certain of our product candidates and out-licensing arrangements depend on patents and/or patent applications owned by other companies or institutions with which we have entered into intellectual property licenses. In particular, we hold exclusive licenses from St. Vincent’s for therapeutic applications that benefit from inhibition or decreased expression or activity of MIC-1, which we refer to as GDF15 and which we used in our AV-380 program, and from KHK for tivozanib. We may 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, a licensor could claim that we have materially breached a license agreement and terminate the license, thereby removing our or our licensees' ability to obtain regulatory approval for and to market any product covered by such license. 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, identical products. In addition, the partners to which we have sublicensed certain rights under these licenses, including Novartis and Pharmstandard, would likely have grounds for terminating our partnerships if these licenses are terminated or the underlying patents are not maintained or enforced. This could have a material adverse effect on our results of operations, our competitive business position and our business prospects.

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

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

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

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

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

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

- Others may be able to make compounds that are similar to our product candidates but that are not covered by the claims of the patents that we own or have exclusively licensed.
- We or our licensors or strategic partners might not have been the first to make the inventions covered by the issued patent or pending patent application that we own or have exclusively licensed.
- We or our licensors or strategic partners might not have been the first to file patent applications covering certain of our inventions.
- Others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights.
- It is possible that our pending patent applications will not lead to issued patents.
    - Issued patents that we own or have exclusively licensed may not provide us with a competitive advantage; for example, our issued patents may not be broad enough to prevent the commercialization of competitive antibodies that are biosimilar to one or more of our antibody products, or may be held invalid or unenforceable, as a result of legal challenges by our competitors.
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Our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets.

- We may not develop additional proprietary technologies that are patentable.
- The patents of others may have an adverse effect on our business.

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

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

Risks Related to Regulatory Approval and Marketing of Our Product Candidates and Other Legal Compliance Matters

Even if we complete the necessary preclinical studies and clinical trials, the marketing approval process is expensive, time-consuming and uncertain and may prevent us from obtaining approvals for the commercialization of some or all of our product candidates. If we or our collaborators are not able to obtain, or if there are delays in obtaining, required regulatory approvals, we or they will not be able to commercialize our product candidates, and our ability to generate revenue will be materially impaired.

Our product candidates and the activities associated with their development and commercialization, including their design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale and distribution, export and import, are subject to comprehensive regulation by the FDA and other regulatory agencies in the United States and by the European Medicines Agency and comparable regulatory authorities in other countries. Failure to obtain marketing approval for a product candidate will prevent us from commercializing the product candidate. We and our collaborators have not received approval to market any of our product candidates from regulatory authorities in any jurisdiction. We have only limited experience in filing and supporting the applications necessary to gain marketing approvals and expect to rely on third-party contract research organizations to assist us in this process.

Securing marketing approval requires the submission of extensive preclinical and clinical data and supporting information to the various regulatory authorities for each therapeutic indication to establish the product candidate’s safety and efficacy. Securing regulatory approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the relevant regulatory authority. Our product candidates may not be effective, may be only moderately effective or may prove to have undesirable or unintended side effects, toxicities or other characteristics that may preclude our obtaining marketing approval or prevent or limit commercial use.

The process of obtaining marketing approvals, both in the United States and abroad, is expensive, may take many years if additional clinical trials are required, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidates involved. Changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted product application, may cause delays in the approval or rejection of an application. The FDA and comparable authorities in other countries have substantial discretion in

the approval process and may refuse to accept any application or may decide that our data is insufficient for approval and require additional preclinical, clinical or other studies. In addition, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit or prevent marketing approval of a product candidate. Any marketing approval we or our collaborators ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved product not commercially viable.

Accordingly, if we or our collaborators experience delays in obtaining approval or if we or they fail to obtain approval of our product candidates, the commercial prospects for our product candidates may be harmed and our ability to generate revenues will be materially impaired.

Failure to obtain marketing approval in foreign jurisdictions would prevent our product candidates from being marketed in such jurisdictions.

In order to market and sell our medicines in the European Union and many other jurisdictions, we or our third party collaborators must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval may differ substantially from that required to obtain FDA approval. The regulatory approval process outside the United States generally includes

all of the risks associated with obtaining FDA approval. In addition, in many countries outside the United States, a product be approved for reimbursement before the product can be approved for sale in that country. We or our third party collaborators may not obtain approvals from regulatory authorities outside the United States on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. We may not be able to file for marketing approvals and may not receive necessary approvals to commercialize our products in any market.

We, or any future collaborators, may not be able to obtain orphan drug designation or orphan drug exclusivity for our product candidates and, even if we do, that exclusivity may not prevent the FDA or the EMA from approving other competing products.

Regulatory authorities in some jurisdictions, including the United States and Europe, may designate drugs and biologics for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals annually in the United States. We, or any future collaborators, may seek orphan drug designations for other product candidates and may be unable to obtain such designations.

Even if we, or any future collaborators, obtain orphan drug designation for a product candidate, we, or they, may not be able to obtain orphan drug exclusivity for that candidate. Generally, a product with orphan drug designation only becomes entitled to orphan drug exclusivity if it receives the first marketing approval for the indication for which it has such designation, in which case the FDA or the EMA will be precluded from approving another marketing application for the same product for that indication for the applicable exclusivity period. The applicable exclusivity period is seven years in the United States and ten years in Europe. The European exclusivity period can be reduced to six years if a product no longer meets the criteria for orphan drug designation or if the product is sufficiently profitable so that market exclusivity is no longer justified. Orphan drug exclusivity may be lost if the FDA or the EMA determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the product to meet the needs of patients with the rare disease or condition.

Even if we, or any future collaborators, obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different products can be approved for the same condition. Even after an orphan drug is approved, the FDA can subsequently approve the same drug or biologic for the same condition if the FDA concludes that the later product is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care.

Even if we, or any current or future collaborators, obtain marketing approvals for our product candidates, the terms of approvals and ongoing regulation of our products may limit how we, or they, manufacture and market our products, which could materially impair our ability to generate revenue.

Once marketing approval has been granted, an approved product and its manufacturer and marketer are subject to ongoing review and extensive regulation. We, and any current or future collaborators, must therefore comply with requirements concerning advertising and promotion for any of our product candidates for which we or they obtain marketing approval. Promotional communications with respect to prescription products are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the product's approved labeling. Thus, we and any current or future collaborators will not be able to promote any products we develop for indications or uses for which they are not approved.

In addition, manufacturers of approved products and those manufacturers' facilities are required to comply with extensive FDA requirements, including ensuring that quality control and manufacturing procedures conform to cGMPs, which include requirements relating to quality control and quality assurance as well as the corresponding maintenance of records and documentation and reporting requirements. We, our contract manufacturers, any current

or future collaborators and their contract manufacturers could be subject to periodic unannounced inspections by the FDA to monitor and ensure compliance with cGMPs.

Accordingly, assuming we, or any current or future collaborators, receive marketing approval for one or more of our product candidates, we, and any current or future collaborators, and our and their contract manufacturers will continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production, product surveillance and quality control.

If we, and any current or future collaborators, are not able to comply with post-approval regulatory requirements, we, and any current or future collaborators, could have the marketing approvals for our products withdrawn by regulatory authorities and our, or any current or future collaborators', ability to market any products could be limited, which could adversely affect our ability to achieve or sustain profitability. Further, the cost of compliance with post-approval regulations may have a negative effect on our operating results and financial condition.

Any product candidate for which we or our collaborators obtain marketing approval could be subject to restrictions or withdrawal from the market and we may be subject to substantial penalties if we fail to comply with regulatory requirements or if we experience unanticipated problems with our product candidates, when and if any of them are approved.

Any product candidate for which we or our collaborators obtain marketing approval, along with the manufacturing processes, post-approval clinical data, labeling, advertising and promotional activities for such product, will be subject to continual requirements of and review by the FDA and other regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, registration and listing requirements, cGMP requirements relating to quality control and manufacturing, quality assurance and corresponding maintenance of records and documents, and requirements regarding the distribution of samples to physicians and recordkeeping. Even if marketing approval of a product candidate is granted, the approval may be subject to limitations on the indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for costly post-marketing testing and surveillance to monitor the safety or efficacy of the medicine, including the requirement to implement a risk evaluation and mitigation strategy.

The FDA and other agencies, including the Department of Justice, or the DOJ, closely regulate and monitor the post-approval marketing and promotion of products to ensure that they are marketed and distributed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA and DOJ impose stringent restrictions on manufacturers' communications regarding off-label use and if we do not market our products for their approved indications, we may be subject to enforcement action for off-label marketing. Violations of the Federal Food, Drug, and Cosmetic Act and other statutes, including the False Claims Act, relating to the promotion and advertising of prescription products may lead to investigations and enforcement actions alleging violations of federal and state health care fraud and abuse laws, as well as state consumer protection laws.

In addition, later discovery of previously unknown adverse events or other problems with our products, manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may yield various results, including:

- restrictions on such products, manufacturers or manufacturing processes;
- restrictions on the labeling or marketing of a product;
- restrictions on distribution or use of a product;
- requirements to conduct post-marketing studies or clinical trials;
- warning letters or untitled letters;
- withdrawal of the products from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recall of products;
- damage to relationships with any potential collaborators;
- unfavorable press coverage and damage to our reputation;
- fines, restitution or disgorgement of profits or revenues;
- suspension or withdrawal of marketing approvals;
- refusal to permit the import or export of our products;
- product seizure;
- injunctions or the imposition of civil or criminal penalties; and
- litigation involving patients using our products.

Non-compliance with European Union requirements regarding safety monitoring or pharmacovigilance, and with requirements related to the development of products for the pediatric population, can also result in significant financial penalties. Similarly, failure to comply with the European Union's requirements regarding the protection of personal information can also lead to significant penalties and sanctions.

Our relationships with healthcare providers, physicians and third party payors will be subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which, in the event of a violation, could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.

Healthcare providers, physicians and third party payors will play a primary role in the recommendation and prescription of any product candidates for which we obtain marketing approval. Our future arrangements with healthcare providers, physicians and third party payors may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute any products for which we obtain marketing approval. Restrictions under applicable federal and state healthcare laws and regulations include the following:

- the federal Anti-Kickback Statute prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, order or recommendation or arranging of, any good or service, for which payment may be made under a federal healthcare program such as Medicare and Medicaid;
- the federal False Claims Act imposes criminal and civil penalties, including through civil whistleblower or qui tam actions, against individuals or entities for, among other things, knowingly presenting, or causing to be presented, false or fraudulent claims for payment by a federal healthcare program or making a false statement or record material to payment of a false claim or avoiding, decreasing or concealing an obligation to pay money to the federal government, with potential liability including mandatory treble damages and significant per-claim penalties, currently set at $5,500 to $11,000 per false claim;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act and its implementing regulations, also imposes obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;
- the federal Physician Payments Sunshine Act requires applicable manufacturers of covered products to report payments and other transfers of value to physicians and teaching hospitals, with data collection beginning in August 2013; and
- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws and transparency statutes, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third party payors, including private insurers.

Some state laws require pharmaceutical companies to comply with the pharmaceutical industry’s voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government and may require product manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures. State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

If our operations are found to be in violation of any of the laws described above or any governmental regulations that apply to us, we may be subject to penalties, including civil and criminal penalties, damages, fines and the curtailment or restructuring of our operations. Any penalties, damages, fines, curtailment or restructuring of our operations could adversely affect our financial results. We are developing and implementing a corporate compliance program designed to ensure that we will market and sell any future products that we successfully develop from our product candidates in compliance with all applicable laws and regulations, but we cannot guarantee that this program will protect 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.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, imprisonment, exclusion of products from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations. If any of the physicians or other healthcare providers or entities with whom we expect to do business is found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

Current and future legislation may increase the difficulty and cost for us and any collaborators to obtain marketing approval of our other product candidates and affect the prices we, or they, may obtain.

In the United States and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could, among other things, prevent or delay marketing approval of our other product candidates, restrict or regulate post-approval activities and affect our ability, or the ability of any collaborators, to profitably sell any products for which we, or they, obtain marketing approval. We expect that current laws, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we, or any collaborators, may receive for any approved products.

For example, in March 2010, President Obama signed into law the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, or collectively the PPACA. Among the provisions of the PPACA of potential importance to our business and our product candidates are the following:

- an annual, non-deductible fee on any entity that manufactures or imports specified branded prescription products and biologic agents;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program;
- a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for products that are inhaled, infused, instilled, implanted or injected;
- expansion of healthcare fraud and abuse laws, including the civil False Claims Act and the federal Anti-Kickback Statute, new government investigative powers and enhanced penalties for noncompliance;
- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts off negotiated prices of applicable brand products to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient products to be covered under Medicare Part D;
- extension of manufacturers' Medicaid rebate liability to individuals enrolled in Medicaid managed care organizations;
- expansion of eligibility criteria for Medicaid programs;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- new requirements to report certain financial arrangements with physicians and teaching hospitals;
- a new requirement to annually report product samples that manufacturers and distributors provide to physicians;
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research;
- a new Independent Payment Advisory Board, or IPAB, which has authority to recommend certain changes to the Medicare program to reduce expenditures by the program that could result in reduced payments for prescription products; and
- established the Center for Medicare and Medicaid Innovation within CMS to test innovative payment and service delivery models.

Other legislative changes have been proposed and adopted since the PPACA was enacted. These changes include the Budget Control Act of 2011, which, among other things, led to aggregate reductions to Medicare payments to providers of up to 2% per fiscal year that started in 2013 and, due to subsequent legislation, will continue until 2025. In addition, the American Taxpayer Relief Act of 2012, among other things, reduced Medicare payments to several providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our product candidates for which regulatory approval is obtained.

We expect that the PPACA, as well as other healthcare reform measures that may be adopted in the future, may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, new payment methodologies and in additional downward pressure on the price that we receive for any approved product. Any

reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our products. Moreover, legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. We cannot be sure whether additional legislative changes will be enacted, or whether the FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our product candidates, if any, may be. In addition, increased scrutiny by the United States Congress of

the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us and any collaborators to more stringent product labeling and post-marketing testing and other requirements.

Laws and regulations governing any international operations we may have in the future may preclude us from developing, manufacturing and selling certain products outside of the United States and require us to develop and implement costly compliance programs.

If we expand our operations outside of the United States, we must dedicate additional resources to comply with numerous laws and regulations in each jurisdiction in which we plan to operate. The Foreign Corrupt Practices Act, or FCPA, prohibits any U.S. individual or business from paying, offering, authorizing payment or offering of anything of value, directly or indirectly, to any foreign official, political party or candidate for the purpose of influencing any act or decision of the foreign entity in order to assist the individual or business in obtaining or retaining business. The FCPA also obligates companies whose securities are listed in the United States to comply with certain accounting provisions requiring the company to maintain books and records that accurately and fairly reflect all transactions of the corporation, including international subsidiaries, and to devise and maintain an adequate system of internal accounting controls for international operations.

Compliance with the FCPA is expensive and difficult, particularly in countries in which corruption is a recognized problem. In addition, the FCPA presents particular challenges in the pharmaceutical industry, because, in many countries, hospitals are operated by the government, and doctors and other hospital employees are considered foreign officials. Certain payments to hospitals in connection with clinical trials and other work have been deemed to be improper payments to government officials and have led to FCPA enforcement actions.

Various laws, regulations and executive orders also restrict the use and dissemination outside of the United States, or the sharing with certain non-U.S. nationals, of information classified for national security purposes, as well as certain products and technical data relating to those products. If we expand our presence outside of the United States, it will require us to dedicate additional resources to comply with these laws, and these laws may preclude us from developing, manufacturing, or selling certain products and product candidates outside of the United States, which could limit our growth potential and increase our development costs.

The failure to comply with laws governing international business practices may result in substantial civil and criminal penalties and suspension or debarment from government contracting. The Securities and Exchange Commission, or SEC, also may suspend or bar issuers from trading securities on U.S. exchanges for violations of the FCPA's accounting provisions.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on our business.

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. From time to time and in the future, our operations may involve the use of hazardous and flammable materials, including chemicals and biological materials, and may also produce hazardous waste products. Even if we contract with third parties for the disposal of these materials and waste products, we cannot completely eliminate the risk of contamination or injury resulting from these materials. In the event of contamination or injury resulting from the use or disposal of our hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties for failure to comply with such laws and regulations.

We maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, but this insurance may not provide adequate coverage against potential liabilities. However, we do not maintain insurance for environmental liability or toxic tort claims that

may be asserted against us.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. Current or future environmental laws and regulations may impair our research, development or production efforts, which could adversely affect our business, financial condition, results of operations or prospects. In addition, failure to comply with these laws and regulations may result in substantial fines, penalties or other sanctions.

Governments outside the United States tend to impose strict price controls, which may adversely affect our revenues, if any.

In some countries, such as the countries of the European Union, the pricing of prescription pharmaceuticals is subject to governmental control and access. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain reimbursement or pricing approval in some countries, we, or any current or future collaborators, may be required to conduct a clinical trial that compares the cost-effectiveness of our product to other

available therapies. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be materially harmed.

We rely significantly upon information technology and any failure, inadequacy, interruption or security lapse of that technology, including any cyber security incidents, could harm our ability to operate our business effectively.

Despite the implementation of security measures, our internal computer systems and those of third parties with which we contract are vulnerable to damage from cyber-attacks, computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. System failures, accidents or security breaches could cause interruptions in our operations, and could result in a material disruption of our clinical and commercialization activities and business operations, in addition to possibly requiring substantial expenditures of resources to remedy. The loss of clinical trial data could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate public disclosure of confidential or proprietary information, we could incur liability and our product development and commercialization efforts could be delayed.

Risks Related to Employee Matters and Managing Growth

If we fail to attract and keep senior management, 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 personnel. We are highly dependent upon our senior management, as well as others on our management team. The reduction in force related to the restructuring we completed this year could make it more difficult to retain or attract employees in the future. The loss of services of employees, and in particular, of a member of management could delay or prevent our ability to successfully maintain or enter into new licensing arrangements or collaborations, the successful development of our product candidates, the completion of our planned clinical trials or the commercialization of our product candidates. We do not carry “key person” insurance covering any members of our senior management. Our employment arrangements with all of these individuals are “at will,” meaning they or we can terminate their service at any time.

We face intense competition for qualified individuals from numerous pharmaceutical and biotechnology companies, universities, governmental entities and other research institutions, many of which have substantially greater resources with which to reward qualified individuals than we do. We may face challenges in retaining our existing senior management and key employees and recruiting new employees to join our company as our business needs change. We may be unable to attract and retain suitably qualified individuals, and our failure to do so could have an adverse effect on our ability to implement our future business plans.

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.

Risks Related to Ownership of Our Common Stock

If we fail to meet the requirements for continued listing on the NASDAQ Global Select Market, our common stock could be delisted from trading, which would decrease the liquidity of our common stock and our ability to raise additional capital.

Our common stock is currently listed for quotation on the NASDAQ Global Select Market. We are required to meet specified financial requirements in order to maintain our listing on the NASDAQ Global Select Market. One such requirement is that we maintain a minimum bid price of at least $1.00 per share for our common stock. If our bid price falls below $1.00 per share for 30 consecutive business days, we will receive a deficiency notice from NASDAQ advising us that we have 180 days to regain compliance by maintaining a minimum bid price of at least $1.00 for a minimum of ten consecutive business days. Under certain circumstances, NASDAQ could require that the minimum bid price exceed $1.00 for more than ten consecutive days before determining that a company complies. If in the future we fail to satisfy the NASDAQ Global Select Market's continued listing requirements, we may transfer to the NASDAQ Capital Market, which generally has lower financial requirements for initial listing, to avoid delisting, or, if we fail to meet its listing requirements, the OTC Bulletin Board. Any potential delisting of our common stock from the NASDAQ Global Select Market would make it more difficult for our stockholders to sell our stock in the public market and would likely result in decreased liquidity and increased volatility for 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. A significant decline in the value of our stock price could also result in securities class-action litigation against us.

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, 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;
- actual or anticipated changes in earnings estimates, development timelines or recommendations by securities analysts;
- general economic and market conditions and other factors that may be unrelated to our operating performance or the operating performance of our competitors, including changes in market valuations of similar companies; and
- sales of common stock by us or our stockholders in the future, as well as the overall trading volume of our common stock.

In addition, the stock market in general and the market for biotechnology and biopharmaceutical companies in particular have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of those companies. These broad market and industry factors may seriously harm the market price of our common stock, regardless of our operating performance.

Periods of volatility in the market for a company's stock are often followed by litigation against the company. For example, since our May 2, 2013 announcement regarding the vote of the Oncologic Drugs Advisory Committee of the

FDA, we and certain of our former officers and directors have been involved in a number of legal proceedings, including those described below under the heading “Legal Proceedings” in Part I—Item 3 of this Form 10-K. These proceedings and other similar 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.

We may not achieve 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 expected timing for certain accomplishments, such as the initiation and completion of clinical trials, filing and approval of regulatory applications for 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 collaborators' preclinical studies or clinical trials, the amount of time, effort and resources committed to our programs by us and our current and potential 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 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 collaborators will make regulatory submissions or receive regulatory approvals as planned or that we or our current and potential 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 the milestones described above as planned, our business could be materially adversely affected and the price of our common stock could decline.

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

Our management has broad discretion on where and how to use our cash and cash equivalents and you will be relying on the judgment of our management regarding the application of our available cash and cash equivalents to fund our operations. Our management might not apply our cash or cash equivalents in ways that increase the value of your investment. We expect to use a substantial portion of our cash to fund existing and future research and development of our preclinical and clinical product candidates, 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.

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 our preclinical and clinical development candidates;
- any intellectual property infringement lawsuit or other litigation in which we may become involved;
- the implementation of our current 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;
- costs associated with lawsuits against us, including the current purported class action and derivative lawsuits described elsewhere in this report under "Part I, Item 3—Legal Proceedings;"
- changes in our loan agreement with Hercules, including the existence of any event of default that may accelerate payments due thereunder; 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 volatility, and in some cases, disruptions, over the past several years, in many cases, over extended periods. Although certain of these trends have recently showed signs of reversing, there can be no assurance that rapid or extended periods of deterioration in credit and financial markets and confidence in economic conditions will not occur. Our general business strategy may be adversely affected by external economic conditions and a volatile business environment or unpredictable and unstable market conditions. If the equity and credit markets are

not favorable at any time we seek to raise capital, it may make any necessary debt or equity financing more difficult, more costly, and more dilutive. Failure to secure any necessary financing in a timely manner and on favorable terms could have a material adverse effect on our growth strategy, financial performance and stock price and could require us to delay or abandon clinical development plans. In addition, there is a risk that one or more of our current service providers, manufacturers or other partners may not survive economically turbulent times, which could directly affect our ability to attain our operating goals on schedule and on budget.

At December 31, 2015, we had $34.1 million of cash, cash equivalents and marketable securities consisting of cash on deposit with banks, money market funds, U.S. government agency securities, 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. However, no assurance can be given that deterioration in conditions of the global credit and financial markets would not negatively impact our current portfolio of cash equivalents or our ability to meet our financing objectives. Dislocations in the credit market may adversely impact the value and/or liquidity of cash equivalents owned by us.

There is a possibility that our stock price may decline because of volatility of the stock market and general economic conditions.

Future sales of shares of our common stock, including shares issued upon the exercise of currently outstanding options, 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. The exercise of these options 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.

If securities or industry analysts do not publish research or publish inaccurate or unfavorable research about our business, our share price and trading volume could decline.

The trading market for our common stock may depend in part on the research and reports that securities or industry analysts publish about us or our business. We do not have any control over these analysts. There can be no assurance that analysts will cover us, or provide favorable coverage. A lack of research coverage may negatively impact the market price of our common stock. To the event we do have analyst coverage, if one or more analysts downgrade our stock or change their opinion of our stock, our share price would likely decline. In addition, if one or more analysts cease coverage of our company or fail to regularly publish reports on us, we could lose visibility in the financial markets, which could cause our share price or trading volume to decline.

A decline in our stock price may affect future fundraising efforts.

We currently have no product revenues, and depend entirely on funds raised through other sources. One source of such funding is future debt and/or equity offerings. Our ability to raise funds in this manner depends upon, among other things, our stock price, which may be affected by capital market forces, evaluation of our stock by securities analysts, product development success (or failure), and internal management operations and controls.

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.

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 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.

We might not be able to utilize a significant portion of our net operating loss carryforwards and research and development tax credit carryforwards.

As of December 31, 2015, we had federal and state net operating loss carryforwards of $444.5 million and $338.7 million, respectively, and federal and state research and development tax credit carryforwards of $10.1 million and $4.0 million, respectively, each of which if not utilized will expire at various dates through 2035. These net operating loss and tax credit carryforwards could expire unused and be unavailable to offset future income tax liabilities. In addition, under Section 382 of the Internal Revenue Code of 1986, as amended, and corresponding provisions of state law, if a corporation undergoes an "ownership change," which is generally defined as a greater than 50% change, by value, in its equity ownership over a three year period, the corporation's ability to use its pre change net operating loss carryforwards and other pre change tax attributes to offset its post change income may be limited. We may experience ownership changes in the future as a result of subsequent shifts in our stock ownership, some of which may be outside of our control. We have not conducted a detailed study to document whether our historical activities qualify to support the research and development credit carryforwards. A detailed study could result in adjustment to our research and development credit carryforwards. If we determine that an ownership change has occurred and our ability to use our historical net operating loss and tax credit carryforwards is materially limited, or if our research and development carryforwards are adjusted, it would harm our future operating results by effectively increasing our future tax obligations.

ITEM 1B. Unresolved Staff Comments

None.

ITEM 2. Properties

We sublease our principal facilities, which consist of approximately 5,000 square feet of office space located at 1 Broadway, Cambridge, Massachusetts. Our lease arrangement is cancellable with 30 days' notice to our landlord. We believe that our existing facilities are sufficient for our current needs for the foreseeable future.

ITEM 3. Legal Proceedings

Two class action lawsuits have been filed against us and certain of our former officers and members of our board of directors, (Tuan Ha-Ngoc, David N. Johnston, William Slichenmyer and Ronald DePinho), in the United States District Court for the District of Massachusetts, one captioned Paul Sanders v. Aveo Pharmaceuticals, Inc., et al., No. 1:13-cv-11157-JLT, filed on May 9, 2013, and the other captioned Christine Krause v. AVEO Pharmaceuticals, Inc., et al., No. 1:13-cv-11320-JLT, filed on May 31, 2013. On December 4, 2013, the District Court consolidated the complaints as In re AVEO Pharmaceuticals, Inc. Securities Litigation et al., No. 1:13-cv-11157-DJC, and an amended complaint was filed on February 3, 2014. The amended complaint purported to be brought on behalf of shareholders who purchased our common stock between January 3, 2012 and May 1, 2013. The amended complaint generally alleged that we and certain of our present and former officers and directors violated Sections 10(b) and/or 20(a) of the Securities Exchange Act of 1934 and Rule 10b-5 promulgated thereunder by making allegedly false and/or misleading statements concerning the phase 3 trial design and results for our TIVO-1 study in an effort to lead investors to believe

that the drug would receive approval from the FDA. The lawsuit seeks unspecified damages, interest, attorneys' fees, and other costs. The consolidated amended complaint was dismissed without prejudice on March 20, 2015, and the lead plaintiffs then filed a second amended complaint bringing similar allegations. We moved to dismiss again, and after a second round of briefing and oral argument, the court ruled in our favor and dismissed the second amended complaint with prejudice on November 18, 2015. The lead plaintiffs have appealed the court's decision to the United States Court of Appeals for the First Circuit. We deny any allegations of wrongdoing and intend to continue to vigorously defend against this lawsuit. However, there is no assurance that we will be successful in our defense or that insurance will be available or adequate to fund any settlement or judgment or the litigation costs of the action. Moreover, we are unable to predict the outcome or reasonably estimate a range of possible loss at this time.

On April 4, 2014, Karen J. van Ingen, a purported purchaser of AVEO stock, filed a derivative complaint allegedly on behalf of AVEO in the United States District Court for the District of Massachusetts, Civil Action No. 1:14-cv-11672-DJC, naming AVEO, as a nominal defendant and also naming as defendants present and former members of our board of directors, including Tuan Ha-Ngoc, Henri A. Termeer, Kenneth M. Bate, Anthony B. Evnin, Robert Epstein, Raju Kucherlapati, Robert C. Young, and Kenneth E. Weg. The complaint alleged breach of fiduciary duty and abuse of control between January 2012 and May 2013 with respect to allegedly misleading statements and omissions regarding tivozanib. The lawsuit seeks, among other relief, unspecified damages, costs and expenses, including attorneys' fees, an order requiring us to implement certain corporate governance reforms, restitution from the defendants and such other relief as the court might find just and proper. We filed a motion to dismiss the derivative complaint, and after briefing and oral argument, on March 18, 2015 the Court ruled in our favor and dismissed the case with prejudice. The plaintiff then filed a motion seeking to vacate the Court's order of dismissal and permit filing of an amended complaint, which we opposed, and which the Court denied on June 30, 2015. The plaintiff has appealed the Court's decision to the United States Court of Appeals for the First Circuit. We deny any allegations of wrongdoing and intend to continue to vigorously defend this lawsuit. However, there

is no assurance that we will be successful in our defense or that insurance will be available or adequate to fund any settlement or judgment or the litigation costs of this action. Moreover, we are unable to predict the outcome or reasonably estimate a range of possible loss at this time.

On July 3, 2013, the staff (the "SEC Staff") of the United States Securities and Exchange Commission (the "Commission") served a subpoena on us for documents and information concerning tivozanib, including related communications with the FDA, investors and others. We have fully cooperated with the inquiry. In September 2015, the SEC Staff invited us to discuss the settlement of potential claims that the SEC Staff may recommend that the Commission bring against us asserting that we violated federal securities laws by omitting to disclose to investors the recommendation made to us by the staff of the U.S. Food and Drug Administration, on May 11, 2012, that we conduct an additional clinical trial with respect to tivozanib. Based on the progress in the settlement process thus far, we believe that we could potentially settle with the SEC for a total amount of $4,000,000. There can be no assurance, however, that a settlement will be approved by the Commission, or that any settlement on terms agreeable to us will be achieved. If settlement discussions conclude without a settlement proposal that is acceptable to the Commission and us, the Commission may authorize the SEC Staff to pursue claims against us. There can be no assurance that we will be able to resolve the potential claims of the Commission or that any settlement will not have a material adverse impact on our ability to execute on our proposed plans or on our financial position or results of operations.

The SEC Staff also invited three of our former officers to discuss the settlement of potential claims that the SEC Staff may recommend that the Commission bring against them. We are not a party to any discussions between the SEC Staff and the former officers, and we can make no assurance regarding such potential claims.

Refer to Footnote 16 in the Notes to Consolidated Financial Statements below for further discussion.

ITEM 4. Mine Safety Disclosures

Not applicable.

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 is traded on the NASDAQ Global Select Market under the symbol "AVEO". The following table sets forth the high and low sale prices per share for our common stock for the periods indicated:

	High	Low
2014		
First Quarter	$2.07	$1.49
Second Quarter	$1.85	$1.00
Third Quarter	$1.92	$1.06
Fourth Quarter	$1.19	$0.61

	High	Low
2015		
First Quarter	$2.02	$0.78
Second Quarter	$3.50	$1.16
Third Quarter	$2.59	$1.14
Fourth Quarter	$1.47	$0.92

Holders

At March 9, 2016, there were approximately 48 holders of record of our common stock. We believe that the number of beneficial owners of our common stock at that date was substantially greater.

Dividends

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

Securities Authorized for Issuance under Equity Compensation Plans

The information required by this item will be set forth in the definitive proxy statement we will file in connection with our 2016 Annual Meeting of Stockholders and is incorporated by reference herein.

Purchase of Equity Securities

We did not purchase any of our equity securities during the period covered by this Annual Report on Form 10-K.

Recent Sales of Unregistered Securities

We did not issue any unregistered securities during the period covered by this Annual Report on Form 10-K.

Comparative Stock Performance Graph

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

The graph below matches AVEO Pharmaceuticals, Inc.'s cumulative 5-Year total shareholder return on common stock with the cumulative total returns of the NASDAQ Composite index and the NASDAQ Biotechnology index. The graph tracks the performance of a $100 investment in our common stock and in each index (with the reinvestment of all dividends) from 12/31/2010 to 12/31/2015.

The stock price performance included in this graph is not necessarily indicative of future stock price performance.

Company/Market/Peer Group	12/2010	12/2011	12/2012	12/2013	12/2014	12/2015
AVEO Pharmaceuticals	$100.00	$117.65	$55.06	$12.52	$5.75	$8.62
NASDAQ Composite Index	$100.00	$100.53	$116.92	$166.19	$188.78	$199.95
NASDAQ Biotechnology Index	$100.00	$113.92	$153.97	$263.29	$348.49	$369.06

ITEM 6. Selected Financial Data

The following selected consolidated financial data should be read in conjunction with our Consolidated Financial Statements and the Accompanying Notes thereto and Management's Discussion and Analysis of Financial Condition and Results of Operations included elsewhere in this Annual Report on Form 10-K. The Balance Sheet Data at December 31, 2015 and 2014 and the Statement of Operations Data for each of the three years in the period ended December 31, 2015 have been derived from our audited Consolidated Financial Statements for such years, included elsewhere in this Annual Report on Form 10-K. The Balance Sheet Data at December 31, 2013, 2012 and 2011, and the Statement of Operations Data for each of the two years in the period ended December 31, 2012 have been derived from the audited Consolidated Financial Statements for such years not included in this Annual Report on Form 10-K.

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

	Years Ended December 31,				
	2015	2014	2013	2012	2011
	(in thousands, except per share data)				
Statement of operations data:					
Revenue	$19,024	$18,123	$1,293	$19,286	$164,849
Operating expenses:					
Research and development	12,875	38,254	68,468	91,358	101,735
General and administrative	14,217	18,589	28,712	36,932	29,167
Restructuring and lease exit	4,358	11,729	8,017	2,633	—
Total operating expenses	31,450	68,572	105,197	130,923	130,902
(Loss) income from operations	(12,426)	(50,449)	(103,904)	(111,637)	33,947
Other income and expense:					
Other (expense) income, net	(289)	66	(123)	247	10
Interest expense	(2,307)	(2,388)	(3,127)	(3,501)	(3,836)
Interest income	21	32	125	497	527
Other expense, net	(2,575)	(2,290)	(3,125)	(2,757)	(3,299)
Net (loss) income before benefit for income taxes	(15,001)	(52,739)	(107,029)	(114,394)	30,648
Net (loss) income	$(15,001)	$(52,739)	$(107,029)	$(114,394)	$30,648
Net (loss) income per share—basic	$(0.27)	$(1.01)	$(2.10)	$(2.64)	$0.77
Weighted average number of common shares used in net (loss) income per share calculation—basic	55,701	52,289	50,928	43,374	39,715
Net (loss) income per share—diluted	$(0.27)	$(1.01)	$(2.10)	$(2.64)	$0.74
Weighted average number of common shares and dilutive common share equivalents used in net (loss) income per share calculation—diluted	55,701	52,289	50,928	43,374	41,473

	As of December 31,				
	2015	2014	2013	2012	2011
	(in thousands)				
Balance sheet data:					
Cash, cash equivalents, and marketable securities	$34,135	$52,306	$118,506	$160,602	$275,440
Working capital	27,978	18,773	97,511	151,551	199,786
Total assets	40,542	70,662	146,346	207,469	295,050
Loans payable, including current portion, net of discount	9,471	20,652	19,205	26,037	24,170
Accumulated deficit	(495,029)	(480,028)	(427,289)	(320,260)	(205,866)
Total stockholders' equity	17,227	20,606	69,938	118,938	223,541

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

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

Overview

We are a biopharmaceutical company dedicated to advancing a broad portfolio of targeted therapeutics for oncology and other areas of unmet medical need. Our proprietary platform has delivered unique insights into cancer and related diseases. Our strategy is to leverage these biomarker insights and partner resources to advance the development of our clinical pipeline. We are focused on developing our lead candidate tivozanib in North America as a treatment for Renal Cell Carcinoma and other cancers. We have entered into partnerships to fund the further development of three of our four clinical stage assets, including AV-380, ficlatuzumab, and tivozanib in non-oncologic indications worldwide and oncology indications outside North America. We are also seeking a partnership for AV-203, our fourth development program. These programs and partnerships are described as follows:

- Tivozanib: Tivozanib is a potent, selective, long half-life vascular endothelial growth factor ("VEGF") tyrosine kinase inhibitor ("TKI") of VEGF receptors 1, 2 and 3. In 2006, we acquired the exclusive rights to develop and commercialize tivozanib in all countries outside of Asia under a license from Kyowa Hakko Kirin Co., Ltd. (formerly Kirin Brewery Co. Ltd.), or KHK. We have programs to evaluate tivozanib in several tumor types, including renal cell, colorectal and breast cancer.

RCC First Line Phase 3 Trial (TIVO-1): We conducted a global phase 3 clinical trial comparing the efficacy and safety of tivozanib with Nexavar® (sorafenib), an approved therapy, for first-line treatment of renal cell carcinoma, or RCC. The trial met its primary endpoint for progression-free survival, or PFS, but showed a non-statistically significant trend favoring the sorafenib arm in overall survival, or OS. In June 2013, the U.S. Food and Drug Administration, or FDA, issued a complete response letter informing us that it would not approve tivozanib for the treatment of first line advanced RCC based on the study data from this trial, and recommended that we perform an additional study adequately sized to assure the FDA that there is no adverse effect on OS.

In January 2015, we announced our receipt of confirmation from the European Medicines Agency, or EMA, that tivozanib is eligible for submission of an application for a European Union Marketing Authorization under the Agency's centralized procedure for the treatment of RCC. Confirmation of eligibility for submission is not predictive of the EMA's approval of a Marketing Authorization Application, or MAA. Tivozanib has previously been granted orphan drug designation in Europe for the treatment of RCC. Our partner, EUSA Pharma (UK) Limited, or EUSA, submitted a MAA for tivozanib for the treatment of RCC with the EMA in February 2016 based on our existing dataset, which includes the results from the TIVO-1 study of tivozanib in the first-line treatment of RCC.

TIVO-1 Extension Study (One-way crossover from sorafenib to tivozanib): We have completed a TIVO-1 extension study, known as Study 902, in which patients with advanced RCC received tivozanib as second-line treatment subsequent to disease progression on the sorafenib arm in the TIVO-1 first-line RCC trial. We presented the final results at the 2015 American Society of Clinical Oncology (ASCO) Annual Meeting on June 1, 2015. The final results show a median PFS of 11.0 months and median OS of 21.6 months, demonstrating the clinically meaningful efficacy of tivozanib in a VEGF treatment refractory population. We believe that the long OS derived from tivozanib following sorafenib in Study 902 contributed to the discordance in the results between the PFS benefit which significantly favored tivozanib and the OS which trended in favor of sorafenib in the TIVO-1 trial.

RCC Third Line Phase 3 Trial (TIVO-3): We are planning to conduct a phase 3 trial of tivozanib in the third-line treatment of patients with refractory RCC. The study will use PFS as the primary endpoint and OS as a secondary endpoint to support a request for regulatory approval of tivozanib as a third-line treatment and to address the overall survival concerns from TIVO-1 as a first-line treatment presented in the June 2013 complete response letter from the FDA. Our study design, which we have shared with the FDA, contemplates a randomized, controlled, multi-center, open-label phase 3 study of approximately 322 subjects randomized 1:1 to receive either tivozanib or sorafenib. Subjects enrolled in the study may include those who have received prior immunotherapy, including immune checkpoint (PD-1) inhibitors, reflecting a potentially evolving treatment landscape. The primary objective of the study would be to show improved PFS. Secondary endpoints would include OS and objective response rate, or ORR, as well as safety and pharmacokinetic endpoints. We are evaluating all options for funding, including partnerships, for the clinical and regulatory advancement of tivozanib in RCC as well as colorectal cancer, or CRC.

RCC PD-1 Combination Trial: We are designing a phase 1 study of tivozanib combined with a PD-1 inhibitor for the treatment of patients with RCC. We are evaluating all options for funding, including partnerships, for the clinical and regulatory advancement of tivozanib in combination with PD-1 inhibitors in RCC.

CRC Phase 2 Results: In March 2015, we announced results from a predefined biomarker analysis of our BATON-CRC study, a randomized phase 2 clinical trial of modified FOLFOX6, a commonly used chemotherapy, combined with tivozanib or Avastin® (bevacizumab), which both target angiogenesis signaling pathways, in first line treatment of metastatic CRC. In this study, among prospectively defined biomarkers, patients with low (below the median, representing 50% of the population) serum neuropilin-1, or NRP-1, a cell surface protein that modulates blood vessel development, showed an improved PFS versus patients with high serum NRP-1 in both treatment arms, supporting the value of serum NRP-1 as a potential prognostic marker for angiogenesis inhibitors. Further, in the subgroup with samples available at the interim analysis, patients identified using a research-use assay to have low serum NRP-1 demonstrated longer PFS when treated with tivozanib compared to bevacizumab, which suggests that first line colorectal cancer patients with low NRP-1 levels may benefit from treatment with tivozanib over bevacizumab, a standard of care in this disease. In April 2015, we presented the results from the phase 2 BATON-CRC study and the Company's ongoing assay development efforts to the FDA in connection with our evaluation of a proposed pivotal phase 3 trial of tivozanib in CRC. In response to questions we posed to the FDA regarding this proposed trial, the FDA suggested that we continue work on the development of our biomarker assay to address variability between assays presented. As such, we hope to identify a commercially viable assay, which may enable a prospectively defined, randomized Phase 2 or Phase 3 study.

Tivozanib Partnerships:

EUSA License Agreement: In December 2015, we entered into a license agreement with EUSA under which we granted EUSA the right to develop and commercialize tivozanib for all diseases and conditions in humans, excluding non-oncologic diseases or conditions of the eye, in Europe (excluding Russia, Ukraine and the Commonwealth of Independent States), Latin America (excluding Mexico), Africa, Australasia and New Zealand. EUSA submitted a MAA for tivozanib for the treatment of RCC with the EMA in February 2016.

Pharmstandard License Agreement: In August 2015, we entered into a license agreement under which we granted to a subsidiary of Pharmstandard OJSC, or Pharmstandard, the exclusive right to develop, manufacture and commercialize tivozanib in the territories of Russia, Ukraine and the Commonwealth of Independent States, or CIS, for all conditions excluding non-oncologic ocular conditions. Under this agreement, Pharmstandard is responsible for all activities and costs associated with the further development, regulatory filings, health services and commercialization of tivozanib in the specified territories. In December 2015, Pharmstandard submitted an application for marketing authorization for tivozanib based on TIVO-1 results in Russia that was accepted by the Ministry of Health in February 2016.

Ophthotech Option for Ocular Conditions (Non-Oncologic): In November 2014, we entered into a research and exclusive option agreement with Ophthotech Corporation, or Ophthotech, under which we granted Ophthotech an option to develop and commercialize tivozanib outside of Asia for the potential diagnosis, prevention and treatment of non-oncologic diseases or conditions of the eye in humans.

- Ficlatuzumab: Ficlatuzumab is a potent Hepatocyte Growth Factor, or HGF, inhibitory antibody. HGF is the sole known ligand of the c-Met receptor which is believed to trigger many activities that are involved in cancer development and metastasis. We have completed two phase 1 clinical studies of ficlatuzumab administered as a single agent and in combination with erlotinib, a TKI, of the epidermal growth factor receptor, or EGFR, and a phase 2 clinical study evaluating ficlatuzumab in combination with gefitinib, an EGFR TKI, in first line non-small cell lung cancer, or NSCLC. The phase 2 trial failed to demonstrate a statistically significant benefit in the intent-to-treat population. However, an exploratory analysis using a serum-based proteomic diagnostic test, known as VeriStrat®, identified a sub-population of patients who experienced a progression free survival and overall survival benefit from the addition of ficlatuzumab to gefitinib. VeriStrat is commercially available to help physicians guide treatment

decisions for patients with second line advanced NSCLC. Data from the exploratory analyses with VeriStrat prompted the development of a separate investigational companion diagnostic test called BDX004. Based upon the exploratory analyses, BDX004 may be indicative of a predictive biomarker for the combination of ficlatuzumab and EGFR TKI over EGFR TKI alone in the first line EGFR mutation patients who have been previously identified to not respond well to the current standard of care.

In April 2014, we entered into a worldwide agreement with Biodesix, Inc., or Biodesix, to develop and commercialize ficlatuzumab with BDX004, a serum based diagnostic test which has been derived from the VeriStrat test, employing the same methodology and data processing algorithms as VeriStrat, for use in a confirmatory clinical trial. Pursuant to the Biodesix agreement, in December 2014 we initiated a phase 2 confirmatory study of ficlatuzumab, which we refer to as the FOCAL study, in combination with erlotinib in first line advanced NSCLC patients who have an EGFR mutation and who are identified by the BDX004 test as being most likely to benefit from the addition of ficlatuzumab to the EGFR TKI. We began enrolling patients during the second half of 2015. Biodesix will fund up to $15 million of the cost of this study,

as well as all of the costs associated with development and registration of BDX004, and any additional development, regulatory and commercial costs for ficlatuzumab will be shared equally. Under the Biodesix agreement, subject to regulatory approval, AVEO would lead worldwide commercialization of ficlatuzumab.

- AV-203: AV-203 is a potent anti-ErbB3 (also known as HER3) specific monoclonal antibody with high ErbB3 affinity. We have observed potent anti-tumor activity in mouse models. AV-203 selectively inhibits the activity of the ErbB3 receptor, and our preclinical studies suggest that neuregulin-1, or NRG1 (also known as heregulin), levels predict AV-203 anti-tumor activity in preclinical models. We have completed a phase 1 dose escalation study of AV-203, which established a recommended phase 2 dose of AV-203 at 20mg/kg intravenously every 2 weeks, demonstrated good tolerability and promising early signs of activity, and reached the maximum planned dose of AV-203 monotherapy. No anti-drug antibodies were detected, and pharmacokinetic results indicated a dose-proportional increase in levels of AV-203.

The expansion cohort of this study among patients with a specific biomarker has been discontinued. We are seeking to pursue further clinical development of AV-203 with a strategic partner.

- AV-380: AV-380 is a potent humanized IgG1 inhibitory monoclonal antibody targeting growth differentiating factor-15, or GDF15, a divergent member of the TGF-ß family, for the potential treatment or prevention of cachexia. Cachexia is defined as a multi-factorial syndrome of involuntary weight loss characterized by an ongoing loss of skeletal muscle mass (with or without loss of fat mass) that cannot be fully reversed by conventional nutritional support and leads to progressive functional impairment. Cachexia is associated with various cancers as well as diseases outside of cancer including chronic kidney disease, congestive heart failure, and chronic obstructive pulmonary disease, or COPD. We believe that AV-380 represents a unique approach to treating cachexia because it addresses key underlying mechanisms of the syndrome and focuses on a significant area of patient need. It is estimated that approximately 30% of all cancer patients die due to cachexia and over half of cancer patients who die do so with cachexia present. (J Cachexia Sarcopenia Muscle 2010). In the United States alone, the estimated prevalence of cancer cachexia is over 400,000 patients, and the prevalence of cachexia due to cancer, COPD, congestive heart failure, frailty and end stage renal disease combined is estimated to total more than 5 million patients (Am J Clin Nutr 2006).

In September 2014, we presented the results from four preclinical studies of AV-380 in various in vivo cachexia models and in vitro assays at the 2nd Cancer Cachexia Conference held in Montreal Canada. Our research was also selected for presentation in an oral session at the conference. In April 2015, we also presented the results from a preclinical study of AV-380 in a cachectic human tumor xenograft model at the Annual Meeting of the American Association of Cancer Research. We have established preclinical proof of concept for GDF15 as a key driver of cachexia by demonstrating, in animal models, that the administration of GDF15 induces cachexia, and that inhibition of GDF15 reverses cachexia and provides a potential indication of an overall survival benefit.

In August 2015, we entered into a license agreement under which we granted Novartis International Pharmaceutical Ltd., or Novartis, the exclusive right to develop and commercialize AV-380 and related AVEO antibodies. Under this agreement, Novartis is responsible for all activities and costs associated with the further development, regulatory filing and commercialization of AV-380 worldwide.

In connection with the AV-380 program, we have in-licensed certain patents and patent applications from St. Vincent's Hospital in Sydney, Australia. We have demonstrated preclinical proof-of-concept for AV-380 in multiple cancer cachexia models and have completed cell line development.

We have devoted substantially all of our resources to our drug discovery efforts, comprising research and development, conducting clinical trials for our product candidates, protecting our intellectual property and the general and administrative functions relating to these operations. We have generated no revenue from product sales through December 31, 2015, and through such date have principally funded our operations through the proceeds from our strategic partnerships, sales of stock to investors and loan agreements with Hercules Technology II, L.P. and Hercules Technology III, L.P.

We do not have a history of being profitable and, as of December 31, 2015, we had an accumulated deficit of $495.0 million. We anticipate that we will continue to incur significant operating costs over the next several years as we continue our planned development activities for our preclinical and clinical products. We will need additional financing to support our operating activities, and the timing and nature of activities contemplated for 2016 and thereafter will be conducted subject to the availability of sufficient financial resources.

Strategic Partnerships

EUSA

In December 2015, we entered into a license agreement with EUSA under which we granted to EUSA the exclusive, sublicensable right to develop, manufacture and commercialize tivozanib in the territories of Europe (excluding Russia, Ukraine and the Commonwealth of Independent States), Latin America (excluding Mexico), Africa, Australasia and New Zealand for all diseases and conditions in humans, excluding non-oncologic diseases or conditions of the eye. For additional information regarding the terms of this agreement, see "Part I, Business – Strategic Partnerships."

Under the license agreement, EUSA made a research and development funding payment to us of $2.5 million and is required to make a payment of $4.0 million upon the grant by the European Medicines Agency, or the EMA, of marketing approval for tivozanib for treatment of renal cell carcinoma. We are eligible to receive additional research funding from EUSA, including up to $20.0 million if EUSA elects to utilize data generated by our planned phase 3 study in third line renal cell carcinoma, and up to $2.0 million for a potential phase 1 combination study with a checkpoint inhibitor. We will be entitled to receive milestone payments of $2.0 million per country upon reimbursement approval for renal cell carcinoma in each of France, Germany, Italy, Spain and the United Kingdom, and an additional $2.0 million for the grant of marketing approval in three of the following five countries: Argentina, Australia, Brazil, South Africa and Venezuela. We will also be eligible to receive a payment of $2.0 million in connection with EUSA's filing with the EMA for marketing approval for tivozanib for the treatment of each of up to three additional indications and $5.0 million per indication in connection with the EMA's grant of marketing approval for each of up to three additional indications, as well as potentially up to $335.0 million upon EUSA's achievement of certain sales thresholds. We will also be eligible to receive tiered double digit royalties on net sales, if any, of licensed products in the licensed territories ranging from a low double digit up to mid-twenty percent depending on the level of annual net sales. A percentage of any milestone and royalty payments we receive are due to Kyowa Hakko Kirin Co., Ltd. (formerly Kirin Brewery Co., Ltd.), or KHK, as a sublicensing fee under the license agreement between us and KHK dated as of December 21, 2006.

EUSA is obligated to use commercially reasonable efforts to develop and commercialize tivozanib throughout the licensed territories. With the exception of certain support to be provided by us prior to the grant of marketing approval by the EMA, EUSA has responsibility for all activities and costs associated with the further development, manufacture, regulatory filings and commercialization of tivozanib in the licensed territories. EUSA submitted an application with the EMA for approval of marketing authorization for tivozanib for the treatment of renal cell carcinoma in February 2016.

Activities under the agreement were evaluated under ASC 605-25 Revenue Recognition—Multiple Element Arrangements, or ASC 605-25, to determine whether such activities represented a multiple element revenue arrangement. The agreement with EUSA includes the following non-contingent deliverables: (i) our grant of an exclusive license to develop and commercialize tivozanib in the licensed territories; (ii) our obligation to transfer all technical knowledge and data useful in the development and manufacture of tivozanib; (iii) our obligation to cooperate with EUSA and support its efforts to file for marketing approval in the licensed territories, (iv) our obligation to provide access to certain regulatory information resulting from our ongoing development activities outside of the licensed territories and (v) our participation in a joint steering committee. We determined that the delivered license did not have stand-alone value from the undelivered elements and have accounted for these items as a single bundled deliverable. We allocated up-front consideration of $2.5 million to the bundled unit of accounting and are recognizing it over our performance period through April 2022, the remaining patent life of tivozanib. We recognized approximately $14,000 as revenue during the year ended December 31, 2015.

We believe the regulatory milestones that may be achieved under the EUSA agreement are consistent with the definition of a milestone included in ASU 2010-17, Revenue Recognition—Milestone Method, and, accordingly, we will

recognize payments related to the achievement of such milestones, if any, when such milestone is achieved. Factors considered in this determination included scientific and regulatory risks that must be overcome to achieve each milestone, the level of effort and investment required to achieve each milestone, and the monetary value attributed to each milestone.

Novartis

In August 2015, we entered into a license agreement with Novartis International Pharmaceutical Ltd., which we refer to as Novartis, under which we granted Novartis the exclusive right to develop and commercialize AV-380 and our related antibodies that bind to GDF15 worldwide. Under this agreement, Novartis is responsible for all activities and costs associated with the further development, regulatory filing and commercialization of AV-380 worldwide. For additional information regarding the terms of this agreement, see “Part I, Item 1, Business – Strategic Partnerships.”

Novartis made an upfront payment to us of $15.0 million during September 2015. We will also be eligible to receive (a) up to $53 million in potential clinical milestone payments and up to $105 million in potential regulatory milestone payments tied to the commencement of clinical trials and to regulatory approvals of products developed under the license agreement in the United States, the European Union and Japan; and (b) up to $150 million in potential sales based milestone payments based on annual net sales of

such products. Upon commercialization, we are eligible to receive tiered royalties on net sales of approved products ranging from the high single digits to the low double digits. Novartis has responsibility under the license agreement for the development, manufacture and commercialization of the licensed antibodies and any resulting approved therapeutic products.

Novartis also exercised its right under the license agreement to acquire our inventory of clinical quality drug substance in December 2015, reimbursing us approximately $3.5 million for such existing inventory.

Activities under the agreement with Novartis were evaluated under ASC 605-25 to determine whether such activities represented a multiple element revenue arrangement. The agreement with Novartis includes the following non-contingent deliverables: (i) our grant of an exclusive, worldwide license to develop and commercialize the licensed antibodies; (ii) our obligation to transfer all technical knowledge and data useful in the development and manufacture of the licensed antibodies; and (iii) our obligation to cooperate with Novartis' requests for transition assistance during a 90 day period. Novartis' option to acquire our inventory of clinical quality drug substance was determined to be a contingent deliverable at the inception of the agreement.

We determined the delivered license and obligation to transfer technical knowledge and data have standalone value from the undelivered cooperation. We allocated up-front consideration of $15.0 million to the delivered license and technical knowledge. The relative selling price of the undelivered cooperation had de minimis value.

We received cash payments of $15.0 million during the year ended December 31, 2015. We recognized the $15.0 million upfront payment allocated to the delivered license and technical knowledge during 2015 upon delivery. We recognized revenue of $3.5 million during 2015 related to the delivery of our inventory of clinical quality drug substance to Novartis pursuant to the terms of the agreement. The amount due to us from Novartis was $3.5 million as of December 31, 2015.

Pharmstandard Group

In August 2015, we entered into an exclusive license agreement with JSC "Pharmstandard-Ufimskiy Vitamin Plant", or Pharmstandard, a subsidiary of Pharmstandard OJSC, under which we granted Pharmstandard the exclusive right to develop, manufacture and commercialize tivozanib in the territories of Russia, Ukraine and the Commonwealth of Independent States for all conditions excluding non-oncologic ocular conditions. For additional information regarding the terms of this agreement, see "Part I, Item 1, Business – Strategic Partnerships."

Pharmstandard is obligated to use commercially reasonable efforts to develop and commercialize tivozanib throughout the licensed territories, and Pharmstandard has responsibility for all activities and costs associated with the further development, manufacture, regulatory filings and commercialization of tivozanib in the licensed territories. Pharmstandard has filed an application for marketing authorization in Russia for tivozanib for the treatment of renal cell carcinoma that was accepted by the Ministry of Health of the Russian Federation in February 2016.

Pharmstandard made an upfront payment to us of $1.0 million and will be obligated to pay an additional $0.5 million upon registration of the license agreement with a Russian regulatory agency. We are also eligible to receive $7.5 million in connection with the first marketing authorization of tivozanib in Russia. If Russian regulatory authorities require additional studies to be conducted prior to approval, this amount would be reduced to $3.0 million. In addition, we are eligible to receive $3.0 million for each additional approved indication of tivozanib, if Pharmstandard elects to seek any such approvals, as well as a high single-digit royalty on net sales in the sublicensed territories. A percentage of all upfront, milestone and royalty payments received by us are due to KHK as a sublicensing fee under the license agreement with KHK.

Activities under the agreement with Pharmstandard were evaluated under ASC 605-25 to determine whether such activities represented a multiple element revenue arrangement. The agreement with Pharmstandard includes the following non-contingent deliverables: (i) our grant of an exclusive license to develop and commercialize tivozanib in the licensed territories, (ii) our obligation to provide access, upon request, to all clinical data, regulatory filings, safety data and manufacturing data to Pharmstandard for use in the development and commercialization of tivozanib in the licensed territories, (iii) our obligation to participate in certain development and commercialization planning meetings and (iv) our obligation to provide support for certain development, regulatory or manufacturing activities if requested by Pharmstandard.

We determined the delivered license does not have standalone value from the undelivered items and that the arrangement should be treated as a single unit of accounting. We allocated the upfront payment of $1.0 million to the bundled unit of accounting and are recognizing it over our performance period through April 2022, the remaining patent life of tivozanib. We recognized approximately $61,000 as revenue during the year ended December 31, 2015.

We believe the regulatory milestones that may be achieved under the Pharmstandard agreement are consistent with the definition of a milestone included in ASU 2010-17, Revenue Recognition—Milestone Method, and, accordingly, we will recognize

payments related to the achievement of such milestones, if any, when such milestone is achieved. Factors considered in this determination included scientific and regulatory risks that must be overcome to achieve each milestone, the level of effort and investment required to achieve each milestone, and the monetary value attributed to each milestone.

We incurred $0.3 million of R&D expense associated with sublicensing fees payable to KHK as a result of such payments from Pharmstandard during the year ended December 31, 2015.

Ophthotech Corporation

In November 2014 we entered into a Research and Exclusive Option Agreement, or Option Agreement, with Ophthotech Corporation pursuant to which we provided Ophthotech an exclusive option to enter into a definitive license agreement whereby we would grant Ophthotech the right to develop and commercialize our VEGF factor tyrosine kinase inhibitor, tivozanib, outside of Asia for the potential diagnosis, prevention and treatment of non-oncologic diseases or conditions of the eye in humans.

Pursuant to this Option Agreement, we granted to Ophthotech an exclusive, royalty free license or sublicense, as applicable, under intellectual property rights controlled by us solely to perform the research and development activities related to the use of tivozanib for the specific purposes outlined in the agreement during the option period. These activities include formulation work for ocular administration, preclinical research and the conduct of a Phase 1/2a, proof of concept clinical trial of a product containing tivozanib in patients with wet age-related macular degeneration, or the POC Study.

Ophthotech paid us $500,000 in consideration for the grant of the option. Such amount is non-refundable and not creditable against any other amounts due under the agreement. We are obligated to make available to Ophthotech, at no cost to Ophthotech, certain quantities of tivozanib hydrochloride solely for conducting its option period research including manufacturing additional quantities of tivozanib in the event stability data indicates that the current supply will expire prior to the end of February 2017. For additional information regarding the terms of the Option Agreement, see “Item 1, Business – Strategic Partnerships.”

Activities under the Option Agreement were evaluated under ASC 605-25 to determine whether such activities represented a multiple element revenue arrangement. The Option Agreement includes the following non-contingent deliverables: (i) our obligation to grant an exclusive option to Ophthotech to enter into a License Agreement to develop and commercialize products incorporating tivozanib for treatment of AMD and other diseases of the eye outside of Asia during the Option Period; (ii) our obligation to enter into an amendment with KHK to modify the terms of the existing KHK agreement to negotiate a mutually acceptable form of license agreement; and (iii) our obligation to transfer research-grade tivozanib API for Ophthotech to conduct the Option Period research.

We determined that the delivered Option Grant Deliverable, or our obligation to grant an exclusive option to Ophthotech to enter into a License Agreement to develop and commercialize products incorporating tivozanib for treatment of AMD and other diseases of the eye outside of Asia during the Option Period, did not have standalone value from the remaining deliverables since Ophthotech could not obtain the intended benefit of the option without the remaining deliverables. Similarly, the remaining deliverables have no standalone value without the Option Grant Deliverable. We are accounting for the deliverables as one unit of accounting.

During the year ended December 31, 2014, we received an up-front cash payment of $0.5 million. We deferred the upfront payment and are recording the deferred revenue over our period of performance which is estimated to be through December 2016, or the life of the agreement. We recorded approximately $0.2 million and $38,000 of revenue associated with the Option Grant Deliverable during the years ended December 31, 2015 and 2014, respectively.

Biodesix

In April 2014, we entered into a worldwide agreement with Biodesix to develop and commercialize our HGF inhibitory antibody ficlatuzumab, with BDX004, a proprietary companion diagnostic test developed by Biodesix and based upon an exploratory analyses with VeriStrat®, a serum protein test that is commercially available to help physicians guide treatment decisions for patients with advanced NSCLC. For additional information regarding the terms of this agreement, see "Part I, Item 1, Business – Strategic Partnerships."

Pursuant to a joint development plan, we retain primary responsibility for clinical development of ficlatuzumab in a proof of concept, or POC, clinical study of ficlatuzumab for NSCLC, in which VeriStrat will be used to select clinical trial subjects, referred to as the NSCLC POC Trial. The NSCLC POC Trial will be fully funded by Biodesix up to a maximum of $15.0 million, referred to as the "Cap". After the Cap is reached, Biodesix will share equally in the costs of the NSCLC trial with us, and we will each be responsible for 50% of development and regulatory costs associated with all future clinical trials agreed-upon by both parties, including all milestone payments and royalties payable to third parties, if any.

Activities under the agreement with Biodesix were evaluated under ASC 605-25 to determine such activities represented a multiple element revenue arrangement. The agreement with Biodesix includes the following non-contingent deliverables: (i) perpetual, non-exclusive rights to certain intellectual property including clinical and biomarker data related to ficlatuzumab for use in developing and commercializing BDX004; (ii) our obligation to deliver technology improvements and data developed during the FOCAL study to Biodesix; (iii) our obligation to participate in the joint steering committee during the FOCAL study; (iv) our obligation to perform certain development activities associated with the FOCAL study; (v) our obligation to supply clinical material for use in conducting the FOCAL study; and (vi) our obligation to deliver clinical specimens and data during the FOCAL study. We concluded that any deliverables that would be delivered after the FOCAL study is complete are contingent deliverables because these services are contingent upon the results of the FOCAL study. As these deliverables are contingent, and are not at an incremental discount, they are not evaluated as deliverables at the inception of the arrangement. These contingent deliverables will be evaluated and accounted for separately as each related contingency is resolved. As of December 31, 2015, no contingent deliverables had been provided by us.

We have determined that the delivered item, or the perpetual, non-exclusive rights to certain intellectual property for use in developing and commercializing BDX004 did not have standalone value from the remaining deliverables since Biodesix could not obtain the intended benefit of the license without the remaining deliverables. Since the remaining deliverables will be performed over the same period of performance there is no difference in accounting for the deliverables as one unit or multiple units of accounting, and therefore, we are accounting for the deliverables as one unit of accounting.

We record the consideration earned while conducting the FOCAL Study, which consists of reimbursement by Biodesix for expenses related to the trial under the Cap, as a reduction to research and development expense using the proportional performance method over the respective period of performance. As a result of the cost sharing provisions in the agreement, we reduced research and development expenses by approximately $3.5 million and $2.7 million during the years ended December 31, 2015 and 2014, respectively. The amount due to us from Biodesix pursuant to the cost-sharing provision was $1.1 million and $1.8 million at December 31, 2015 and 2014, respectively.

St. Vincent’s Hospital

In July 2012, we entered into a license agreement with St. Vincent’s Hospital Sydney Limited, which we refer to as St. Vincent’s, under which we obtained an exclusive, worldwide license to research, develop, manufacture and commercialize products for therapeutic applications that benefit from inhibition or decreased expression or activity of MIC-1, which is also known as GDF15. We believe GDF15 is a novel target for cachexia and we are exploiting this license in our AV-380 program for cachexia. Under the agreement, we have the right to grant sublicenses subject to certain restrictions. We have a right of first negotiation to obtain an exclusive license to certain improvements that St. Vincent’s or third parties may make to licensed therapeutic products. Under the license agreement, St. Vincent’s also granted us non-exclusive rights for certain related diagnostic products and research tools. For additional information regarding the terms of the agreement with St. Vincent’s, see “Part I, Item 1, Business – Strategic Partnerships.”

In August 2015, in connection with the execution of our license agreement with Novartis, we entered into an amended and restated agreement with St. Vincent’s, pursuant to which we made an upfront payment to St. Vincent’s of $1.5 million. St. Vincent’s is also eligible to receive up to approximately $18.9 million in connection with development and regulatory milestones. Royalties for approved products resulting from the license agreement will also be payable to St. Vincent’s, and we and Novartis will share that obligation equally.

Biogen Idec

In March 2009, we entered into an exclusive option and license agreement with Biogen Idec International GmbH, or 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 were 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. In March 2014, we amended our agreement with Biogen Idec, whereby Biogen Idec agreed to the termination of its rights and obligations under the agreement, including Biogen Idec's option to (i) obtain a co-exclusive (with us) license to develop and manufacture ErbB3 targeted antibodies and (ii) obtain exclusive commercialization rights to ErbB3 products in countries in the world other than North America. As a result, we retain worldwide rights to AV-203, a clinical stage ErbB3-targeted antibody. Pursuant to the amendment, we are obligated to in good faith use reasonable efforts to seek a collaboration partner for the purpose of funding further development and commercialization of ErbB3-targeted antibodies. Pursuant to the amendment, we are obligated to pay Biogen Idec a percentage of milestone payments received by us from future partnerships after March 28, 2016 and single digit royalty payments on net sales related to the sale of ErbB3 products, up to cumulative maximum amount of $50.0 million. For additional information regarding the terms of Biogen Idec agreement, see "Part I, Item 1, Business – Strategic Partnerships."

The deliverables under the original Biogen Idec agreement included an option for a co-exclusive, worldwide license to develop and manufacture ErbB3 antibody products and an option for an exclusive license to commercialize ErbB3 antibody products in all countries in the world other than North America. We determined that these deliverables did not have standalone value due to the fact that the program was still in preclinical development and required our experience to advance development of the product candidates. As such, we determined that the agreement should be accounted for as one unit of accounting.

Under the terms of the original agreement, Biogen Idec made up-front and milestone-based cash payments totaling $20.0 million. Of the $20.0 million received, $10.0 million was associated with milestones that were considered substantive and these amounts were included in revenue when earned. The remaining $10.0 million was amortized as additional license revenue over our period of substantial involvement.

We concluded that the amendment entered into in March 2014 materially modified the terms of the agreement and, as a result, required application of the guidance included in ASC 605-25. Based upon the terms of the amended arrangement, the remaining deliverables included our obligation to seek a collaboration partner to fund further development of the program and our obligation to continue development and commercialization of the licensed products if a collaboration partner is secured. We concluded that our obligation to use best efforts to seek a collaboration partner does not have standalone value from our efforts to continue development and commercialization of the licensed products and thus the deliverables should be treated as a single unit of accounting.

Upon modifying the arrangement, we had $14.7 million of deferred revenue remaining to be recognized. We are not entitled to receive any further consideration from Biogen Idec under the amended arrangement. We allocated a portion of the remaining deferred revenue to the undelivered unit of accounting based upon our best estimate of the selling price. We determined the best estimate of the selling price to be approximately $0.6 million and recognized the remaining $14.1 million as collaboration revenue in the three months ended March 31, 2014. The deferred revenue associated with the undelivered unit of accounting is being recognized on a straight-line basis over the expected period of performance, or through March 2016, based upon our historical experience with marketing our product candidates to potential partners.

The best estimate of the selling price was based upon a cost approach pursuant to which we estimated the costs expected to be incurred in executing a partnership agreement and then applied a reasonable markup. We estimated future cash outflows for several possible outcomes, including the execution of a partnership at different times within a reasonable range and partnerships of differing complexity. We estimated our cash outflows for each scenario based upon the expected costs associated with the relevant employees and the expected level of effort to be expended to seek and execute a partnership. Our analysis also considered the legal charges we anticipate we will incur. Changes to the assumptions within the reasonable range of possible values would not have a material impact on the amounts recorded in current or future periods.

Under the agreement, we recorded revenue of $0.3 million, $14.5 million and $0.9 million during the years ended December 31, 2015, 2014 and 2013, respectively.

Astellas Pharma

In February 2011, we entered into a collaboration and license agreement with Astellas and certain of its indirect wholly-owned subsidiaries pursuant to which we and Astellas made plans to develop and seek to commercialize tivozanib for the treatment of a broad range of cancers. On February 12, 2014, Astellas exercised its right to terminate the agreement. The termination of the agreement became effective August 11, 2014, at which time tivozanib rights returned to us. In accordance with the collaboration and license agreement, we and Astellas agreed to equally share committed development costs, including the costs of completing certain tivozanib clinical development activities that were initiated as part of our partnership with Astellas.

In connection with the agreement, we received an initial cash payment of $125.0 million, comprised of a $75.0 million license fee and $50.0 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 for the treatment of patients with advanced RCC. We have accounted for the joint development and commercialization activities in North America and Europe as a joint risk-sharing collaboration in accordance with Accounting Standards Codification, or ASC, 808 Collaborative Arrangements. In addition, these joint development and commercialization activities were not deemed to be separate deliverables under the agreement with Astellas.

Payments from Astellas with respect to Astellas' share of tivozanib development and commercialization costs incurred by us pursuant to the joint development plan are recorded as a reduction to research and development expense and general and administrative expense in the accompanying consolidated financial statements due to the joint risk-sharing nature of the activities in North America and Europe. As a result of the cost-sharing provisions in the Astellas Agreement, we reduced research and

development expense by $0.7 million, $3.5 million and $15.8 million during the years ended December 31, 2015, 2014, and 2013, respectively. We also reduced general and administrative expense by $0.1 million, $0.1 million and $2.8 million as a result of the cost-sharing provisions in the Astellas Agreement during the years ended December 31, 2015, 2014 and 2013, respectively. The net amount due to us from Astellas pursuant to the cost-sharing provisions was $0.1 million and $0.6 million at December 31, 2015 and 2014, respectively.

Activities under the agreement with Astellas outside of the joint development and commercialization activities in North America and Europe were evaluated under ASC 605-25 to determine if they represented a multiple element revenue arrangement. The agreement with Astellas included the following deliverables outside of the joint development and commercialization activities in North America and Europe: (i) a co-exclusive license to develop and commercialize tivozanib in North America and Europe; (ii) a royalty-bearing license to develop and commercialize tivozanib in the royalty territory, which includes our obligation to provide access to clinical and regulatory information resulting from the activities in North America and Europe to Astellas for its development and commercialization of tivozanib in the royalty territory; and (iii) our obligation to supply clinical material to Astellas for development of tivozanib in the royalty territory. All of these deliverables were deemed to have stand-alone value and to meet the criteria to be accounted for as separate units of accounting under ASC 605-25.

We allocated the up-front consideration of $125.0 million to the deliverables based on our best estimate of selling price of each deliverable using the relative selling price method as we did not have vendor specific objective evidence or third-party evidence for such deliverables. We allocated $120.2 million of the up-front consideration from Astellas to the co-exclusive license in North America and Europe and $4.8 million of the up-front consideration from Astellas to the combined deliverable representing a royalty-bearing license to develop and commercialize tivozanib in the royalty territory along with our obligation to provide access to clinical and regulatory information resulting from the activities in North America and Europe to Astellas for its use in the royalty territory. The relative selling price for our obligation to supply clinical material to Astellas for development in the royalty territory had de minimis value.

We recorded the $120.2 million relative selling price of the co-exclusive license granted in North America and Europe as collaboration revenue upon delivery of the license, and deferred approximately $4.8 million of revenue representing the relative selling price of the royalty-bearing license to develop and commercialize tivozanib in the royalty territory along with our obligation to provide access to clinical and regulatory information resulting from the activities in North America and Europe to Astellas for its use in the royalty territory. We were recording the $4.8 million ratably over the period of our performance through April 2022, the remaining patent life of tivozanib. Upon being notified that the collaboration would be terminated effective August 2014, we reassessed the period of performance associated with the royalty territory deliverable and accelerated the recognition of the remaining deferred revenue such that the balance would be recognized through August 2014. This change in estimate resulted in the recognition of an additional $3.2 million during the year ended December 31, 2014. We recorded approximately $3.6 million and $0.4 million of revenue associated with the Royalty Territory Deliverable during the years ended December 31, 2014 and 2013.

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 KHK 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. For additional information regarding the terms of the license agreement with KHK, see “Item 1, Business – Strategic Partnerships.”

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. 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. The total remaining payments for clinical and regulatory milestones under our license agreement with KHK are $38.0 million, in the aggregate, provided that the associated clinical and regulatory milestones specific to

licensed territories would be replaced by a specified percentage of any non-research and development amounts we receive from any third party sublicensees.

We also 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 that we entered into in February 2011. We are required to pay to KHK 30% of certain amounts we receive from sublicensees, including up-front license fees, milestone payments and royalties, other than amounts we receive in respect of research and development funding or equity investments, subject to certain limitations.

We are also required to pay tiered royalty payments on net sales we make of tivozanib in our territory, which range from the low to mid-teens as a percentage of net sales. The royalty rate escalates within this range based on increasing tivozanib sales. Our royalty payment obligations in a particular country in our territory begin on the date of the first commercial sale of tivozanib in that country, and end on the later of 12 years after the date of first commercial sale of tivozanib in that country or the date of the last to expire of the patents covering tivozanib that have been issued in that country. In the event we sublicense the rights licensed to us under the license agreement with KHK, we are required to pay KHK a specified percentage of any amounts we receive from any third party sublicensees, other than amounts we receive in respect of research and development funding or equity investments, subject to certain limitations.

Financial Overview

In January 2015, our Board of Directors approved a strategic restructuring that eliminated our internal research function to better align our resources with our future clinically focused strategic plans given that our material programs were at preclinical and clinical stages of development. As part of this restructuring, we eliminated approximately two thirds of our workforce, or 40 positions, across the organization. The restructuring was fully completed during 2015.

Revenue

To date, we have not generated any revenue from product sales. All of our revenue to date has been derived from license fees, milestone payments, premium over the fair value of convertible preferred shares sold to our strategic partners, and research and development payments received from our strategic partners.

In the future, we may generate revenue from a combination of product sales, license fees, milestone payments and research and development payments in connection with strategic partnerships, and royalties resulting from the sales of products developed under licenses of our intellectual property. We expect that any revenue we generate will fluctuate from year to year as a result of the timing and amount of license fees, research and development reimbursements, milestone and other payments received under our strategic partnerships, and the amount and timing of payments that we receive upon the sale of our products, to the extent any are successfully commercialized. We do not expect to generate revenue from product sales in the near term. If we or our strategic partners fail to complete the development of our drug candidates in a timely manner or obtain regulatory approval for them, our ability to generate future revenue, and our results of operations and financial position, would be materially adversely affected.

Research and Development Expenses

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

- employee-related expenses, which include salaries, benefits and stock-based compensation expense;
- expenses incurred under agreements with contract research organizations, investigative sites and consultants that conduct our clinical trials and a substantial portion of our preclinical studies;
-

the cost of acquiring and manufacturing clinical trial materials, as well as commercial materials prior to our anticipated launch of tivozanib;

- the cost of completing certain tivozanib clinical development activities that were initiated as part of our prior partnership with Astellas;
- facilities, depreciation and other allocated expenses, which include direct and allocated expenses for rent and maintenance of facilities and equipment, and depreciation of fixed assets;
- license fees for, and milestone payments related to, in-licensed products and technology; and
- costs associated with outsourced development activities, regulatory approvals and medical affairs.

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

Research and development expenses are net of amounts reimbursed under our agreements with Astellas and Biodesix for Astellas' and Biodesix' respective shares of development costs incurred by us under our joint development plans with each respective partner.

We track external development expenses and personnel expense on a program-by-program basis and allocate common expenses, such as scientific consultants and laboratory supplies, to each program based on the personnel resources allocated to such program. Facilities, depreciation, stock-based compensation, research and development management and research and development support services are not allocated among programs and are considered overhead. We expect our overhead expenses to decrease in future periods as a result of our January 2015 restructuring which reduced our facilities requirement by more than 80% of our prior space, including the elimination of lab and vivarium needs. Below is a summary of our research and development expenses for the years ended December 31, 2015, 2014 and 2013:

	Years Ended December 31,		
	2015	2014	2013
	(in thousands)		
Tivozanib	$8,513	$9,530	$25,060
AV-380 Program in Cachexia	2,408	12,968	4,308
AV-203	532	1,843	5,698
Ficlatuzumab	80	1,579	12,573
Other pipeline programs	11	72	1,299
Other research and development	10	67	376
Platform collaborations	—	—	—
Overhead	1,321	12,195	19,154
Total research and development expenses	$12,875	$38,254	$68,468

Tivozanib

On November 27, 2012, the FDA accepted for filing our NDA for tivozanib, our lead product candidate, with the proposed indication for the treatment of patients with advanced renal cell carcinoma, or RCC. On May 2, 2013, we were informed by the FDA that its Oncologic Drugs Advisory Committee believed that our NDA for investigational agent tivozanib did not demonstrate a favorable benefit-to-risk evaluation for the treatment of advanced RCC, and in June 2013, we received a complete response letter from the FDA informing us that the FDA will not approve in its present form our NDA for our investigational agent tivozanib for the treatment of patients with advanced RCC.

Our strategy for development of tivozanib included a focus on the exploration of various biomarkers which could provide insights into tivozanib's potential clinical benefit. Accordingly, we conducted biomarker studies referred to as the BATON (Biomarker Assessment of Tivozanib in Oncology) trials. The first, which was a single-arm phase 2 trial of tivozanib (BATON-RCC) to evaluate various biomarkers for tivozanib activity in treatment naïve advanced RCC patients, was completed in 2014. In another, we evaluated tivozanib in colorectal cancer (BATON-CRC) through a randomized phase 2 clinical trial, to evaluate tivozanib in combination with mFOLFOX6 compared to Avastin in combination with mFOLFOX6 as first-line therapy in patients with advanced metastatic colorectal cancer, or CRC. On December 13, 2013, we announced that, based on data from a September 2013 interim analysis, the BATON-CRC trial was unlikely to meet the primary endpoint of demonstrating superiority over bevacizumab in the intent-to-treat

population; and on February 14, 2014, we announced that the study would be discontinued.

We entered into a collaboration and license agreement with Astellas in February 2011, pursuant to which we and Astellas shared responsibility for tivozanib, including expenses for continued development and commercialization of tivozanib, in North America and Europe. We have included $0.8 million, $3.5 million and $15.8 million in research and development cost reimbursements as a reduction in tivozanib-related expenses for the years ended December 31, 2015, 2014 and 2013, respectively. We also 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 of our NDA filing for tivozanib. On August 11, 2014, our collaboration and license agreement with Astellas terminated pursuant to Astellas' election to terminate and tivozanib rights were returned to us.

We and Astellas will share the costs of completing certain tivozanib clinical development activities. We do not expect the amount that we will incur in 2016 to be significant. The actual amount that we will incur may differ from this estimate depending upon our ability to expedite the termination of our existing obligations while continuing to satisfy our patient and regulatory requirements.

In November 2014, we entered into a research and exclusive option agreement with Ophthotech Corporation, or Ophthotech, under which we granted Ophthotech an option to develop and commercialize tivozanib for the potential diagnosis, prevention and treatment of non-oncologic diseases or conditions of the eye in humans.

In August 2015, we entered into a license agreement under which we granted to a subsidiary of Pharmstandard OJSC, or Pharmstandard, the exclusive right to develop, manufacture and commercialize tivozanib in the territories of Russia, Ukraine and the Commonwealth of Independent States for all conditions excluding non-oncologic ocular conditions. Under this agreement, Pharmstandard is responsible for all activities and costs associated with the further development, regulatory filings, health services and commercialization of tivozanib in the specified territories. In December 2015, Pharmstandard submitted an application for marketing authorization in Russia.

In December 2015, we entered into a license agreement with EUSA under which we granted EUSA the right to develop and commercialize tivozanib for all diseases and conditions in humans, excluding non-oncologic diseases or conditions of the eye, in Europe (excluding Russia, Ukraine and the Commonwealth of Independent States), Latin America (excluding Mexico), Africa, Australasia and New Zealand. We expect EUSA to file a Marketing Authorization Application, or MAA, for tivozanib for the treatment of RCC with the European Medicines Agency, or EMA, in the first quarter of 2016. Under the license agreement, EUSA has responsibility for all activities and costs associated with the further development, manufacture, regulatory approval and commercialization of tivozanib in the licensed territories.

We are also evaluating the opportunity to conduct an additional phase 3 trial of tivozanib vs. sorafenib in approximately 322 patients in the refractory RCC setting using PFS as the primary endpoint and OS as a secondary endpoint, in order to support the approval of tivozanib as a third-line treatment and to address the overall survival concerns presented in the June 2013 complete response letter from the FDA. We expect the remaining uncommitted costs of this trial to be between $34.0 and $36.0 million through completion. The timing and nature of activities contemplated for 2016 and thereafter will be conducted subject to the availability of sufficient financial resources.

AV-380 Program in Cachexia

In 2012, we initiated a program focusing on cachexia, which we now refer to as our AV-380 program. Our primary research focus is in the area of cancer cachexia which we believe represents a significant are of patient need. In addition, cachexia is also associated with diseases outside of cancer including CKD, CHF, and COPD. In connection with our cachexia program, we have in-licensed certain patents and patent applications from St. Vincent’s. Appropriate IND-enabling efforts, including cell line development and manufacturing of our first cGMP batch, have been completed in preparation for potential future clinical development.

In August 2015, we entered into a license agreement with Novartis, under which we granted Novartis the exclusive right to develop and commercialize AV-380 and related AVEO antibodies that bind to Growth Differentiation Factor 15 worldwide. Under this agreement, Novartis is responsible for all activities and costs associated with the further development, regulatory filing and commercialization of AV-380 worldwide. We do not expect to incur any significant costs related to AV-380 in future periods beyond any milestone fees and royalties payable to St. Vincent’s pursuant to our in-licensing agreement.

AV-203

In March 2014, we regained our worldwide rights from Biogen Idec to develop, manufacture and commercialize AV-203, and we are actively pursuing partnerships or collaborations to further advance the development of AV-203. Because obtaining a partnership or collaboration may be complex and unpredictable in timing and nature of terms, we are unable to estimate with any certainty the costs we will incur in the future development of AV-203.

Ficlatuzumab

In April 2014, we entered into a worldwide agreement with Biodesix to develop and commercialize AVEO's potent HGF inhibitory antibody ficlatuzumab, with BDX004, a proprietary companion diagnostic test, developed by Biodesix and based upon an exploratory analyses with VeriStrat®, a serum protein test that is commercially available to help physicians guide treatment decisions for patients with advanced NSCLC. Pursuant to the agreement with Biodesix, Biodesix will provide up to $15 million for a phase 2 trial of ficlatuzumab in combination with erlotinib in ^{first} line advanced NSCLC patients selected using BDX004, a diagnostic test derived from VeriStrat, and fund the further development and registration of BDX004 as a companion diagnostic. After the

completion of the phase 2 trial, any additional development, regulatory or commercial expenses for ficlatuzumab will be equally shared, as well as profits, if any.

Due to the unpredictable nature of clinical development, we are unable to estimate with any certainty the costs we will incur in the future development of ficlatuzumab.

Uncertainties of Estimates Related to Research and Development Expenses

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

At this time, we cannot reasonably estimate or know the nature, specific timing and estimated costs of the efforts that will be necessary to complete the development of our product candidates, or the period, if any, in which material net cash inflows may commence from sales of any approved products. This uncertainty is due to the numerous risks and uncertainties associated with developing drugs, including the uncertainty of:

- our ability to establish and maintain strategic partnerships, the terms of those strategic partnerships and the success of those strategic partnerships, if any, including the timing and amount of payments that we might receive from strategic partners;
- the scope, progress, results and costs of preclinical development, laboratory testing and clinical trials for any product candidate;
- the progress and results of our clinical trials;
- the costs, timing and outcome of regulatory review of our product candidates;
- the emergence of competing technologies and products and other adverse market developments; and
- the costs of preparing, filing and prosecuting patent applications and maintaining, enforcing and defending intellectual property-related claims.

As a result of the uncertainties associated with developing drugs, including those discussed above, we are unable to determine the duration and completion costs of current or future clinical stages of our product candidates, or when, or to what extent, we will generate revenues from the commercialization and sale of any of our product candidates. Development timelines, probability of success and development costs vary widely. We anticipate that we will make determinations as to which additional programs to pursue and how much funding to direct to each program on an ongoing basis in response to the scientific and clinical success, if any, of each product candidate, as well as ongoing assessment of each product candidate's commercial potential. We will need to raise substantial additional capital in the future in order to fund the development of our preclinical and clinical product candidates.

General and Administrative Expenses

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

We anticipate that our general and administrative expenses will continue to decrease due to the January 2015 restructuring. This decrease may be partially offset by an increase in legal costs associated with the ongoing shareholder litigation and SEC investigation described above in this report under the heading "Legal Proceedings" in Part I—Item 3.

Interest Income and Interest Expense

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

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

Income Taxes

We calculate our provision for income taxes on ordinary income based on our projected annual tax rate for the year. We recorded a loss for the years ended December 31, 2015, 2014, and 2013, and since we maintain a full valuation allowance on all of our deferred tax assets, we have recorded no income tax provision or benefit during the years ended December 31, 2015, 2014, and 2013.

Critical Accounting Policies and Significant Judgments and Estimates

Our discussion and analysis of our financial condition and results of operations are based on our consolidated financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States. The preparation of these financial statements requires us to make estimates and judgments that affect the reported amounts of assets, liabilities, revenues and expenses and the disclosure of contingent assets and liabilities in our financial statements. On an ongoing basis, we evaluate our estimates and judgments, including those related to revenue recognition, accrued clinical expenses, and stock-based compensation. We base our estimates on historical experience, known trends and events and various other factors that we and our management believe to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

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

Revenue Recognition

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

When evaluating multiple element arrangements, we consider whether the deliverables under the arrangement represent separate units of accounting. This evaluation requires subjective determinations and requires management to make judgments about the individual deliverables and whether such deliverables are separable from the other aspects of the contractual relationship. In determining the units of accounting, management evaluates certain criteria, including whether the deliverables have standalone value, based on the consideration of the relevant facts and circumstances for each arrangement. The consideration received is allocated among the separate units of accounting using the relative selling price method, and the applicable revenue recognition criteria are applied to each of the separate units.

We determine the estimated selling price for deliverables within each agreement using vendor-specific objective evidence, or VSOE, of selling price, if available, third-party evidence, or TPE, of selling price if VSOE is not available, or best estimate of selling price if neither VSOE nor TPE is available. Determining the best estimate of selling price for a deliverable requires significant judgment. We typically use best estimate of selling price to estimate the selling price for licenses to our proprietary technology, since we often do not have VSOE or TPE of selling price for these deliverables. In those circumstances where we utilize best estimate of selling price to determine the estimated selling price of a license to our proprietary technology, we consider market conditions as well as entity-specific factors, including those factors contemplated in negotiating the agreements as well as internally

developed models that include assumptions related to the market opportunity, estimated development costs, probability of success and the time needed to commercialize a product candidate pursuant to the applicable license. In validating our best estimate of selling price, we evaluate whether changes in the key assumptions used to determine the best estimate of selling price will have a significant effect on the allocation of arrangement consideration between multiple deliverables.

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

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

At the inception of each agreement that includes milestone payments, we evaluate whether each milestone is substantive and at risk to both parties on the basis of the contingent nature of the milestone. This evaluation includes an assessment of whether (a) the consideration is commensurate with either (1) the entity's performance to achieve the milestone, or (2) the enhancement of the value of the delivered item(s) as a result of a specific outcome resulting from the entity's performance to achieve the milestone, (b) the consideration relates solely to past performance, and (c) the consideration is reasonable relative to all of the deliverables and payment terms within the arrangement. We evaluate factors such as the scientific, regulatory, commercial and other risks that must be overcome to achieve the respective milestone, the level of effort and investment required to achieve the respective milestone and whether the milestone consideration is reasonable relative to all deliverables and payment terms in the arrangement in making this assessment. The conclusion as to whether milestone payments are substantive involves management judgment regarding the factors noted above.

We classify each of our milestones into one of four categories: (i) clinical and development milestones, (ii) regulatory milestones, (iii) commercial milestones, and (iv) patent-related milestones. Clinical and development milestones are typically achieved when a product candidate advances into a defined phase of clinical research or completes such phase. For example, a milestone payment may be due to us upon the initiation of a phase 3 clinical trial for a new indication, which is the last phase of clinical development and could eventually contribute to marketing approval by the FDA or other regulatory authorities. Regulatory milestones are typically achieved upon acceptance of the submission for marketing approval of a product candidate or upon approval to market the product candidate by the FDA or other regulatory authorities. For example, a milestone payment may be due to us upon the FDA's acceptance of an NDA. Commercial milestones are typically achieved when an approved pharmaceutical product reaches certain defined levels of net sales by the licensee, such as when a product first achieves global sales or annual sales of a specified amount. Patent-related milestones are typically achieved when a patent application is filed or a patent is issued with respect to certain intellectual property related to the applicable collaboration.

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

Accrued Clinical Expenses

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

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

- fees paid to investigative sites in connection with clinical studies;
- fees paid to contract manufacturers in connection with the production of clinical trial materials; and
- fees paid to vendors in connection with preclinical development activities.

We determine our expenses related to clinical studies based on our estimates of the services received and efforts expended pursuant to contracts with multiple research institutions and contract research organizations that conduct and manage clinical studies on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. Payments under some of these contracts depend on factors such as the successful enrollment of patients and the completion of clinical trial milestones. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies

from our estimate, we adjust the accrual accordingly. Although we do not expect our estimates to be materially different from amounts actually incurred, and our estimates have not historically been materially different, our estimates of the status and timing of services performed relative to the actual status and timing of services performed may vary and may result in us reporting amounts that are too high or too low in any particular period. Based on our accrued clinical trial expenses as of December 31, 2015, if our previous estimates are 5% too high or too low, this may result in an adjustment to our accrued clinical trial expenses in future periods of approximately $0.1 million.

Estimated SEC Settlement

The Company is involved in various legal proceedings and accrues anticipated costs of settlement, damages, and/or losses to the extent such amounts are probable and estimable. If the estimate of a probable loss is a range and no amount within the range is more likely, the Company accrues the minimum amount of the range.

On July 3, 2013, the staff (the "SEC Staff") of the United States Securities and Exchange Commission (the "Commission") served a subpoena on us for documents and information concerning tivozanib, including related communications with the FDA, investors and others. We have fully cooperated with the inquiry. In September 2015, the SEC Staff invited us to discuss the settlement of potential claims that the SEC Staff may recommend that the Commission bring against us asserting that we violated federal securities laws by omitting to disclose to investors the recommendation made to us by the staff of the U.S. Food and Drug Administration, on May 11, 2012, that we conduct an additional clinical trial with respect to tivozanib. Based on the progress in the settlement process thus far, we believe that we could potentially settle with the SEC for a total amount of $4,000,000 and, accordingly, we have accrued an estimated settlement liability, for accounting purposes, in that amount in our financial statements as of December 31, 2015. There can be no assurance, however, that a settlement will be approved by the Commission, or that any settlement on terms agreeable to us will be achieved. If settlement discussions conclude without a settlement proposal that is acceptable to the Commission and us, the Commission may authorize the SEC Staff to pursue claims against us. There can be no assurance that we will be able to resolve the potential claims of the Commission or that any settlement will not have a material adverse impact on our ability to execute on our proposed plans or on our financial position or results of operations.

The SEC Staff also invited three of our former officers to discuss the settlement of potential claims that the SEC Staff may recommend that the Commission bring against them. We are not a party to any discussions between the SEC Staff and the former officers, and we can make no assurance regarding such potential claims.

Stock-Based Compensation

Under our stock-based compensation programs, we periodically grant stock options and restricted stock to employees, directors and nonemployee consultants. We also issue shares under an employee stock purchase plan. The fair value of all awards is recognized in our statements of operations over the requisite service period for each award. Awards that vest as the recipient provides service are expensed on a straight-line basis over the requisite service period. Other awards, such as performance-based awards that vest upon the achievement of specified goals, are expensed using the accelerated attribution method if achievement of the specified goals is considered probable. We have also granted awards that vest upon the achievement of market conditions. Per ASC 718 Share-Based Payments, market conditions must be considered in determining the estimated grant-date fair value of share-based payments and the market conditions must be considered in determining the requisite service period over which compensation cost is recognized. We estimate the fair value of the awards with market conditions using a Monte Carlo simulation, which utilizes several assumptions including the risk-free interest rate, the volatility of our stock and the exercise behavior of award recipients. The grant-date fair value of the awards is then recognized over the requisite service period, which represents the derived service period for the awards as determined by the Monte Carlo simulation. Determining the amount of stock-based compensation to be recorded requires us to develop estimates of fair values of stock options as of the grant date using highly subjective assumptions.

We use the Black-Scholes option pricing model to value our stock option awards without market conditions, which requires us to make certain assumptions regarding the expected volatility of our common stock price, the expected term of the option grants, the risk-free interest rate and the dividend yield with respect to our common stock. Our expected stock price volatility is based on an average of our own historical volatility and that of several peer companies. We utilized a weighted average method using our own volatility data for the time that we have been public, along with similar data for peer companies that are publicly traded. For purposes of identifying peer companies, we considered characteristics such as industry, length of trading history, similar vesting terms and in-the-money option status. Due to the lack of available quarterly data for these peer companies and a lack of our own historical data, we elected to use the “simplified” method for “plain vanilla” options to estimate the expected term of our stock option grants. Under this approach, the weighted-average expected life is presumed to be the average of the vesting term and the contractual term of the option. The risk-free interest rate used for each grant is based on the U.S. Treasury yield curve in effect at the time of grant for instruments with a similar expected life. We utilize a dividend yield of zero based on the fact that we have never paid cash dividends and have no present intention to pay cash dividends.

During the years ended December 31, 2015, 2014 and 2013, respectively, the assumptions used in the Black-Scholes pricing model for new grants were as follows:

	Years Ended December 31,		
	2015	2014	2013
Volatility	73.04%-78.70%	69.38%-77.92%	64.22%-72.65%
Expected Term (in years)	5.50-6.25	5.50-6.25	5.50-6.25
Risk-Free Interest Rates	1.54%-1.93%	1.81%-2.02%	1.01%-2.10%
Dividend Yield	—	—	—

We recognized stock-based compensation expense of approximately $1.1 million, $2.8 million and $3.9 million for the years ended December 31, 2015, 2014, and 2013, respectively. During the years ending December 31, 2015, 2014 and 2013, we estimated our expected forfeiture rates to be 71%, 62% and 49%, respectively. As of December 31, 2015, we had approximately $0.7 million of total unrecognized stock-based compensation expense for stock options, which we expect to recognize over a weighted-average period of approximately 2.9 years.

As of December 31, 2015, we had $6,000 of total unrecognized stock-based compensation expense related to restricted stock awards granted under our 2010 Stock Incentive Plan. We expect to recognize the expense over a weighted-average period of 0.1 years.

We record compensation expense only for those awards that we ultimately expect will vest. We have performed an historical analysis of option awards that were forfeited prior to vesting and recorded total stock option expense that reflected this estimated forfeiture rate. We cannot currently predict the total amount of stock-based compensation expense to be recognized in any future period because such amounts will depend on levels of stock-based payments granted in the future as well as the portion of the awards that actually vest. Forfeitures are estimated each period and adjusted if actual forfeitures differ from those estimates. Actual forfeitures may differ from our estimates as a result of significant changes in our operations, such as those stemming from our October 2012, June 2013 and January 2015 restructurings.

We have historically granted stock options at exercise prices that are not less than the fair market value of our common stock.

Results of Operations

Comparison of Years Ended December 31, 2015 and 2014

The following tables summarize the results of our operations for each of the years ended December 31, 2015 and 2014, together with the changes in those items in dollars and as a percentage:

	Years Ended December 31,		Increase/ (decrease)	%	
	2015	2014			
	(in thousands)				
Revenue	$19,024	$18,123	$901	5	%
Operating expenses:					

Research and development	12,875	38,254	(25,379)	(66)%
General and administrative	14,217	18,589	(4,372)	(24)%
Restructuring and lease exit	4,358	11,729	(7,371)	(63)%
Total operating expenses	31,450	68,572	(37,122)	(54)%
Loss from operations	(12,426)	(50,449)	38,023	(75)%
Other (expense) income, net	(289)	66	(355)	(538)%
Interest expense	(2,307)	(2,388)	81	(3)%
Interest income	21	32	(11)	(34)%
Net loss	$(15,001)	$(52,739)	$37,738	(72)%

Revenue	Years Ended December 31, 2015	2014	Increase/ (decrease)	%
	(in thousands)			
Strategic Partner:				
Novartis	$18,450	$—	$18,450	100 %
Biogen Idec	268	14,520	(14,252)	(98)%
Ophthotech	231	39	192	492 %
Pharmstandard	61	—	61	100 %
EUSA	14	—	14	100 %
Astellas	—	3,564	(3,564)	(100)%
	$19,024	$18,123	$901	5 %

Revenue. Revenue for the year ended December 31, 2015 was $19.0 million compared to $18.1 million for the year ended December 31, 2014, an increase of approximately $0.9 million, or 5%. The increase was primarily due to the recognition of $18.5 million of revenue associated with the receipt of a $15.0 million upfront payment for our license of AV-380 to Novartis and Novartis' subsequent purchase of clinical material for $3.5 million. These amounts were partially offset by a decrease of $3.6 million of revenue from Astellas following the termination of our collaboration agreement in 2014 and a decrease of $14.3 million of revenue recognized from our arrangement with Biogen due to the one-time recognition of previously deferred revenue following an amendment to our agreement in 2014.

Research and development. Research and development expenses for the year ended December 31, 2015 were $12.9 million compared to $38.3 million for the year ended December 31, 2014, a decrease of $25.4 million, or 66%. The decrease is primarily attributable to a $7.8 million decrease in employee compensation, benefits, contract labor and consulting and a decrease of $9.2 million in facilities, IT, and other costs following our January 2015 restructuring; a decrease of $7.6 million in outsourced services costs primarily related to the completion of the manufacture of AV-380 material in 2014; and a decrease of $0.8 million in medical affairs and external clinical trial costs associated with the decreased number of active patients enrolled in our clinical trials.

Included in research and development expenses were stock-based compensation expenses of approximately $0.3 million and $0.9 million for the years ended December 31, 2015 and 2014, respectively.

General and administrative. General and administrative expenses for the year ended December 31, 2015 were $14.2 million compared to $18.6 million for the year ended December 31, 2014, a decrease of $4.4 million, or 24%. The decrease is primarily the result of a $4.1 million decrease in salaries, benefits, contract labor and consulting and a decrease of $4.5 million in facilities, IT, insurance and other infrastructure costs following our January 2015 restructuring as well as a $2.0 million decrease in external legal costs associated with various ongoing legal matters. These amounts were partially offset by $4.0 million in expense incurred in 2015 related to the accrual of an estimated settlement liability, for accounting purposes, related to the potential SEC claims and an increase in depreciation expense of $2.2 million due to the acceleration of depreciation in connection with the termination of our lease agreement of 650 East Kendall Street in September 2014.

Included in general and administrative expenses were stock-based compensation expenses of approximately $0.8 million and $1.9 million for the years ended December 31, 2015 and 2014, respectively.

Restructuring and lease exit. Restructuring and lease exit expense for the year ended December 31, 2015 was $4.4 million, compared to $11.7 million for the year ended December 31, 2014. The expenses incurred during 2015 relate to costs associated with elimination of our research function and the associated reductions in headcount as part of our January 2015 restructuring. The expenses incurred during 2014 relate to costs associated with partially vacating and

subsequently terminating the agreement for our leased space at 650 East Kendall Street, which occurred in September 2014.

Other (expense) income, net. Other (expense) income, net for the year ended December 31, 2015 was ($0.3) million compared to $0.1 million for the year ended December 31, 2014, a decrease of $0.4 million or 538%. Other (expense) for 2015 is primarily due to losses incurred upon disposing of certain assets following our January 2015 restructuring. Other income for 2014 is primarily due to proceeds from the sale of lab equipment.

Interest expense. Interest expense for the year ended December 31, 2015 was $2.3 million compared to $2.4 million for the year ended December 31, 2014, a decrease of $0.1 million, or 3%. The decrease is primarily attributable to the declining average outstanding balance on our loan with Hercules Technology Growth.

Interest income. Interest income for the year ended December 31, 2015 was $21,000 compared to $32,000 for the year ended December 31, 2014, a decrease of $11,000, or 34%. The decrease in interest income is primarily due to overall lower average cash, cash equivalent and marketable securities balances during the year ended December 31, 2015 compared to the year ended December 31, 2014.

Comparison of Years Ended December 31, 2014 and 2013

The following tables summarize the results of our operations for each of the years ended December 31, 2014 and 2013, together with the changes in those items in dollars and as a percentage:

	Years Ended December 31,		Increase/ (decrease)	%
	2014	2013		
	(in thousands)			
Revenue	$18,123	$1,293	$16,830	1,302%
Operating expenses:				
Research and development	38,254	68,468	(30,214)	(44)%
General and administrative	18,589	28,712	(10,123)	(35)%
Restructuring and lease exit	11,729	8,017	3,712	46%
Total operating expenses	68,572	105,197	(36,625)	(35)%
Loss from operations	(50,449)	(103,904)	53,455	(51)%
Other income (expense), net	66	(123)	189	(154)%
Interest expense	(2,388)	(3,127)	739	(24)%
Interest income	32	125	(93)	(74)%
Net loss	$(52,739)	$(107,029)	$54,290	(51)%

Revenue	Years Ended December 31,		Increase/ (decrease)	%
	2014	2013		
	(in thousands)			
Strategic Partner:				
Astellas	$3,564	$430	$3,134	729%
Ophthotech	39	—	39	100%
Biogen Idec	14,520	863	13,657	1,583%
	$18,123	$1,293	$16,830	1,302%

Revenue. Revenue for the year ended December 31, 2014 was $18.1 million compared to $1.3 million for the year ended December 31, 2013, an increase of approximately $16.8 million, or 1,302%. The increase was primarily due to the recognition of an additional $13.7 million of previously deferred revenue as a result of the amendment to our arrangement with Biogen. Pursuant to the amendment, Biogen agreed to the termination of its rights and obligations under the previous arrangement. As a result, we recognized as revenue all previously deferred amounts in excess of the estimated selling price of the remaining deliverables under the modified arrangement. In addition, we recognized an additional $3.1 million in connection with the change in the estimated period of performance associated with our collaboration with Astellas as a result of the termination of the agreement in August 2014.

Research and development. Research and development expenses for the year ended December 31, 2014 were $38.3 million compared to $68.5 million for the year ended December 31, 2013, a decrease of $30.2 million, or 44%. The decrease is primarily attributable to a $14.0 million decrease in employee compensation, benefits, and contract labor as well as a decrease of $6.2 million in facilities, IT, and other costs following our June 2013 restructuring; a decrease of $11.9 million in outsourced services costs primarily related to the completion of the manufacture of ficlatuzumab material in 2013; and a decrease of $11.7 million in external clinical trial, research, and medical affairs costs associated with decreased tivozanib clinical development activity. The decrease for 2014 was partially offset by a decrease of $9.5 million in reimbursements to us by Astellas for tivozanib development costs due to the corresponding decrease in tivozanib expenses, which we recorded as a reduction in R&D expense in the prior year period, and an increase of $4.1 million in manufacturing costs related primarily to the completion of the manufacture of AV-380 material in 2014.

Included in research and development expenses were stock-based compensation expenses of approximately $0.9 million and $2.0 million for the years ended December 31, 2014 and 2013, respectively.

General and administrative. General and administrative expenses for the year ended December 31, 2014 were $18.6 million compared to $28.7 million for the year ended December 31, 2013, a decrease of $10.1 million, or 35%. The decrease is primarily the

result of a $6.0 million decrease in salaries and benefits as well as a decrease of $2.5 million in facilities and IT costs following our June 2013 restructuring, and a $6.7 million decrease in marketing and consulting costs due to termination of tivozanib pre-commercialization activities. These amounts were partially offset by a $1.6 million increase in external legal costs associated with various ongoing legal matters, an increase in depreciation expense of $0.9 million due to the acceleration of depreciation following the termination of our lease agreement of 650 East Kendall Street in September 2014, and by a $2.6 million decrease in reimbursements to us from Astellas for shared tivozanib general and administrative costs, which we recorded as a reduction in general and administrative expense in the prior year period.

Included in general and administrative expenses were stock-based compensation expenses of approximately $1.9 million and $1.8 million for the years ended December 31, 2014 and 2013, respectively.

Restructuring and lease exit. Restructuring and lease exit expense for the year ended December 31, 2014 was $11.7 million, compared to $8.0 million for the year ended December 31, 2013. The expenses incurred during 2014 relate to costs associated with partially vacating and subsequently terminating the agreement for our leased space at 650 East Kendall Street, which occurred in September 2014. The expenses incurred during 2013 relate to severance and employee benefits incurred as part of the June 2013 strategic restructuring.

Other income (expense), net. Other income (expense), net for the year ended December 31, 2014 was $0.1 million compared to $(0.1) million for the year ended December 31, 2013, an increase of $0.2 million or 154%. Other income for 2014 is primarily due to proceeds from the sale of lab equipment, while expense for 2013 is primarily due to losses on foreign exchange rates and fixed asset disposals.

Interest expense. Interest expense for the year ended December 31, 2014 was $2.4 million compared to $3.1 million for the year ended December 31, 2013, a decrease of $0.7 million, or 24%. The decrease is primarily attributable to the declining outstanding balance on our loan with Hercules Technology Growth during the first three quarters of 2014.

Interest income. Interest income for the year ended December 31, 2014 was $32,000 compared to $125,000 for the year ended December 31, 2013, a decrease of $93,000, or 74%. The decrease in interest income is primarily due to overall lower average cash, cash equivalent and marketable securities balances during the year ended December 31, 2014 compared to the year ended December 31, 2013.

Contractual Obligations and Commitments

The following table summarizes our non-cancellable contractual obligations at December 31, 2015:

	Payment due by period				
Contractual Obligations	Total	Less than 1 Year	1 to 3 Years	3 to 5 Years	More than 5 Years
	(in thousands)				
Long-term debt (including interest)	$12,413	$3,499	$8,914	—	—
Operating lease obligations[1]	46	46	—	—	—
License agreements[2][3]	25	25	—	—	—
Total contractual cash obligations	$12,484	$3,570	$8,914	—	—

(1) As discussed in Note 14 to our consolidated financial statements, we provided notice in February 2015 of our election to surrender our space at 650 E. Kendall Street in Cambridge on May 29, 2015. In conjunction with our departure from our prior space, we began subleasing our principal facilities at One Broadway in Cambridge in April, 2015. Our lease arrangement is cancellable within 30 days' notice to our landlord. As a result, our operating lease obligation as of December 31, 2015 is the January rent payable to our landlord.

(2) Under our license agreement with Kyowa Hakko Kirin, we are required to make certain milestone payments upon the achievement of specified regulatory milestones. We are also required to pay 30% of certain amounts we receive from sublicensees, including up-front license fees, milestone payments and royalties, other than amounts we receive in respect of research and development funding or equity investments, subject to certain limitations. Additionally, under our license agreement with St. Vincent's Hospital, we are required to make certain milestone payments upon the achievement of specified regulatory or clinical milestones. At this time, we cannot reasonably estimate when or if we may be required to make other additional payments to Kyowa Hakko Kirin or St. Vincent's Hospital and have not included any additional amounts in the table above.

(3) As discussed in Note 7 to our consolidated financial statements, we have executed license agreements for patented technology and other technology related to research projects, including technology to humanize ficlatuzumab and other antibody product candidates. The license agreements required us to pay non-refundable license fees upon execution, and in certain cases, require

milestone payments upon the achievement of defined development goals. We have not included any additional milestone payments in the table above as we are not able to make a reasonable estimate of the probability and timing of such payments, if any. In addition to the amounts in the table above, these four agreements include sales and development milestones of up to $22.5 million, $5.5 million and $4.2 million per product, respectively, and single digit royalties as a percentage of sales.

Liquidity and Capital Resources

We have funded our operations principally through the sale of equity securities sold in private placements and underwritten public offerings of equity securities, revenue and expense reimbursements from strategic partnerships, debt financing and interest income. Through December 31, 2015, we have received gross proceeds of $89.7 million from the sale of common stock in our initial public offering, $68.3 million from private placements of shares of our common stock to institutional and accredited investors, $168.7 million from a follow-on public offering of shares of our common stock, and $169.6 million from the sale of convertible preferred stock prior to becoming a public company. As of December 31, 2015, we have received an aggregate of $420.5 million in cash from our agreements with strategic partners, and $36.5 million in funding from our debt financing with Hercules Technology Growth and certain of its affiliates. As of December 31, 2015, we had cash, cash equivalents and marketable securities of approximately $34.1 million. Currently, our funds are invested in money market funds, U.S. government agency securities, and corporate debt securities, including commercial paper. The following table sets forth the primary sources and uses of cash for each of the periods set forth below:

	Years Ended December 31,		
	2015	2014	2013
	(in thousands)		
Net cash used in operating activities	$(18,230)	$(54,248)	$(84,402)
Net cash (used in) provided by investing activities	(6,316)	54,710	12,070
Net cash (used in) provided by financing activities	(1,126)	1,018	46,998
Net (decrease) increase in cash and cash equivalents	$(25,672)	$1,480	$(25,334)

During the years ended December 31, 2015, 2014 and 2013, our operating activities used cash of $18.2 million, $54.2 million and $84.4 million, respectively. Cash used by operations for the year ended December 31, 2015 was due primarily to our net loss adjusted for non-cash items. Cash used by operations for the year ended December 31, 2014 was due primarily to our net loss adjusted for non-cash items, including a $7.6 million impairment of property due to the lease exit costs incurred upon us meeting the cease use criteria for certain of our facilities during 2014, an $18.0 million recognition of deferred revenue related to the termination of our collaboration with Astellas and Biogen during the same period, and working capital changes. Cash used by operations for the year ended December 31, 2013 was due primarily to our net losses adjusted for non-cash items.

During the years ended December 31, 2015, 2014 and 2013, our investing activities (used) provided cash of ($6.3) million, $54.7 million and $12.1 million, respectively. The cash used in investing activities for the year ended December 31, 2015 was the result of the purchase of $19.1 million of marketable securities, partially offset by the sale of $11.6 million of marketable securities and the receipt of $1.2 million in proceeds from the sale of property and equipment. The cash provided by investing activities for the years ended December 31, 2014 and 2013 was the result of fewer purchases of marketable securities than the proceeds from maturities and sales of marketable securities in order to fund our ongoing operations, partially offset by purchases of property and equipment of $12.9 million and $3.7 million during the years ended December 31, 2013 and 2012, respectively.

During the years ended December 31, 2015, 2014 and 2013, our financing activities (used) provided ($1.1) million, $1.0 million and $47.0 million, respectively. The cash used in financing activities in 2015 was due to $11.6 million in principal payments on our loan agreement, partially offset by proceeds from the issuance of common stock totaling $10.2 million. The cash provided by financing activities in 2014 was due to net proceeds of $8.6 million from the amendment of our loan agreement entered into with affiliates of Hercules Technology Growth, offset partially by principal payments on loans payable in the amount of $7.8 million. The cash provided by financing activities in 2013 was primarily due to the net proceeds of $53.6 million from our public offering of stock, offset by $7.1 million in principal payments on our loan from Hercules Technology Growth.

At-The-Market Issuance Sales Agreements with FBR

In February 2015, we entered into an at-the-market issuance sales agreement, which we refer to as the Sales Agreement, with FBR & Co., or FBR, (formerly MLV & Co. LLC), pursuant to which we could issue and sell shares of our common stock from time to time up to an aggregate amount of $17.9 million, at our option, through FBR as our sales agent.

On May 7, 2015, we filed a shelf registration statement on Form S-3 with the SEC, which we refer to as the 2015 Shelf. The 2015 Shelf covers the offering, issuance and sale of up to $100 million of our common stock, preferred stock, debt securities, warrants

and/or units. The 2015 Shelf was filed to replace our existing $250 million shelf registration statement, which expired at the end of May 2015, and which we refer to as the 2012 Shelf. On May 7, 2015, we also amended the Sales Agreement to provide for the offering, issuance and sale of up to $15 million of our common stock under the 2015 Shelf. The prior at-the-market offering initiated under the Sales Agreement expired along with the 2012 Shelf. As of December 31, 2015, we have sold approximately 5.9 million shares pursuant to the Sales Agreement, as amended, resulting in proceeds of approximately $10.2 million, net of commissions and issuance costs. Approximately $9.0 million remains available for sale under the Sales Agreement.

Sales of common stock through FBR may be made by any method that is deemed an “at-the-market” offering as defined in Rule 415 promulgated under the Securities Act of 1933, as amended, including by means of ordinary brokers’ transactions at market prices, in block transactions or as otherwise agreed by the Company and FBR. Subject to the terms and conditions of the Sales Agreement, FBR will use commercially reasonable efforts to sell our common stock based upon our instructions (including any price, time or size limits or other customary parameters or conditions we may impose). We are not obligated to make any sales of common stock under the amended Sales Agreement. Any shares sold will be sold pursuant to an effective shelf registration statement on Form S-3. We are required to pay FBR a commission of up to 3% of the gross proceeds. The Sales Agreement may be terminated by us at any time.

Credit Facilities. On September 24, 2014, we amended our loan and security agreement, which we refer to as the Amended Loan Agreement, with Hercules Technology II, L.P. and Hercules Technology III, L.P., affiliates of Hercules Technology Growth, which we originally entered into on May 28, 2010 and amended on December 21, 2011 and March 31, 2012. Pursuant to the Amended Loan Agreement, we received a new loan in an aggregate principal amount of $10.0 million and amended the terms of our original loan with Hercules, which had an outstanding principal balance of $11.6 million at the date of the amendment. We are not required to make any principal payments on the new loan of $10.0 million until May 1, 2016. The date on which we will be required to begin making principal payments was extended in August 2015 and may be further extended if we continue to achieve performance milestones, after which time we will be required to make monthly principal and interest payments with the entire loan due and payable on January 1, 2018.

The Amended Loan Agreement has an end-of-term payment of approximately $0.5 million due on January 1, 2018 or on such earlier date as the new loan is prepaid. The Amended Loan Agreement also has a financial covenant with respect to the new loan, whereby we have agreed to maintain a liquidity ratio equal to or greater than 1.25 to 1.00, or the equivalent of $12.5 million based on the outstanding principal balance as of December 31, 2015, in unrestricted and unencumbered cash and cash equivalents. This financial covenant will not apply after such time as we receive favorable data both with respect to our phase 2 clinical study of ficlatuzumab and a phase 1 clinical study of AV-380. We continued to be in compliance with all financial covenants under the Amended Loan Agreement at December 31, 2015. We must make interest payments on both loans each month the loans remains outstanding. Per annum interest is payable on each loan at the greater of 11.9% and an amount equal to 11.9% plus the prime rate minus 4.75%, provided, however, that the per annum interest shall not exceed 15.0%. Our annual interest rate as of December 31, 2015 was 11.9%.

We have determined that the risk of subjective acceleration under the material adverse events clause included in this loan and security agreement is remote and, therefore, have classified the outstanding principal amount in current and long-term liabilities based on the timing of scheduled principal payments. As of December 31, 2015 and through the date of this filing, the lenders have not asserted any events of default under the loan.

The loans are secured by a lien on all of our personal property (other than intellectual property), whether owned as of, or acquired after, the date of the amended loan agreement. As of December 31, 2015, the principal balance outstanding was $10.0 million.

Operating Capital Requirements. We anticipate that we will continue to incur significant operating losses for the next several years as we incur expenses to continue to execute on our clinical development strategy to advance our clinical

stage assets. In particular, we estimate that the remaining uncommitted costs of a Phase 3 trial for RCC such as the one contemplated by us could cost in the range of $34-36 million through 2018.

We believe that our cash resources would allow us to fund our current operations into the fourth quarter of 2017. This estimate does not include our payment of potential licensing milestones or the uncommitted costs of conducting any contemplated clinical trials and assumes no milestone payments from our partners, no additional funding from new partnership agreements, no equity financings, no debt financings, no accelerated repayment thereof and no further sales of equity under our ATM. This estimate also does not include any amount we may agree to pay in excess of the estimated settlement liability, for accounting purposes, that we have established with respect to a settlement of claims with the SEC, as described above under the heading “Legal Proceedings” in Part I—Item 3 of this Form 10-K.

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 and the period in which we will have working capital to fund our operations. Accordingly, the timing and nature of activities contemplated for 2016 and thereafter will be conducted subject to the availability of sufficient financial resources.

Our future funding requirements will depend on many factors, including, but not limited to:

- our ability to establish and maintain strategic partnerships, licensing or other arrangements and the financial terms of such agreements;
- the number and characteristics of the product candidates we pursue;
- the scope, progress, results and costs of researching and developing our product candidates, and conducting preclinical and clinical trials;
- the timing of, and the costs involved in, obtaining regulatory approvals for our product candidates;
- the costs involved in preparing, filing, prosecuting, maintaining, defending and enforcing patent claims, including litigation costs and the outcome of such litigation;
- the absence of any breach, acceleration event or event of default under our loan agreement with Hercules or under any other agreements with third parties;
- the outcome of legal actions against us, including the current lawsuits and SEC proceedings described above under "Part I, Item 3—Legal Proceedings," including whether we enter into a settlement with the SEC within the estimated settlement liability we have established for accounting purposes;
- the cost of commercialization activities if any of our product candidates are approved for sale, including marketing, sales and distribution costs;
- the cost of manufacturing our product candidates and any products we successfully commercialize; and
- the timing, receipt and amount of sales of, or royalties on, our future products, if any.

If our available cash and cash equivalents are insufficient to satisfy our liquidity requirements, or if we identify additional opportunities to do so, we may seek to sell additional equity or debt securities or obtain additional credit facilities. The sale of additional equity or convertible debt securities may result in additional dilution to our stockholders. If we raise additional funds through the issuance of debt securities or preferred stock or through additional credit facilities, these securities and/or the loans under credit facilities could provide for rights senior to those of our common stock and could contain covenants that would restrict our operations. We may require additional capital beyond our currently forecasted amounts. 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 our clinical trials or other development activities for one or more of our product candidates; and/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, if approved.

Off-Balance Sheet Arrangements

We did not have, during the periods presented, and we do not currently have, any off-balance sheet arrangements, as defined under applicable SEC rules.

ITEM 7A. Quantitative and Qualitative Disclosures About Market Risk

We are exposed to market risk related to changes in interest rates. As of December 31, 2015, we had cash, cash equivalents and marketable securities of $34.1 million, consisting of cash on deposit with banks, money market funds, U.S. government agency securities, and corporate debt, including commercial paper. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates, particularly because our investments are in short-term cash equivalents. Our cash equivalents are subject to interest rate risk and could fall in value if market interest rates increase. Due to the short-term duration of our investment portfolio and the low risk profile of our investments, an immediate 10% change in interest rates would not have a material effect on the fair market value of our portfolio. We have the ability to hold our cash equivalents until maturity, and therefore we would not expect our operating results or cash flows to be affected to any significant degree by the effect of a change in market interest rates on our investments. We do not currently have any auction rate securities.

Our long-term debt bears interest at variable rates. In May 2010, we entered into a loan agreement with affiliates of Hercules Technology Growth Capital pursuant to which we received a loan in the aggregate principal amount of $25.0 million. In March 2012, we entered into an amendment to the loan agreement, pursuant to which we increased the principal amount to $26.5 million. In September 2014, we entered into a further amendment to the loan agreement, pursuant to which we borrowed a new loan of $10.0 million, which is in addition to the existing loan which had an outstanding principal balance of $11.6 million. As of December 31, 2015, our aggregate principal balance outstanding on our loans was $10.0 million. Per annum interest is payable at the greater of 11.9% and 11.9% plus the prime rate of interest minus 4.75%, not to exceed 15%. As a result of the 15% maximum per annum interest rate under the amended loan agreement, we have limited exposure to changes in interest rates on borrowings under this loan agreement. For every 1% increase in the prime rate over 4.75%, given the amount of debt outstanding under the loan agreement as of December 31, 2015, and expected loan payments during 2015, we would have a decrease in future annual cash flows of approximately $0.1 million over the next twelve month period as a result of such 1% increase.

We are also exposed to market risk related to change in foreign currency exchange rates. We contract with contract research organizations and investigational sites that are located around the world. We are subject to fluctuations in foreign currency rates in connection with these agreements. We do not currently hedge our foreign currency exchange rate risk.

ITEM 8. Financial Statements and Supplementary Data

AVEO PHARMACEUTICALS, INC.

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Board of Directors and Stockholders of

AVEO Pharmaceuticals, Inc.

We have audited the accompanying consolidated balance sheets of AVEO Pharmaceuticals, Inc. as of December 31, 2015 and 2014, and the related consolidated statements of operations, comprehensive loss, stockholders' equity, and cash flows for each of the three years in the period ended December 31, 2015. These financial statements are the responsibility of AVEO Pharmaceuticals, Inc.'s management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the consolidated financial position of AVEO Pharmaceuticals, Inc. at December 31, 2015 and 2014, and the consolidated results of its operations and its cash flows for each of the three years in the period ended December 31, 2015, in conformity with U.S. generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), AVEO Pharmaceuticals, Inc.'s internal control over financial reporting as of December 31, 2015, based on criteria established in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) and our report dated March 15, 2016 expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP

Boston, Massachusetts

March 15, 2016

AVEO Pharmaceuticals, Inc.

Consolidated Balance Sheets

(In thousands, except par value amounts)

	2015	2014
Assets		
Current assets:		
Cash and cash equivalents	$26,634	$52,306
Marketable securities	7,501	—
Accounts receivable	4,641	2,341
Restricted cash	—	2,997
Prepaid expenses and other current assets	1,600	1,484
Total current assets	40,376	59,128
Property and equipment, net	23	11,295
Other assets	143	239
Total assets	$40,542	$70,662
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$1,425	$3,245
Accrued expenses	4,106	9,301
Lease exit obligation	—	4,981
Loans payable, net of discount	2,053	11,722
Deferred revenue	814	537
Estimated settlement liability (Note 16)	4,000	—
Deferred rent	—	10,569
Total current liabilities	12,398	40,355
Loans payable, net of current portion and discount	7,418	8,930
Deferred revenue, net of current portion	2,881	231
Other liabilities	618	540
Commitments and contingencies (Note 8)		
Stockholders' equity:		
Preferred stock, $.001 par value: 5,000 shares authorized; no shares issued and outstanding	—	—
Common stock, $.001 par value: 200,000 and 100,000 shares authorized at December 31, 2015 and 2014, respectively; 58,182 and 52,289 shares issued and outstanding at December 31, 2015 and 2014, respectively	58	52
Additional paid-in capital	512,201	500,582
Accumulated other comprehensive loss	(3)	—
Accumulated deficit	(495,029)	(480,028)
Total stockholders' equity	17,227	20,606
Total liabilities and stockholders' equity	$40,542	$70,662

See accompanying notes

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AVEO Pharmaceuticals, Inc.

Consolidated Statements of Operations

(In thousands, except per share amounts)

	Year Ended December 31,		
	2015	2014	2013
Collaboration revenue	$19,024	$18,123	$1,293
Operating expenses:			
Research and development	12,875	38,254	68,468
General and administrative	14,217	18,589	28,712
Restructuring and lease exit	4,358	11,729	8,017
	31,450	68,572	105,197
Loss from operations	(12,426)	(50,449)	(103,904)
Other income and expense:			
Other (expense) income, net	(289)	66	(123)
Interest expense	(2,307)	(2,388)	(3,127)
Interest income	21	32	125
Other expense, net	(2,575)	(2,290)	(3,125)
Net loss	$(15,001)	$(52,739)	$(107,029)
Basic and diluted net loss per share:			
Net loss per share	$(0.27)	$(1.01)	$(2.10)
Weighted average number of common shares outstanding	55,701	52,289	50,928

See accompanying notes

AVEO PHARMACEUTICALS, INC.

Consolidated Statements of Comprehensive Loss

(In thousands)

	Year Ended December 31,		
	2015	2014	2013
Net loss	$(15,001)	$(52,739)	$(107,029)
Other comprehensive (loss) income:			
Unrealized (losses) gains on available-for-sale securities	(3)	2	(9)
Foreign currency translation adjustment	—	—	26
Comprehensive loss	$(15,004)	$(52,737)	$(107,012)

See accompanying notes

AVEO Pharmaceuticals, Inc.

Consolidated Statements of Stockholders' Equity

(In thousands)

Transaction	Common Shares Shares	Par Value	Additional Paid-in Capital	Accumulated Other Comprehensive Loss	Accumulated Deficit	Total Stockholders' Equity
Balance at December 31, 2012	43,780	$ 44	$439,173	$ (19)	$ (320,260)	$ 118,938
Exercise of stock options	185	1	271	—	—	272
Stock-based compensation expense related to equity-classified awards	—	—	3,791	—	—	3,791
Issuance of common stock to settle liability-classified share awards granted to directors	39	—	119	—	—	119
Issuance of common stock under employee stock purchase plan	110	—	193	—	—	193
Issuance of common stock from follow-on stock offering (net of issuance cost of $3,865)	7,667	7	53,630	—	—	53,637
Issuance of restricted stock awards, net of forfeitures	28	—	—	—	—	—
Change in unrealized gain/loss on investments	—	—	—	(9)	—	(9)
Cumulative translation adjustment	—	—	—	26	—	26
Net loss	—	—	—	—	(107,029)	(107,029)
Balance at December 31, 2013	51,809	$ 52	$497,177	$ (2)	$ (427,289)	$ 69,938
Stock-based compensation expense related to equity-classified awards	—	—	2,750	—	—	2,750
Issuance of common stock to settle liability-classified share awards granted to directors	31	—	51	—	—	51
	139	—	191	—	—	191

Issuance of common stock under employee stock purchase plan						
Issuance of warrants in connection with loans payable	—	—	413	—	—	413
Issuance of restricted stock awards, net of forfeitures	310	—	—	—	—	—
Change in unrealized gain/loss on investments	—	—	—	2	—	2
Net loss	—	—	—	—	(52,739)	(52,739)
Balance at December 31, 2014	52,289	$ 52	$ 500,582	$ —	$ (480,028)	$ 20,606
Stock-based compensation expense related to equity-classified awards	—	—	1,132	—	—	1,132
Exercise of stock options	166	—	241	—	—	241
Issuance of common stock to settle liability-classified share awards granted to directors	8		7			7
Issuance of common stock under employee stock purchase plan	7	—	27	—	—	27
Issuance of common stock from at-the-market sales agreement (net of issuance cost of $157)	5,913	6	10,212	—	—	10,218
Forfeiture of restricted stock awards	(201)	—	—	—	—	—
Change in unrealized gain/loss on investments	—	—	—	(3)	—	(3)
Net loss	—	—	—	—	(15,001)	(15,001)
Balance at December 31, 2015	58,182	$ 58	$ 512,201	$ (3)	$ (495,029)	$ 17,227

See accompanying notes

AVEO Pharmaceuticals, Inc.

Consolidated Statements of Cash Flows

(in thousands)

	Year Ended December 31,		
	2015	2014	2013
Operating activities			
Net loss	$(15,001)	$(52,739)	$ (107,029)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	9,567	6,219	3,775
Net loss (gain) on disposal of property and equipment	253	(127)	83
Impairment of property and equipment	232	7,600	65
Stock-based compensation	1,132	2,808	3,940
Non-cash interest expense	655	347	285
Amortization of premiums and discounts on investments	34	221	1,041
Changes in operating assets and liabilities:			
Accounts receivable	(2,300)	(1,357)	19,665
Tenant improvement allowance receivable	—	5,833	(2,593)
Prepaid expenses and other current assets	(116)	1,503	3,179
Other noncurrent assets	96	50	31
Restricted cash	2,997	598	5
Accounts payable	(1,820)	(993)	(6,390)
Accrued expenses	(5,189)	(2,064)	(7,838)
Lease exit obligation	(5,206)	4,981	—
Deferred revenue	2,927	(17,623)	(1,293)
Other liabilities	78	—	—
Estimated settlement liability	4,000	—	—
Deferred rent	(10,569)	(9,505)	8,672
Net cash used in operating activities	(18,230)	(54,248)	(84,402)
Investing activities			
Purchases of property and equipment	(22)	(12,942)	(3,668)
Purchases of marketable securities	(19,085)	(42,306)	(175,391)
Proceeds from maturities and sales of marketable securities	11,550	109,767	191,129
Proceeds from sale of property and equipment	1,241	191	—
Net cash (used in) provided by investing activities	(6,316)	54,710	12,070
Financing activities			
Proceeds from issuance of common stock, net of issuance costs	10,218	—	53,637
Proceeds from issuance of stock for stock-based compensation arrangements	268	191	465
Proceeds from issuance of loans payable	—	10,000	—
Payments of debt issuance cost	—	(1,388)	—
Principal payments on loans payable	(11,612)	(7,785)	(7,104)
Net cash (used in) provided by financing activities	(1,126)	1,018	46,998
Net (decrease) increase in cash and cash equivalents	(25,672)	1,480	(25,334)
Effect of exchange rate changes on cash and cash equivalents	—	—	26
Cash and cash equivalents at beginning of period	52,306	50,826	76,134

Cash and cash equivalents at end of period	$26,634	$52,306	$ 50,826
Supplemental cash flow and noncash investing and financing activities			
Cash paid for interest	$1,983	$2,018	$ 2,916
Non-cash financing activity			
Fair value of warrants issued in connection with long-term debt	$—	$413	—

See accompanying notes

AVEO Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements

December 31, 2015

1. Nature of Business and Organization

AVEO Pharmaceuticals, Inc. (the "Company") is a biopharmaceutical company committed to developing targeted therapies through biomarker insights to provide substantial improvements in patient outcomes where significant unmet medical needs exist. AVEO's proprietary platform has delivered unique insights into cancer and related disease. AVEO's strategy for building value is to leverage these biomarker insights and partner resources to advance the development of its clinical pipeline.

The Company's pipeline of product candidates includes tivozanib, a potent, selective long half-life vascular endothelial growth factor tyrosine kinase inhibitor of all three vascular endothelial growth factors, or VEGF TKI, for which the Company previously demonstrated tivozanib's safety and efficacy in first and second line RCC. However, the U.S. Food and Drug Administration issued a complete response letter denying AVEO's application for approval of the use of tivozanib in first line advanced RCC. The Company is planning to conduct a phase 3 trial of tivozanib in the third-line treatment of patients with refractory RCC to support a request for regulatory approval of tivozanib as a third-line treatment and to address the overall survival concerns presented in the June 2013 complete response letter from the FDA. A strategic partner has submitted a Marketing Authorization Application for tivozanib with the European Medicines Agency for the treatment of RCC in February 2016. Another strategic partner has submitted a registration dossier for tivozanib with the Ministry of Health of the Russian Federation for the treatment of RCC in December 2015 that was accepted in February 2016.

The Company also has a pipeline of monoclonal antibodies, including:

(i) Ficlatuzumab, a potent anti-HFG antibody that inhibits the activity of the HGF/c-Met pathway for which the Company has completed a phase 2 clinical trial, and has entered into a partnership with Biodesix, Inc. ("Biodesix") to advance clinical development,
(ii) AV-203, a potent, high affinity inhibitor of ErbB3 function that has demonstrated anti-tumor activity in multiple preclinical models for which the Company has completed a phase 1 dose escalation trial,
(iii) AV-380, a potent humanized IgG1 inhibitory monoclonal antibody targeting growth differentiating factor-15, or GDF15, a divergent member of the TGF-ß family, for the potential treatment or prevention of cachexia, which the Company has licensed to Novartis.

As used throughout these consolidated financial statements, the terms "AVEO," and the "Company", refer to the business of AVEO Pharmaceuticals, Inc. and its subsidiaries, AVEO Pharma Limited and AVEO Securities Corporation, both of which are wholly-owned.

The Company has an accumulated deficit as of December 31, 2015 of approximately $495.0 million, and will require substantial additional capital for research and product development. The Company believes that its existing cash and cash equivalents are sufficient to fund its operations through at least twelve months from the balance sheet date.

2. Significant Accounting Policies

Revenue Recognition

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

When evaluating multiple element arrangements, the Company considers whether the deliverables under the arrangement represent separate units of accounting. This evaluation requires subjective determinations and requires management to make judgments about the individual deliverables and whether such deliverables are separable from the other aspects of the contractual relationship. In determining the units of accounting, management evaluates certain criteria, including whether the deliverables have standalone value, based on the relevant facts and circumstances for each arrangement. The consideration received is allocated among the separate units of accounting using the relative selling price method, and the applicable revenue recognition criteria are applied to each of the separate units.

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

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

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

At the inception of each agreement that includes milestone payments, the Company evaluates whether each milestone is substantive and at risk to both parties on the basis of the contingent nature of the milestone. This evaluation includes an assessment of whether (a) the consideration is commensurate with either (1) the entity's performance to achieve the milestone, or (2) the enhancement of the value of the delivered item(s) as a result of a specific outcome resulting from the entity's performance to achieve the milestone, (b) the consideration relates solely to past performance, and (c) the consideration is reasonable relative to all of the deliverables and payment terms within the arrangement. The Company evaluates factors such as the scientific, regulatory, commercial and other risks that must be overcome to achieve the respective milestone, the level of effort and investment required to achieve the respective milestone and whether the milestone consideration is reasonable relative to all deliverables and payment terms in the arrangement in making this assessment.

The Company aggregates its milestones into four categories: (i) clinical and development milestones, (ii) regulatory milestones, (iii) commercial milestones, and (iv) patent-related milestones. Clinical and development milestones are typically achieved when a product candidate advances into a defined phase of clinical research or completes such phase. For example, a milestone payment may be due to the Company upon the initiation of a phase 3 clinical trial for a new indication, which is the last phase of clinical development and could eventually contribute to marketing approval by the U.S. Food and Drug Administration ("FDA") or other global regulatory authorities. Regulatory milestones are typically achieved upon acceptance of the submission for marketing approval of a product candidate or upon approval to market the product candidate by the FDA or other global regulatory authorities. For example, a

milestone payment may be due to the Company upon the FDA's acceptance of a New Drug Application ("NDA"). Commercial milestones are typically achieved when an approved pharmaceutical product reaches certain defined levels of net sales by the licensee, such as when a product first achieves global sales or annual sales of a specified amount. Patent-related milestones are typically achieved when a patent application is filed or a patent is issued with respect to certain intellectual property related to the applicable collaboration.

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

Principles of Consolidation

The Company's consolidated financial statements include the Company's accounts and the accounts of the Company's wholly-owned subsidiaries, AVEO Pharma Limited and AVEO Securities Corporation. All intercompany transactions have been eliminated.

Research and Development Expenses

Research and development expenses are charged to expense as incurred. Research and development expenses consist of costs incurred in performing research and development activities, including personnel-related costs such as salaries and stock-based compensation, facilities, research-related overhead, clinical trial costs, manufacturing costs and costs of other contracted services, license fees, and other external costs. Nonrefundable advance payments for goods and services that will be used in future research and development activities are expensed when the activity has been performed or when the goods have been received.

Cash and Cash Equivalents

The Company considers highly liquid investments with a maturity of three months or less when purchased to be cash equivalents. Cash equivalents at December 31, 2015 consisted of money market funds, U.S. government agency securities, and corporate debt securities, including commercial paper, maintained by an investment manager totaling $16.3 million. Cash equivalents at December 31, 2014 consisted of money market funds, U.S. government agency securities, and corporate debt securities, including commercial paper, maintained by an investment manager totaling $36.6 million. The carrying values of our cash equivalent securities approximate fair value due to their short term maturities.

Marketable Securities

Marketable securities at December 31, 2015 consisted of municipal bonds, asset-backed securities, and corporate debt securities, including commercial paper, maintained by an investment manager. There were no marketable securities held by the Company at December 31, 2014. Credit risk is reduced as a result of the Company's policy to limit the amount invested in any one issue. Marketable securities consist primarily of investments which have expected average maturity dates in excess of three months, but not longer than 24 months. The Company classifies these investments as available-for-sale. Unrealized gains and losses are included in other comprehensive (loss) income until realized. The cost of securities sold is based on the specific identification method. There were no realized gains or losses recognized on the sale or maturity of securities during the years ended December 31, 2015 and 2014.

Available-for-sale securities at December 31, 2015 consisted of the following:

	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
	(in thousands)			
Corporate debt securities (Due within 1 year)	$6,504	$ —	$ (3)	$6,501
Government agency securities (Due within 1 year)	1,000	—	—	1,000
	$7,504	$ —	$ (3)	$7,501

The aggregate fair value of securities in an unrealized loss position for less than 12 months at December 31, 2015 was $5.1 million, representing 6 securities. There were no securities in an unrealized loss position for greater than 12

months at December 31, 2015. The unrealized loss was caused by a temporary change in the market for these securities primarily caused by changes in markets interest rates. There was no change in the credit risk of the securities. To determine whether an other-than-temporary impairment exists, the Company performs an analysis to assess whether it intends to sell, or whether it would more likely than not be required to sell, the security before the expected recovery of the amortized cost basis. Where the Company intends to sell a security, or may be required to do so, the security's decline in fair value is deemed to be other-than-temporary and the full amount of the unrealized loss is recorded in the statement of operations as an other-than-temporary impairment charge. When this is not the case, the Company performs additional analyses on all securities with unrealized losses to evaluate losses associated with the creditworthiness of the security. Credit losses are identified where the Company does not expect to receive cash flows, based on using a single best estimate, sufficient to recover the amortized cost basis of a security and these are recognized in other income (expense), net.

Marketable securities in an unrealized loss position at December 31, 2015 consisted of the following:

	Aggregate Fair Value	Unrealized Losses
	(in thousands)	
Corporate debt securities (Due within 1 year)	$ 4,100	$ (3)
Government agency securities (Due within 1 year)	1,000	—
	$ 5,100	$ (3)

Concentrations of Credit Risk

Financial instruments that potentially subject the Company to credit risk primarily consist of cash, cash equivalents and available-for-sale marketable securities. The Company maintains deposits in federally insured financial institutions in excess of federally insured limits.

The Company's credit risk related to marketable securities is reduced as a result of the Company's policy to limit the amount invested in any one issue.

The Company's accounts receivable primarily consist of amounts due to the Company from licensees and collaborators. As of December 31, 2015, the Company had $4.6 million of receivables outstanding, including $3.5 million due from Novartis for the purchase of clinical material pursuant to our licensing arrangement for AV-380 (refer to Note 7) and $1.1 million due from Biodesix pursuant to our collaboration arrangement for AV-299 (refer to Note 7). The Company has not experienced any material losses related to receivables from individual licensees or collaborators.

Fair Value Measurements

The Company records cash equivalents and marketable securities at fair value. The accounting standards for fair value measurements establish a hierarchy that distinguishes between fair value measurements based on market data (observable inputs) and those based on the Company's own assumptions (unobservable inputs). The hierarchy consists of three levels:

- Level 1—Quoted market prices in active markets for identical assets or liabilities. Assets that are valued utilizing only Level 1 inputs include money market funds.
- Level 2—Inputs other than Level 1 inputs that are either directly or indirectly observable, such as quoted market prices, interest rates and yield curves. Assets that are valued utilizing Level 2 inputs include U.S. government agency securities, asset-backed securities, and corporate bonds, including commercial paper. These investments have been initially valued at the transaction price and are subsequently valued, at the end of each reporting period, utilizing third party pricing services or other observable market data. The pricing services utilize industry standard valuation models, including both income and market based approaches and observable market inputs to determine value. These observable market inputs include reportable trades, benchmark yields, credit spreads, broker/dealer quotes, bids, offers, current spot rates, and other industry and economic events. The Company validates the prices provided by third party pricing services by reviewing their pricing methods and matrices, obtaining market values from other pricing sources, analyzing pricing data in certain instances and confirming that the relevant markets are active. After completing its validation procedures, the Company did not adjust or override any fair value measurements provided by pricing services as of December 31, 2015 or December 31, 2014.

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Level 3—Unobservable inputs developed using estimates and assumptions developed by the Company, which reflect those that a market participant would use. The Company currently has no assets or liabilities measured at fair value on a recurring basis that utilize Level 3 inputs.

The following tables summarize the cash equivalents and marketable securities measured at fair value on a recurring basis in the accompanying consolidated balance sheets as of December 31, 2015 and 2014.

	Fair Value Measurements of Cash Equivalents and Marketable Securities as of December 31, 2015			
	Level 1	Level 2	Level 3	Total
	(in thousands)			
Cash equivalents	$11,462	$4,812	$ —	$16,274
Marketable securities	—	7,501	—	7,501
	$11,462	$12,313	$ —	$23,775

	Fair Value Measurements of Cash Equivalents			
	as of December 31, 2014			
	Level 1	Level 2	Level 3	Total
	(in thousands)			
Cash equivalents	$28,777	$7,834	$ —	$36,611

The Company recorded a liability totaling $7.3 million associated with the exit of a portion of its leased facilities during the year ended December 31, 2014. The Company measured the fair value of the liability based on the present value of the remaining termination payments. The net cash outflows were discounted using a credit-risk adjusted rate. The Company has classified this lease liability as a Level 3 fair value measurement.

The fair value of the Company's loans payable at December 31, 2015 and 2014, computed pursuant to a discounted cash flow technique using the effective interest rate under the loan, was $10.0 million and $21.3 million, respectively. These fair values are considered a level 3 fair value measurement. The effective interest rate considers the fair value of the warrant issued in connection with the loan, loan issuance costs and a deferred charge, which approximates a market interest rate.

Property and Equipment

Property and equipment are stated at cost and are depreciated using the straight-line method over the estimated useful lives of the respective assets. Maintenance and repair costs are charged to expense as incurred.

Long-lived Assets

The Company reviews long-lived assets, including property and equipment, for impairment whenever changes in business circumstances indicate that the carrying amount of the asset may not be fully recoverable. The Company recognized $0.2 million, $7.6 million and $0.1 million of impairment losses for the years ended December 31, 2015, 2014 and 2013. The impairment charges incurred during these years primarily related to leasehold improvements.

Stock-Based Compensation

Under the Company's stock-based compensation programs, the Company periodically grants stock options and restricted stock to employees, directors and nonemployee consultants. The Company also issues shares under an employee stock purchase plan. The fair value of all awards is recognized in the Company's statements of operations over the requisite service period for each award. Awards that vest as the recipient provides service are expensed on a straight-line basis over the requisite service period. Other awards, such as performance-based awards that vest upon the achievement of specified goals, are expensed using the accelerated attribution method if achievement of the specified goals is considered probable. The Company has also granted awards that vest upon the achievement of market conditions. Per ASC 718 Share-Based Payments, market conditions must be considered in determining the estimated grant-date fair value of share-based payments and the market conditions must be considered in determining the requisite service period over which compensation cost is recognized. The Company estimates the fair value of the awards with market conditions using a Monte Carlo simulation, which utilizes several assumptions including the risk-free interest rate, the volatility of the Company's stock and the exercise behavior of award recipients. The grant-date fair value of the awards is then recognized over the requisite service period, which represents the derived service period for the awards as determined by the Monte Carlo simulation.

The fair value of equity-classified awards to employees and directors are measured at fair value on the date the awards are granted. Awards to nonemployee consultants are recorded at their fair values and are re-measured as of each balance sheet date until the recipient's services are complete. During the years ended December 31, 2015, 2014 and 2013, the Company recorded the following stock-based compensation expense:

	Years Ended December 31,		
	2015	2014	2013
	(in thousands)		
Research and development	$298	$899	$1,991
General and administrative	765	1,909	1,949
Restructuring	69	—	—
Total stock-based compensation expense	$1,132	$2,808	$3,940

Stock-based compensation expense is allocated to research and development and general and administrative expense based upon the department of the employee to whom each award was granted. No related tax benefits of the stock-based compensation expense have been recognized.

Legal Contingencies

The Company is involved in various legal proceedings and accrues anticipated costs of settlement, damages, and/or losses to the extent such amounts are probable and estimable. If the estimate of a probable loss is a range and no amount within the range is more likely, the Company accrues the minimum amount of the range. See Footnote 16 for discussion of our individual material legal proceedings.

Income Taxes

The Company provides for income taxes using the asset-liability method. Under this method, deferred tax assets and liabilities are recognized based on differences between financial reporting and tax bases of assets and liabilities, and are measured using the enacted tax rates and laws that will be in effect when the differences are expected to reverse. Uncertain tax positions are recognized if the position is more-likely-than-not to be sustained upon examination by a tax authority. Unrecognized tax benefits represent tax positions for which reserves have been established. The Company maintains a full valuation allowance on all deferred tax assets.

Segment and Geographic Information

Operating segments are defined as components of an enterprise engaging in business activities for which discrete financial information is available and regularly reviewed by the chief operating decision maker in deciding how to allocate resources and in assessing performance. The Company views its operations and manages its business in one operating segment principally in the United States. As of December 31, 2015 and 2014, the Company has $1.0 million of net assets located in the United Kingdom.

Use of Estimates

The preparation of financial statements in conformity with accounting principles generally accepted in the United States (“GAAP”) requires the Company’s management to make estimates and assumptions that affect the amounts reported in the financial statements and accompanying notes. Actual results could differ from those estimates.

Recent Accounting Pronouncements

In May 2014, the Financial Accounting Standards Board (“FASB”) issued a comprehensive new revenue recognition standard that will supersede nearly all existing revenue recognition guidance under US GAAP. The standard was originally scheduled to be effective for public entities for annual and interim periods beginning after December 15, 2016. In July 2015, the standard was deferred and will now be effective for annual and interim periods beginning after December 15, 2017. Early adoption is permitted for annual and interim periods beginning after December 15, 2016. The Company is currently evaluating the effect this standard will have on its revenue recognition policies and its financial statements, including how the standard will be adopted.

In August 2014, the FASB issued Accounting Standards Update (“ASU”) No. 2014-15, Presentation of Financial Statements—Going Concern (Subtopic 205-40): Disclosure of Uncertainties about an Entity’s Ability to Continue as a Going Concern. This ASU is intended to define management’s responsibility to evaluate whether there is substantial doubt about an organization’s ability to continue as a going concern within one year of the date of issuance of the entity’s financial statements and to provide related footnote disclosures. This guidance is effective for fiscal years beginning after December 15, 2016, with early application permitted. The adoption of this standard may have an effect on the Company’s disclosures in future periods.

In April 2015, the FASB issued a standard that will require that debt issuance costs be presented in the balance sheet as a reduction of the carrying amount of the associated liability, consistent with debt discounts. The standard is effective for public entities for annual and interim periods beginning after December 15, 2015. The Company does not

believe the adoption of this standard will have a material effect on its financial statements.

3. Loss Per Common Share

Basic loss per share is computed by dividing net loss by the weighted-average number of common shares outstanding during the period. Diluted loss per share is computed by dividing net loss by the weighted-average number of common shares and dilutive common share equivalents then outstanding. Potential common share equivalents consist of restricted stock awards and the incremental common shares issuable upon the exercise of stock options and warrants. Since the Company had a net loss for all periods presented, the effect of all potentially dilutive securities is anti-dilutive. Accordingly, basic and diluted net loss per common share is the same.

The following table sets forth for the periods presented the potential common shares (prior to consideration of the treasury stock method) excluded from the calculation of net loss per common share because their inclusion would have been anti-dilutive:

	Outstanding at Years Ended December 31,		
	2015	2014	2013
	(in thousands)		
Options outstanding	4,796	5,817	4,297
Warrants outstanding	609	609	—
	5,405	6,426	4,297

4. Property and Equipment

Property and equipment consists of the following:

	Estimated Useful Life	December 31, 2015	December 31, 2014
		(in thousands)	
Laboratory equipment	5 years	$ —	$ 7,671
Computer equipment and software	3 years	187	3,913
Office furniture	5 years	—	893
Leasehold improvements	Shorter of asset's useful life or remaining term of lease	—	14,433
		187	26,910
Less accumulated depreciation and amortization		(164)	(15,615)
Property and equipment, net		$ 23	$ 11,295

Depreciation expense for the years ended December 31, 2015, 2014 and 2013 was $9.6 million, $6.2 million and $3.8 million, respectively. In September 2014, the Company entered into a Lease Termination Agreement, pursuant to which the Company agreed to surrender the remaining 49,185 square feet of leased space no later than September 24, 2015. As a result, the Company revised the estimated useful life of its leasehold improvements related to this space, resulting in an increase in depreciation expense of approximately $2.4 million during the year ended December 31, 2014. In February 2015, the Company provided notice that it would surrender the remaining space on May 29, 2015. Accordingly, the Company again revised the estimated useful life of its leasehold improvements related to this office space and amortized such assets through May 2015, resulting in an additional $2.9 million of depreciation expense during the year ended December 31, 2015.

5. Accrued Expenses

Accrued expenses consisted of the following:

	December 31, 2015	December 31, 2014
	(in thousands)	
Clinical expenses	$1,793	$ 2,312
Salaries and benefits	938	1,744
Professional fees	573	685
Restructuring	357	—
Manufacturing and distribution	173	3,216
Other	272	1,344
	$4,106	$ 9,301

6. Loans Payable

On May 28, 2010, the Company entered into a loan and security agreement (the “Loan Agreement”) with Hercules Technology II, L.P. and Hercules Technology III, L.P., affiliates of Hercules Technology Growth (collectively, “Hercules”), pursuant to which the Company received a loan in the aggregate principal amount of $25.0 million. The Company was required to repay the aggregate principal balance under the Loan Agreement in 30 equal monthly installments of principal starting on January 1, 2012. On March 31, 2012, the Company entered into an amendment to the Loan Agreement, pursuant to which the Company increased the principal

amount under the Loan Agreement to $26.5 million. Under the amendment to the Loan Agreement, the date on which the Company was required to begin repaying the aggregate principal balance was extended to April 1, 2013, at which point the Company began repaying such balance in 30 equal monthly installments.

On September 24, 2014, the Company further amended the Loan Agreement with Hercules (the "Amended Loan Agreement"). Pursuant to the Amended Loan Agreement, the Company received a new loan in the aggregate principal amount of $10.0 million and amended the terms of the original Loan Agreement with an outstanding principal balance of $11.6 million. The Company was not required to pay principal on the original loan until January 1, 2015, at which time the Company was required to commence making 12 principal and interest payments ending December 1, 2015. The original loan was fully paid as of December 31, 2015.

Pursuant to the Amended Loan Agreement, the Company is not required to make principal payments on the new $10.0 million loan until May 1, 2016. The period during which the Company is not required to pay principal was extended six months from November 1, 2015 to May 1, 2016 upon executing the Company's license agreement with Novartis and may be further extended if the Company continues to achieve certain performance milestones, after which time, the Company is required to make monthly principal and interest payments with the last principal and interest payment due on January 1, 2018. The Amended Loan Agreement has an end-of-term payment of approximately $0.5 million due on January 1, 2018 or on such earlier date as the new loan is prepaid. This end-of-term payment has been recorded as a loan discount and is being amortized to interest expense over the term of the loan agreement using the effective interest rate method. The Company accounted for the Amended Loan Agreement as a loan modification in accordance with ASC 470-50, Debt—Modifications and Extinguishments.

Per annum interest is payable on principal balance of both loans at the greater of 11.9% and an amount equal to 11.9% plus the prime rate of interest minus 4.75%, provided however, that the per annum interest shall not exceed 15.0%.

The Amended Loan Agreement contains a financial covenant whereby the Company has agreed to maintain, with respect to the new loan of $10.0 million, a liquidity ratio equal to or greater than 1.25 to 1.00 of the then outstanding loan balance or the equivalent of $12.5 million in unrestricted and unencumbered cash and cash equivalents as of December 31, 2015 based upon a principal balance of $10.0 million. The financial covenant shall not apply after such time that the Company receives favorable data both with respect to its phase 2 clinical trial of ficlatuzumab and a phase 1 clinical trial of AV-380.

The Loan Agreement required a deferred financing charge of $1.3 million which was paid in May 2012 related to the amendment of the Loan Agreement. The Loan Agreement also included an additional deferred financing charge of $1.2 million which was paid in June 2014. These amounts were recorded as a loan discount and are being amortized to interest expense over the term of the loan borrowed under the Loan Agreement using the effective interest rate method. The Company recorded a liability for the full amount of the charge since the payment of such amount was not contingent on any future event. The Company paid approximately $0.2 million in loan issuance costs directly to Hercules under the Loan Agreement, which were offset against the loan proceeds and are accounted for as a loan discount.

As part of the Loan Agreement, on June 2, 2010, the Company issued warrants to the lenders to purchase up to 156,641 shares of the Company's common stock at an exercise price equal to $7.98 per share to Hercules. The Company recorded the relative fair value of the warrants of approximately $0.8 million as stockholders' equity and as a discount to the related loan outstanding and is amortizing the value of the discount to interest expense over the term of the original loan using the effective interest method. On July 21, 2011, Hercules exercised these warrants and they are no longer outstanding.

As part of the Amended Loan Agreement, on September 24, 2014, the Company issued warrants to the lenders to purchase up to 608,696 shares of the Company's common stock at an exercise price equal to $1.15 per share to Hercules. The Company recorded the relative fair value of the warrants of approximately $0.4 million as stockholders'

equity and as a discount to the related loan outstanding and is amortizing the value of the discount to interest expense over the term of the loan using the effective interest method. The relative fair value of the warrants was calculated using the Black-Scholes option-pricing model with the following assumptions: volatility of 71.81%, an expected term equal to the contractual life of the warrants (five years), a risk-free interest rate of 1.82% and no dividend yield. The resulting effective interest rate for the loans outstanding under the Amended Loan Agreement is approximately 16.14%.

As part of the Loan Agreement, Hercules also received an option, subject to the Company's written consent, not to be unreasonably withheld, to purchase, either with cash or through conversion of outstanding principal under the loan, up to $2.0 million of equity of the Company sold in any sale by the Company to third parties of equity securities resulting in at least $10.0 million in net cash proceeds to the Company, subject to certain exceptions. The Company has evaluated the embedded conversion option, and has concluded that it does not need to be bifurcated and separately accounted for. No amount will be recognized for the conversion feature until such time as the conversion feature is exercised and it can be determined whether a beneficial conversion feature exists. As of December 31, 2015, the outstanding aggregate principal balance under the remaining loan was $10.0 million.

The loans are secured by a lien on all of our personal property (other than intellectual property), whether owned as of, or acquired after, the date of the amended loan agreement. The Amended Loan Agreement defines events of default, including the occurrence of an event that results in a material adverse effect upon the Company's business operations, properties, assets or condition (financial or otherwise), its ability to perform its obligations under and in accordance with the terms of the Amended Loan Agreement, or upon the ability of the lenders to enforce any of their rights or remedies with respect to such obligations, or upon the collateral under the Loan Agreement, the related liens or the priority thereof. As of December 31, 2015, Hercules has not asserted any events of default and the Company does not believe that there has been a material adverse change as defined in the loan agreement. The Company has determined that the risk of subjective acceleration under the material adverse events clause is remote and therefore has classified the outstanding principal in current and long-term liabilities based on the timing of scheduled principal payments.

Future minimum payments under the loans payable outstanding as of December 31, 2015 are as follows (amounts in thousands):

Years Ending December 31:	
2016	$3,499
2017	4,645
2018	4,269
	12,413
Less amount representing interest	(1,872)
Less discount	(530)
Less deferred charges	(540)
Less current portion	(2,053)
Loans payable, net of current portion and discount	$7,418

7. Collaboration and License Agreements
(a) Out-License Agreements

EUSA

In December 2015, the Company entered into a license agreement with EUSA under which the Company granted to EUSA the exclusive, sublicensable right to develop, manufacture and commercialize tivozanib in the territories of Europe (excluding Russia, Ukraine and the Commonwealth of Independent States), Latin America (excluding Mexico), Africa, Australasia and New Zealand (the "Licensed Territories") for all diseases and conditions in humans, excluding non-oncologic diseases or conditions of the eye.

Under the license agreement, EUSA made a research and development funding payment to the Company of $2.5 million during the year ended December 31, 2015 and is required to make a payment of $4.0 million upon the grant by the European Medicines Agency ("EMA") of marketing approval for tivozanib for treatment of renal cell carcinoma. The Company is eligible to receive additional research funding from EUSA, including up to $20.0 million if EUSA elects to utilize data generated by the Company's planned phase 3 study in third line renal cell carcinoma, and up to $2.0 million for a potential phase 1 combination study with a checkpoint inhibitor. The Company will be entitled to receive milestone payments of $2.0 million per country upon reimbursement approval for renal cell carcinoma in each of France, Germany, Italy, Spain and the United Kingdom, and an additional $2.0 million for the grant of marketing approval in three of the following five countries: Argentina, Australia, Brazil, South Africa and Venezuela. The Company will also be eligible to receive a payment of $2.0 million in connection with EUSA's filing

with the EMA for marketing approval for tivozanib for the treatment of each of up to three additional indications and $5.0 million per indication in connection with the EMA's grant of marketing approval for each of up to three additional indications, as well as potentially up to $335.0 million upon EUSA's achievement of certain sales thresholds. The Company will also be eligible to receive tiered double digit royalties on net sales, if any, of licensed products in the Licensed Territories ranging from a low double digit up to mid-twenty percent depending on the level of annual net sales. A percentage of any milestone and royalty payments received by AVEO are due to Kyowa Hakko Kirin Co., Ltd. (formerly Kirin Brewery Co., Ltd.) ("KHK") as a sublicensing fee under the license agreement between AVEO and KHK dated as of December 21, 2006.

EUSA is obligated to use commercially reasonable efforts to develop and commercialize tivozanib throughout the Licensed Territories. With the exception of certain support to be provided by the Company prior to the grant of marketing approval by the EMA, EUSA has responsibility for all activities and costs associated with the further development, manufacture, regulatory filings and commercialization of tivozanib in the Licensed Territories. EUSA is obligated to use commercially reasonable efforts to file an application with the EMA for approval of marketing authorization for tivozanib for the treatment of renal cell carcinoma, which EUSA filed in February 2016.

The term of the license agreement commenced in December 2015 and will continue on a product-by-product and country-by-country basis until the later to occur of (a) the expiration of the last valid patent claim for such product in such country, (b) the

expiration of market or regulatory data exclusivity for such product in such country or (c) the 10th anniversary of the Effective Date. Either party may terminate the license agreement in the event of the bankruptcy of the other party or a material breach by the other party that remains uncured, following receipt of written notice of such breach, for a period of (a) thirty (30) days in the case of breach for nonpayment of any amount due under the license agreement, and (b) ninety (90) days in the case of any other material breach. EUSA may terminate the license agreement at any time upon one hundred eighty (180) days' prior written notice. In addition, the Company may terminate the license agreement upon thirty (30) days' prior written notice if EUSA challenges any of the patent rights licensed under the license agreement.

Activities under the agreement were evaluated under ASC 605-25 Revenue Recognition—Multiple Element Arrangements, or ASC 605-25, to determine whether such activities represented a multiple element revenue arrangement. The agreement with EUSA includes the following non-contingent deliverables: (i) the Company's grant of an exclusive license to develop and commercialize the tivozanib in the licensed territories; (ii) the Company's obligation to transfer all technical knowledge and data useful in the development and manufacture of tivozanib; (iii) the Company's obligation to cooperate with EUSA and support its efforts to file for marketing approval in the licensed territories, (iv) the Company's obligation to provide access to certain regulatory information resulting from the Company's ongoing development activities outside of the licensed territories and (v) the Company's participation in a joint steering committee. The Company determined that the delivered license did not have stand-alone value from the undelivered elements and have accounted for these items as a single bundled deliverable. The Company allocated up-front consideration of $2.5 million to the bundled unit of accounting and is recognizing it over our performance period through April 2022, the remaining patent life of tivozanib. The Company recognized approximately $14,000 as revenue during the year ended December 31, 2015.

The Company believes the regulatory milestones that may be achieved under the EUSA agreement are consistent with the definition of a milestone included in ASU 2010-17, Revenue Recognition—Milestone Method, and, accordingly, the Company will recognize payments related to the achievement of such milestones, if any, when each such milestone is achieved. Factors considered in this determination included scientific and regulatory risks that must be overcome to achieve each milestone, the level of effort and investment required to achieve each milestone, and the monetary value attributed to each milestone.

Novartis

In August 2015, the Company entered into a license agreement with Novartis. Under the license agreement, the Company has granted to Novartis the exclusive right to develop and commercialize worldwide the Company's proprietary antibody AV-380 and related AVEO antibodies that bind to Growth Differentiation Factor 15 ("GDF15") for the treatment and prevention of diseases and other conditions in all indications in humans (the "Product").

Pursuant to the license agreement, Novartis made an upfront payment to the Company of $15.0 million within fifteen days of the effective date. Novartis also has acquired the Company's inventory of clinical quality, AV-380 biological drug substance and reimbursed the Company for approximately $3.5 million for such existing inventory. The Company will also be eligible to receive (a) up to $53.0 million in potential clinical and development milestone payments and up to $105.0 million in potential regulatory milestone payments tied to the commencement of clinical trials and to regulatory approvals of products developed under the license agreement in the United States, the European Union and Japan; and (b) up to $150.0 million in potential commercial milestone payments based on annual net sales of such products. Upon commercialization, the Company is eligible to receive tiered royalties on net sales of approved products ranging from the high single digits to the low double digits. Novartis has responsibility under the license agreement for the development, manufacture and commercialization of the Company's antibodies and any resulting approved therapeutic products.

The term of the license agreement commenced in August 2015 and will continue on a country-by-country basis until the later to occur of the 10th anniversary of the first commercial sale of a product in such country or the expiration of

the last valid patent claim for a product in that country. Either party may terminate the license agreement in the event of a material breach of the license agreement by the other party that remains uncured for a period of sixty days, which period may be extended an additional thirty days under certain circumstances. Novartis may terminate the license agreement, either in its entirety or with respect to any individual products or countries, at any time upon sixty days' prior written notice. In addition, the Company may terminate the license agreement upon thirty days' prior written notice if Novartis challenges certain patents controlled by the Company related to the Company's antibodies.

The Company has agreed that it will not directly or indirectly develop, manufacture or commercialize any GDF15 modulator as a human therapeutic during the term of the license agreement.

Activities under the agreement with Novartis were evaluated under ASC 605-25 Revenue Recognition—Multiple Element Arrangements, or ASC 605-25, to determine whether such activities represented a multiple element revenue arrangement. The agreement with Novartis includes the following non-contingent deliverables: (i) the Company's grant of an exclusive, worldwide

license to develop and commercialize the Product; (ii) the Company's obligation to transfer all technical knowledge and data useful in the development and manufacture of the Product; and (iii) the Company's obligation to cooperate with Novartis' requests for transition assistance during a 90 day period. The Company determined that the option to purchase the Company's existing inventory was a contingent deliverable.

The Company determined the delivered license and obligation to transfer technical knowledge and data have standalone value from the undelivered cooperation. The Company allocated up-front consideration of $15.0 million to the delivered license and technical knowledge. The relative selling price of the undelivered cooperation had de minimis value.

The Company received cash payments of $15.0 million during the year ended December 31, 2015. The Company recognized the $15.0 million upfront payment allocated to the delivered license and technical knowledge upon delivery. The Company recognized revenue of $3.5 million during 2015 related to the delivery of its inventory of clinical quality drug substance to Novartis pursuant to the terms of the agreement. The amount due to the Company from Novartis was $3.5 million as of December 31, 2015.

Pharmstandard Group

In August 2015, the Company entered into a license agreement with JSC "Pharmstandard- Ufimskiy Vitamin Plant," a company registered under the laws of the Russian Federation ("Pharmstandard"). Pharmstandard is a subsidiary of Pharmstandard OJSC. Under the license agreement, the Company has granted to Pharmstandard the exclusive, sublicensable right to develop, manufacture and commercialize tivozanib in the territories of Russia, Ukraine and the Commonwealth of Independent States (the "Licensed Territories") for all diseases and conditions in humans, excluding non-oncologic ocular conditions.

Under the license agreement, Pharmstandard is required to make an upfront payment to AVEO of $1.5 million, of which $1.0 million was paid during the three months ended September 30, 2015 and $0.5 million is payable within fifteen business days of the date the license agreement is registered with the Federal Service for Intellectual Property of the Russian Federation. The Company is also eligible to receive $7.5 million in connection with the first marketing authorization of tivozanib in Russia. If Russian regulatory authorities require additional studies to be conducted by Pharmstandard prior to approval, this amount would be reduced to $3.0 million. In addition, the Company is eligible to receive $3.0 million for each additional approved indication of tivozanib, if Pharmstandard elects to seek any such approvals, as well as a high single-digit royalty on net sales in the Licensed Territories.

Pharmstandard is obligated to use commercially reasonable efforts to develop and commercialize tivozanib throughout the Licensed Territories, and Pharmstandard has responsibility for all activities and costs associated with the further development, manufacture, regulatory filings and commercialization of tivozanib in the Licensed Territories. Pharmstandard filed an application for marketing authorization in Russia for tivozanib for the treatment of renal cell carcinoma in December 2015.

The term of the license agreement commenced in August 2015 and will continue on a product-by-product and country-by-country basis until the later to occur of (a) the expiration of the last valid patent claim for such product in such country, (b) the expiration of the last marketing authorization for such product in such country or (c) the 10th anniversary of the first commercial sale of such product in such country. Either party may terminate the license agreement in the event of a material breach by the other party that remains uncured, following receipt of written notice of such breach, for a period of (a) thirty days, in the case of breach for nonpayment of any amount due under the license agreement, and (b) ninety days, in the case of any other material breach. After the first anniversary of the effective date, Pharmstandard may terminate the license agreement at any time upon ninety days' prior written notice. In addition, the Company may terminate the license agreement upon thirty days' prior written notice if Pharmstandard challenges certain patents controlled by the Company or the Company's licensor, Kyowa Hakko Kirin Co., Ltd. (formerly Kirin Brewery Co. Ltd.) ("KHK"), related to tivozanib.

Activities under the agreement with Pharmstandard were evaluated under ASC 605-25 to determine whether such activities represented a multiple element revenue arrangement. The agreement with Pharmstandard includes the following non-contingent deliverables: (i) the Company's grant of an exclusive license to develop and commercialize tivozanib in the Licensed Territories, (ii) the Company's obligation to provide access, upon request, to all clinical data, regulatory filings, safety data and manufacturing data to Pharmstandard for use in the development and commercialization of tivozanib in the Licensed Territories, (iii) the Company's obligation to participate in certain development and commercialization planning meetings and (iv) the Company's obligation to provide support for certain development, regulatory or manufacturing activities if requested by Pharmstandard.

The Company determined the delivered license does not have standalone value from the undelivered items and that the arrangement should be treated as a single unit of accounting. The Company allocated the upfront payment of $1.0 million to the

bundled unit of accounting and is recognizing it over the Company's performance period through April 2022, the remaining patent life of tivozanib. The Company recognized approximately $61,000 as revenue during the year ended December 31, 2015.

The Company believes the regulatory milestones that may be achieved under the Pharmstandard agreement are consistent with the definition of a milestone included in ASU 2010-17, Revenue Recognition—Milestone Method, and, accordingly, the Company will recognize payments related to the achievement of such milestones, if any, when such milestone is achieved. Factors considered in this determination included scientific and regulatory risks that must be overcome to achieve each milestone, the level of effort and investment required to achieve each milestone, and the monetary value attributed to each milestone.

A percentage of all upfront, milestone and royalty payments received by AVEO are due to KHK as a sublicensing fee under the License Agreement between AVEO and KHK dated as of December 21, 2006. The Company incurred $0.3 million of R&D expense associated with sublicensing fees payable to KHK during the year ended December 31, 2015.

Ophthotech Corporation

In November 2014 the Company entered into a Research and Exclusive Option Agreement, or Option Agreement, with Ophthotech Corporation pursuant to which the Company provided Ophthotech an exclusive option to enter into a definitive license agreement whereby the Company would grant Ophthotech the right to develop and commercialize the Company's VEGF factor tyrosine kinase inhibitor, tivozanib, outside of Asia for the potential diagnosis, prevention and treatment of non-oncologic diseases or conditions of the eye in humans.

Pursuant to this Option Agreement, the Company granted to Ophthotech an exclusive, royalty free license or sublicense, as applicable, under intellectual property rights controlled by the Company solely to perform the research and development activities related to the use of tivozanib for the specific purposes outlined in the agreement during the option period (as defined below). These activities include formulation work for ocular administration, preclinical research and the conduct of a phase 1/2a, proof of concept clinical trial of a product containing tivozanib in patients with wet age-related macular degeneration, (the "POC Study").

Ophthotech paid the Company $500,000 in consideration for the grant of the option. Such amount is non-refundable and not creditable against any other amounts due under the agreement. The Company is obligated to make available to Ophthotech, at no cost to Ophthotech, certain quantities of tivozanib hydrochloride solely for conducting its option period research including manufacturing additional quantities of tivozanib in the event stability data indicates that the current supply will expire prior to the end of February 2017.

During the option period, if Ophthotech elects to continue the development of tivozanib for non-oncologic diseases of the eye, the Company is entitled to receive a one-time milestone payment of $2.0 million upon acceptance of the first Investigational New Drug application for the purpose of conducting a human clinical study of tivozanib in ocular diseases (the "IND Submission Milestone Payment"). The Company is also entitled to receive a one-time milestone payment of $6.0 million (the "Clinical Efficacy Milestone Payment"), on the earlier of (a) December 31, 2016 and (b) the later to occur of: (i) the achievement of a clinical milestone in the POC Study (the "Clinical Efficacy Milestone") and (ii) the earlier of (A) the date twelve (12) months after our and Ophthotech's agreement as to the form and substance of the KHK Amendment (as defined below) or (B) the date ninety (90) days after the entry into the KHK Amendment, subject to the Company's right to terminate the Option Agreement on 90 days' written notice (the date on which such payment is due, referred to as the "Clinical Efficacy Milestone Payment Trigger Date").

Ophthotech may exercise the option at any time until the latest to occur of: (i) twelve (12) months after the achievement of the Clinical Efficacy Milestone, (ii) ninety (90) days after the Clinical Efficacy Milestone Payment Trigger Date, and (iii) thirty (30) days after the Company and Ophthotech agree as to the definitive form of license agreement, which the Company refers to as the option period.

During the Option Period, the Company will not grant a license to any third party that would preclude the Company from being able to grant to Ophthotech the rights and licenses that are contemplated by the definitive license agreement, and the Company will not engage in any research, development or commercialization of tivozanib in the field covered by the contemplated definitive license agreement, except as specified in the Option Agreement.

The terms of the Option Agreement are subject to the Company's obligations to Kyowa Hakko Kirin Co., Ltd. ("KHK"), under a license agreement entered into by the Company with KHK in 2006, pursuant to which the Company acquired exclusive rights to develop and commercialize tivozanib for all human diseases outside of Asia (the "KHK License Agreement"). A percentage of all payments received by the Company under the Option Agreement and any definitive license agreement must be paid to KHK. The Company is required to maintain the KHK Agreement in effect, and not enter into any amendment or termination thereof that would adversely affect the Company's rights, during the option period.

During the option period, the Company and Ophthotech are obligated to negotiate in good faith the form and substance of a definitive license agreement, as well as the form and substance of an amendment to the Company's license agreement with KHK (the "KHK Amendment") to modify certain rights and obligations of the parties and sublicensees thereunder, particularly with respect to rights to improvements that are not specifically related to tivozanib, and regulatory affairs matters.

Upon exercise of the option, Ophthotech is required to pay the Company a one-time option exercise fee of $2.0 million in addition to the IND Submission Milestone Payment if such payment has not then been previously paid. If upon exercise of the option, the Clinical Efficacy Milestone Payment Trigger Date has not yet occurred, the Company shall be entitled to the Clinical Efficacy Milestone Payment at such time that the Clinical Efficacy Milestone Payment Date does occur if the license agreement remains in effect as of such date. The license agreement, if entered into upon Ophthotech's exercise of the Option, will provide for the Company to be entitled to receive (i) $10.0 million upon meeting certain efficacy and safety endpoints in phase 2 clinical trials that would enable the commencement of a phase 3 clinical trial, (ii) $20.0 million upon marketing approval in the United States, (iii) $20.0 million upon marketing approval in the UK, Germany, Spain, Italy and France and (iv) up to $45.0 million in sales-based milestone payments. Ophthotech would also be required to pay tiered, double digit royalties, up to the mid-teens, on net sales of tivozanib or products containing tivozanib.

Either party may terminate the Option Agreement in the event of an uncured material breach of the Option Agreement by the other party which remains uncured for a period of ninety (90) days (or thirty (30) days for a breach relating to non-payment), or upon bankruptcy or like proceedings relating to the other party. Ophthotech may terminate the Option Agreement at any time upon ninety (90) days' prior written notice to us. In addition, the Company may terminate the Option Agreement upon thirty (30) days' prior written notice to Ophthotech if Ophthotech challenges certain patents controlled by the Company related to tivozanib. Unless terminated as provided above, the Option Agreement will expire upon the expiration of the option or the entry into the definitive license agreement.

Activities under the agreement with Ophthotech were evaluated under ASC 605-25 to determine whether such activities represented a multiple element revenue arrangement. The agreement with Ophthotech includes the following non-contingent deliverables: the Company's obligation to grant an exclusive option to Ophthotech to enter into a License Agreement to develop and commercialize products incorporating tivozanib for treatment of AMD and other diseases of the eye outside of Asia during the Option Period; the Company's obligation to enter into an amendment with KHK to modify the terms of the existing KHK agreement to negotiate a mutually acceptable form of license agreement; and the Company's obligation to transfer research-grade tivozanib API for Ophthotech to conduct the Option Period research.

The Company determined that the delivered Option Grant Deliverable, or the Company's obligation to grant an exclusive option to Ophthotech to enter into a License Agreement to develop and commercialize products incorporating tivozanib for treatment of AMD and other diseases of the eye outside of Asia during the Option Period, did not have standalone value from the remaining deliverables since Ophthotech could not obtain the intended benefit of the option without the remaining deliverables. Similarly, the remaining deliverables have no standalone value without the Option Grant Deliverable. The Company is accounting for the deliverables as one unit of accounting.

Under the agreement, the Company received a cash payment of $0.5 million during the year ended December 31, 2014. The Company deferred the payment and is recording the deferred revenue over the Company's period of performance, which is estimated to be through December 2016. The Company recorded approximately $0.2 million and $38,000 of revenue during the years ended December 31, 2015 and 2014, respectively.

Biodesix

In April 2014, the Company entered into a worldwide agreement with Biodesix to develop and commercialize its hepatocyte growth factor ("HGF") inhibitory antibody ficlatuzumab, with BDX004, a proprietary companion diagnostic

test developed by Biodesix and derived from VeriStrat®, a serum protein test that is commercially available to help physicians guide treatment decisions for patients with advanced non-small cell lung cancer ("NSCLC"). Under the agreement, the Company granted Biodesix perpetual, non-exclusive rights to certain intellectual property, including all clinical and biomarker data related to ficlatuzumab, to develop and commercialize BDX004. Biodesix granted the Company perpetual, non-exclusive rights to certain intellectual property, including diagnostic data related to BDX004, with respect to the development and commercialization of ficlatuzumab; each license includes the right to sublicense, subject to certain exceptions. Pursuant to a joint development plan, the Company retains primary responsibility for clinical development of ficlatuzumab in a proof of concept ("POC") clinical study of ficlatuzumab for NSCLC, in which VeriStrat will be used to select clinical trial subjects, referred to as the NSCLC POC Trial. The NSCLC POC Trial will be fully funded by Biodesix up to a maximum of $15.0 million, referred to as the "Cap". After the Cap is reached, the Company and Biodesix will share equally in the costs of the NSCLC trial, and the Company and Biodesix will each be responsible for 50% of development and regulatory costs associated with all future clinical trials agreed-upon by Biodesix and the Company, including all milestone payments and royalties payable to third parties, if any.

Pending marketing approval of ficlatuzumab and subject to a commercialization agreement to be entered into after receipt of results from the NSCLC POC Trial, each party would share equally in commercialization profits and losses, subject to the Company's right to be the lead commercialization party.

Biodesix is solely responsible for the BDX004 development costs, as well as BDX004 sales and marketing costs. Subject to and following the approval of the BDX004 test as a companion diagnostic for ficlatuzumab, Biodesix has agreed to make the BDX004 test available and use commercially reasonable efforts to seek reimbursement in all geographies where ficlatuzumab is approved. The Company has agreed to reimburse Biodesix a pre-specified amount, under certain circumstances for BDX004 tests performed.

Prior to the first commercial sale of ficlatuzumab and after the earlier of (i) the Cap being reached or (ii) the completion of the NSCLC POC Trial, each party has the right to elect to discontinue participating in further development or commercialization efforts with respect to ficlatuzumab, which is referred to as an "Opt-Out". If either AVEO or Biodesix elects to Opt-Out, with such party referred to as the "Opting -Out Party", then the Opting-Out Party shall not be responsible for any future costs associated with developing and commercializing ficlatuzumab other than any ongoing clinical trials. After election of an Opt-Out, the non-opting out party shall have sole decision-making authority with respect to further development and commercialization of ficlatuzumab. Additionally, the Opting-Out Party shall be entitled to receive, if ficlatuzumab is successfully developed and commercialized, a royalty equal to 10% of net sales of ficlatuzumab throughout the world, if any, subject to offsets under certain circumstances.

If Biodesix elects to Opt-Out, it will continue to be responsible for its development and commercialization obligations with respect to BDX004. If AVEO elects to Opt-Out, it will continue to make the existing supply of ficlatuzumab available to Biodesix for the purposes of enabling Biodesix to complete the development of ficlatuzumab, and Biodesix will have the right to commercialize ficlatuzumab.

Prior to any Opt-Out, the parties shall share equally in any payments received from a third party licensee; provided, however, after any Opt-Out, the Opting-Out Party shall be entitled to receive only a reduced portion of such third party payments. The agreement will remain in effect until the expiration of all payment obligations between the parties related to development and commercialization of ficlatuzumab, unless earlier terminated.

Activities under the agreement with Biodesix were evaluated under ASC 605-25 to determine whether such activities represented a multiple element revenue arrangement. The agreement with Biodesix includes the following non-contingent deliverables: perpetual, non-exclusive rights to certain intellectual property including clinical and biomarker data related to ficlatuzumab for use in developing and commercializing BDX004; the Company's obligation to deliver technology improvements and data developed during the NSCLC POC Trial to Biodesix; the Company's obligation to participate in the joint steering committee during the NSCLC POC Trial; the Company's obligation to perform certain development activities associated with the NSCLC POC Trial; and the Company's obligation to supply clinical material for use in conducting the NSCLC POC Trial; and the Company's obligation to deliver clinical specimens and data during the NSCLC POC Trial. The Company concluded that any deliverables that would be delivered after the NSCLC POC Trial is complete are contingent deliverables because these services are contingent upon the results of the NSCLC POC Trial. As these deliverables are contingent, and are not at an incremental discount, they are not evaluated as deliverables at the inception of the arrangement. These contingent deliverables will be evaluated and accounted for separately as each related contingency is resolved. As of December 31, 2015, no contingent deliverables had been provided by the Company.

The Company determined that the delivered item, or the perpetual, non-exclusive rights to certain intellectual property for use in developing and commercializing BDX004 did not have standalone value from the remaining deliverables since Biodesix could not obtain the intended benefit of the license without the remaining deliverables. Since the remaining deliverables will be performed over the same period of performance there is no difference in accounting for the deliverables as one unit or multiple units of accounting, and therefore, the Company is accounting for the deliverables as one unit of accounting.

The Company records the consideration earned while conducting the NSCLC POC Trial, which consists of reimbursements from Biodesix for expenses related to the trial under the Cap, as a reduction to research and development expense using the proportional performance method over the respective period of performance. As a result of the cost sharing provisions in the agreement, the Company reduced research and development expenses by approximately $3.5 million and $2.7 million during the years ended December 31, 2015 and 2014. The amount due to the Company from Biodesix pursuant to the cost-sharing provision was $1.1 million and $1.8 million at December 31, 2015 and 2014, respectively.

Biogen Idec International GmbH

In March 2009, the Company entered into an exclusive option and license agreement with Biogen Idec International GmbH, a subsidiary of Biogen Idec Inc., (collectively “Biogen Idec”) regarding the development and commercialization of the Company’s discovery-stage ErbB3-targeted antibodies for the potential treatment and diagnosis of cancer and other diseases outside of North

America. Under the agreement, the Company is 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.

In March 2014, the Company and Biogen Idec amended the exclusive option and license agreement (the "Amendment"). Pursuant to the Amendment, Biogen agreed to the termination of its rights and obligations under the agreement, including Biogen's option to (i) obtain a co-exclusive (with AVEO) worldwide license to develop and manufacture ErbB3 targeted antibodies and (ii) obtain exclusive commercialization rights to ErbB3 products in countries in the world other than North America. As a result, AVEO has worldwide rights to AV-203. Pursuant to the Amendment, AVEO is obligated to use reasonable efforts to seek a collaboration partner for the purpose of funding further development and commercialization of ErbB3 targeted antibodies. AVEO is also obligated to pay Biogen a percentage of milestone payments received by AVEO from future partnerships after March 28, 2016 and single digit royalty payments on net sales related to the sale of ErbB3 products, if any, up to cumulative maximum amount of $50 million.

The deliverables under the original arrangement included an option for a co-exclusive, worldwide license to develop and manufacture ErbB3 antibody products and an option for an exclusive license to commercialize ErbB3 antibody products in all countries in the world other than North America. The Company determined that these deliverables did not have standalone value due to the fact that the program was still in preclinical development and required the Company's experience to advance development of the product candidates. As such, the Company determined that the original agreement should be accounted for as one unit of accounting.

Under the terms of the original agreement, Biogen Idec made up-front and milestone-based cash payments totaling $20.0 million. Of the $20.0 million received, $10.0 million was associated with milestones that were considered substantive and these amounts were included in revenue when they were earned. The remaining $10.0 million was amortized as additional license revenue over the Company's period of substantial involvement.

The Company concluded that the Amendment materially modified the terms of the agreement and, as a result, required the application of ASC 605-25. Based upon the terms of the Amendment, the remaining deliverables included the Company's obligation to seek a collaboration partner to fund further development of the program and the Company's obligation to continue development and commercialization of the licensed products if a collaboration partner is secured ("Development Deliverable"). The Company concluded that its obligation to use best efforts to seek a collaboration partner does not have standalone value from the Development Deliverable upon delivery and thus the deliverables should be treated as a single unit of accounting.

Upon modifying the arrangement, the Company had $14.7 million of deferred revenue remaining to be amortized. The Company is not entitled to receive any further consideration from Biogen Idec under the amended arrangement. The Company allocated a portion of the remaining deferred revenue to the undelivered unit of accounting based upon the Company's best estimate of the selling price, as the Company determined that neither VSOE or TPE were available. The Company determined the best estimate of selling price to be approximately $0.6 million and recognized the remaining $14.1 million as collaboration revenue in March 2014. The deferred revenue associated with the undelivered unit of accounting is being recognized on a straight-line basis over the expected period of performance, or through March 2016, based upon the Company's historical experience with marketing its product candidates to potential partners.

The best estimate of selling price was based upon a cost approach pursuant to which the Company estimated the costs expected to be incurred in executing a partnership agreement and then applied a reasonable markup. The Company estimated future cash outflows for several possible outcomes, including the execution of a partnership at different times within a reasonable range and partnerships of differing complexity. The Company estimated its cash outflows for each scenario based upon the expected costs associated with the relevant employees and the expected level of effort to be expended to seek and execute a partnership. The Company's analysis also considered the legal charges that it anticipates it will incur. Changes to the Company's assumptions within the reasonable range of possible values

would not have a material impact on the amounts recorded in current or future periods.

Under the agreement, the Company recorded revenue of $0.3 million, $14.5 million and $0.9 million during the years ended December 31, 2015, 2014 and 2013, respectively.

Astellas Pharma Inc.

In February 2011, the Company, together with its wholly-owned subsidiary AVEO Pharma Limited, entered into a Collaboration and License Agreement with Astellas (the “Astellas Agreement”), pursuant to which the Company and Astellas intended to develop and commercialize tivozanib for the treatment of a broad range of cancers. Under the terms of the Astellas Agreement, the Company and Astellas shared responsibility for continued development and commercialization of tivozanib in North America and in Europe under a joint development plan and a joint commercialization plan, respectively. Throughout the rest of the world (the “Royalty Territory”), excluding Asia, where KHK has retained all development and commercialization rights, Astellas had

an exclusive, royalty-bearing license to develop and commercialize tivozanib. The terms of the Astellas Agreement were subject to the Company's obligations to KHK under a license agreement entered into with KHK in 2006 pursuant to which the Company acquired exclusive rights to develop and commercialize tivozanib worldwide outside of Asia.

In January 2014, AVEO and Astellas jointly decided to discontinue a phase 2 breast cancer clinical trial due to insufficient enrollment. Further, Astellas elected in February 2014 to terminate the Astellas Agreement as a result of the limited scope of development for tivozanib moving forward. This termination became effective on August 11, 2014, at which time the tivozanib rights returned to the Company. In accordance with the Astellas Agreement, committed development costs, including the costs of completing certain tivozanib clinical development activities, will be shared equally. There are no refund provisions in the Astellas Agreement.

Under the Astellas Agreement, the Company received an initial cash payment of $125.0 million, comprised of a $75.0 million license fee and $50.0 million in research and development funding. The Company retained net proceeds of approximately $97.6 million of the initial cash payment from Astellas, after payments to KHK and strategic, legal and financial advisors. In December 2012, the Company received a $15.0 million milestone payment from Astellas in connection with the acceptance by the FDA of the NDA filing for tivozanib. The milestone was considered substantive and revenue was recognized upon achievement of the milestone.

The Company accounted for the joint development and commercialization activities in North America and Europe as a joint risk-sharing collaboration in accordance with ASC 808, Collaborative Arrangements. In addition, these activities were not deemed to be separate deliverables under the Astellas Agreement.

Payments from Astellas with respect to Astellas' share of tivozanib development and commercialization costs incurred by the Company pursuant to the joint development plan were recorded as a reduction to research and development expense and general and administrative expense in the accompanying consolidated financial statements due to the joint risk-sharing nature of the activities in North America and Europe. As a result of the cost-sharing provisions in the Astellas Agreement, the Company reduced research and development expense by $0.7 million, $3.5 million and $15.8 million during the years ended December 31, 2015, 2014, and 2013, respectively. The Company also reduced general and administrative expense by $0.1 million, $0.1 million and $2.8 million during the years ended December 31, 2015, 2014 and 2013, respectively, as a result of the cost-sharing provisions in the Astellas Agreement. The net amount due to the Company from Astellas pursuant to the cost-sharing provisions was $0.1 million and $0.6 million at December 31, 2015 and 2014, respectively.

Activities under the Astellas Agreement outside of the joint development and commercialization activities in North America and Europe, including the co-exclusive license to develop and commercialize tivozanib in North America and Europe that was delivered prior to the initiation of the collaborative activities in North America and Europe, were evaluated under ASC 605-25 to determine if they represented a multiple element revenue arrangement. The Astellas Agreement included the following deliverables: (1) a co-exclusive license to develop and commercialize tivozanib in North America and Europe (the "License Deliverable"); (2) a combined deliverable comprised of an exclusive royalty-bearing license to develop and commercialize tivozanib in the Royalty Territory and the Company's obligation to provide access to clinical and regulatory information resulting from the activities in North America and Europe to Astellas for its development and commercialization of tivozanib in the Royalty Territory (the "Royalty Territory Deliverable"); and (3) the Company's obligation to supply clinical material to Astellas for development of tivozanib in the Royalty Territory (the "Clinical Material Deliverable"). All of these deliverables were deemed to have stand-alone value and to meet the criteria to be accounted for as separate units of accounting under ASC 605-25. Factors considered in this determination included, among other things, the subject of the licenses and the research and development and commercial capabilities of Astellas.

The Company allocated the up-front consideration of $125.0 million to the deliverables based on management's best estimate of selling price of each deliverable using the relative selling price method as the Company did not have VSOE or TPE of selling price for such deliverables. The Company's best estimate of selling price considered

discounted cash flow models, the key assumptions of which included the market opportunity for commercialization of tivozanib in North America and Europe and the Royalty Territory, the probability of successfully developing and commercializing tivozanib, the remaining development costs for tivozanib, and the estimated time to commercialization of tivozanib. The Company's analysis included the following market conditions and entity-specific factors: (a) the specific rights provided under the license to develop and commercialize tivozanib in North America and Europe and the Royalty Territory, (b) the potential indications for tivozanib pursuant to the licenses, (c) the relevant territories for the respective licenses, (d) the stage of development of tivozanib by potential indication and estimated remaining development timelines and costs for each indication, (e) the development risk by indication, (f) the market size by indication, (g) the expected product life of tivozanib assuming commercialization and (h) the competitive environment. The Company utilized a discount rate of 15% in its analysis, representing the weighted average cost of capital derived from returns on equity for comparable companies.

The Company concluded that a change in the key assumptions used to determine best estimate of selling price for each license deliverable would not have a significant effect on the allocation of arrangement consideration.

The Company allocated up-front consideration of $120.2 million to the License Deliverable and up-front consideration of $4.8 million to the Royalty Territory Deliverable. The relative selling price of the Company's obligation under the Clinical Material Deliverable had de minimis value.

The Company recorded the $120.2 million relative selling price of the License Deliverable as collaboration revenue during the three months ended March 31, 2011 upon delivery of the license, and deferred approximately $4.8 million of revenue representing the relative selling price of the Royalty Territory Deliverable. The Company was recording the $4.8 million of revenue attributed to the Royalty Territory Deliverable ratably over the Company's period of performance through April 2022, the remaining patent life of tivozanib. Upon being notified that the collaboration would be terminated effective August 2014, the Company reassessed the period of performance associated with the Royalty Territory Deliverable and accelerated the recognition of the remaining deferred revenue such that the balance would be recognized through August 2014. This change in estimate resulted in the recognition of an additional $3.1 million during the year ended December 31, 2014. The Company recorded approximately $3.6 million and $0.4 million of revenue associated with the Royalty Territory Deliverable during the years ended December 31, 2014 and 2013, respectively. The Company recorded no revenue associated with the Royalty Territory Delivery during the year ended December 31, 2015.

Under the agreement, the Company received cash payments related to reimbursable payments and milestone payments of $1.5 million, $4.1 million and $40.1 million during the years ended December 31, 2015, 2014 and 2013, respectively, and recorded revenue of $3.6 million and $0.4 million during the years ended December 31, 2014 and 2013, respectively. The Company did not record revenue related to reimbursable payments and milestone payments during the year ended December 31, 2015.

(b) In-license Agreements

Kirin Brewery Co. Ltd. (KHK)

In December 2006, the Company entered into an exclusive license agreement, with the right to grant sublicenses, subject to certain restrictions, with Kirin Brewery Co. Ltd. (now Kyowa Hakko Kirin) ("KHK") to research, develop, manufacture and commercialize tivozanib, pharmaceutical compositions thereof and associated biomarkers in all territories in the world except for Asia (the "KHK Agreement"). Upon entering into the KHK Agreement, the Company made a cash payment in the amount of $5.0 million.

In March 2010, the Company made a $10.0 million milestone payment to KHK in connection with the dosing of the first patient in the Company's phase 3 clinical trial of tivozanib. The Company recorded $22.5 million of research and development expense during the year ended December 31, 2011 associated with a payment made to KHK related to the up-front license payment received under the Astellas Agreement. In December 2012, the Company made a $12.0 million milestone payment to KHK in connection with the acceptance by the FDA of the Company's NDA filing for tivozanib. In connection with this payment, $6.0 million was reimbursed from Astellas and recorded as a reduction of research and development expense.

Under the KHK Agreement, the Company may be required to (i) 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, (ii) pay tiered royalty payments on net sales it makes of tivozanib in its territory ranging from the low to mid-teens as a percentage of the Company's net sales of tivozanib, and (iii) pay 30% of certain amounts the Company receives under sublicense agreements, including up-front license fees, milestone payments and royalties, other than amounts the Company receives in respect of research and development funding or equity investments, subject to certain limitations.

The license agreement will remain in effect until the expiration of all of the Company's royalty and sublicense revenue obligations to KHK unless either party elects to terminate the license agreement earlier. If the Company fails to meet

its obligations under the agreements and is unable to cure such failure within specified time periods, KHK can terminate the agreement, resulting in a loss of the Company's rights to tivozanib and an obligation to assign or license to KHK any intellectual property rights the Company may have in tivozanib.

St. Vincent's Hospital

In July 2012, the Company entered into a license agreement with St Vincent's Hospital Sydney Limited, which the Company refers to as St. Vincent's, under which the Company obtained an exclusive, worldwide license, with the right to grant sublicenses subject to certain restrictions, under specified patent rights and related know-how, to research, develop, manufacture and commercialize products for human therapeutic, preventative and palliative applications that benefit from inhibition or decreased expression or activity of MIC-1, which the Company refers to as GDF15. The Company is exploiting this license in its AV-380 program for cachexia. The Company has a right of first negotiation to obtain an exclusive license to certain improvements that St. Vincent's or third parties may make to licensed therapeutic products. Under the license agreement, St. Vincent's also granted us non-exclusive rights for certain related diagnostic products and research tools.

Under the license agreement, the Company is obligated to use diligent efforts to conduct research and clinical development and commercially launch at least one licensed therapeutic product, and to maximize profits from licensed therapeutic products for the benefit of us and St. Vincent's. Subject to certain conditions, the Company has also agreed to achieve specified research, development and regulatory milestones by specified dates. If the Company does not achieve a given milestone by the agreed date, the Company has the option of paying the amount the Company would have been obligated to pay had the Company timely achieved the milestone, and, if the Company does so, St. Vincent's will not have the right to terminate the license agreement based on its failure to timely achieve such milestone.

In order to sublicense certain necessary intellectual property rights to Novartis in August 2015, the Company entered into an amendment (the "Amended St. Vincent's Agreement") to the license agreement with St. Vincent's. Under the license agreement with Novartis, the Company is required to maintain the Amended St. Vincent's Agreement in effect, and not enter into any amendment that would adversely affect Novartis' rights during the term of the license agreement with Novartis.

The Company has also agreed that, for as long as there is a valid claim in the licensed patents, the Company will not, and the Company will ensure that its affiliates and its sublicensees do not, develop or commercialize any product, other than a licensed therapeutic product, for the treatment, prevention or prophylaxis of cachexia, decreased appetite or body weight, that binds to GDF15 or the GDF15 receptor and that is a GDF15 antagonist, and will not license or induce any other person to do the same.

In connection with entering into the license agreement with St. Vincent's, the Company paid St. Vincent's an upfront license fee of $0.7 million and a low five-figure amount to reimburse St. Vincent's for patent-related expenses it incurred with respect to a specified licensed patent. In connection with entering into the Amended St. Vincent's Agreement, the Company was required to make an upfront payment to St. Vincent's of $1.5 million in 2015, which has been recorded as R&D expense.

Under the Company's license agreement with St. Vincent's, the Company may be required to:

- make milestone payments, up to an aggregate total of $18.9 million, upon achievement of specified research, development and regulatory milestones for the first three indications for licensed therapeutic products, some of which payments may be increased by a mid to high double-digit percentage rate for milestones payments made after the Company grants any sublicense under the license agreement, depending on the sublicensed territory or territories;
- pay tiered royalty payments equal to a low-single-digit percentage of any net sales the Company or its sublicensees make of licensed therapeutic products. The royalty rate escalates within the low-single-digit range during each calendar year based on increasing licensed therapeutic product sales during such calendar year. Royalties for approved products resulting from the Amended St. Vincent's Agreement will also be payable to St. Vincent's, and the Company and Novartis will share that obligation equally. The Company's royalty payment obligations for a licensed therapeutic product in a particular country end on the later of 10 years after the date of first commercial sale of such licensed therapeutic product in such country or expiration of the last-to-expire valid claim of the licensed patents covering such licensed therapeutic product in such country, and are subject to offsets under certain circumstances; and
- reimburse St. Vincent's for some or all of the reasonable costs and expenses it incurs in patent management, filing, prosecuting and maintaining the licensed patents.

The license agreement will remain in effect until the later of 10 years after the date of first commercial sale of licensed therapeutic products in the last country in which a commercial sale is made, or expiration of the last-to-expire valid claim of the licensed patents, unless the Company elects, or St. Vincent's elects, to terminate the license agreement earlier.

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, or in connection with events relating to the other party's insolvency or bankruptcy, or if a force majeure event continues for more than 4 months.

St. Vincent's has the right to terminate the agreement due to any patent-related challenge by the Company, its affiliates or any sublicensee, or if the Company or its affiliates or any sublicensee cause or induce any other person to make a patent-related challenge, and such challenge continues after a specified cure period.

The Company has the right to terminate the agreement on 6 months' notice if the Company terminates its GDF15 research and development programs as a result of the failure of a licensed therapeutic product in pre-clinical or clinical development, or if the Company forms the reasonable view that further GDF15 research and development is not commercially viable, and the Company is not then in breach of any of its obligations under the agreement. If the Company forms the reasonable view that further GDF15 research and development is not commercially viable and terminate the agreement before the Company starts a phase 1 clinical trial on a licensed therapeutic product, the Company will be required to pay St. Vincent's a low-to-mid six-figure termination payment.

Any termination of the agreement, in whole or in part, will result in a loss of the Company's rights to the relevant licensed patents and know-how. If St. Vincent's terminates the agreement in its entirety due to the Company's breach, insolvency or a patent-related challenge, or the Company terminates the agreement due to a development failure or lack of commercial viability, as described above, St. Vincent's will have a non-exclusive license from us to certain intellectual property rights and know-how relating to the licensed therapeutic products, and the Company must transfer to St. Vincent's certain then-existing regulatory approvals and related documents for the licensed therapeutic products.

Other License Agreements

The Company has entered into various cancelable license agreements for patented technology and other technology related to research projects, including technology to humanize ficlatuzumab, AV-203 and other antibody product candidates. The Company is obligated to pay annual maintenance payments of $25,000, which are recognized as research and development expense over the maintenance period. Under an additional agreement, if the parties agree to the use of the licensed technology in development of a product, the Company will be required to make a $1.0 million license payment per product. Three of these agreements also include development and sales-based milestones of up to $22.5 million, $5.5 million and $4.2 million per product, respectively, and single digit royalties as a percentage of sales.

Certain other research agreements require the Company to remit royalties in amounts ranging from 0.5% to 1.5% based on net sales of products utilizing the licensed technology. No expenses were incurred during the years ended December 31, 2015, 2014 and 2013. The Company has not paid any royalties to date.

8. Commitments and Contingencies

Operating Leases

The Company leases office and has leased lab space and equipment under various operating lease agreements. Rent expense under the operating leases amounted to ($9.1) million, $4.1 million and $9.4 million for the years ended December 31, 2015, 2014 and 2013, respectively. For the year ended December 31, 2014, $3.1 million of rent expense is included within lease exit costs on the Company's statement of operations. The net rent credit for the year ended December 31, 2015 and the net rent credit for the years ended December 31, 2014 and 2013 were recorded within operating expenses and allocated to research and development and general and administrative expense based upon the use of the underlying facility space.

In May 2015, the Company began leasing office space under a cancellable arrangement. The Company recognized rent expense of approximately $0.2 million related to this lease during the year ended December 31, 2015.

On May 9, 2012, the Company entered into a lease agreement with BMR-650 E KENDALL B LLC ("BMR"), under which the Company agreed to lease 126,065 square feet of space located at 650 East Kendall Street, Cambridge, Massachusetts to be used for office, research and laboratory space. The initial term of the lease agreement was approximately twelve years and seven months (the "initial term"). The Company has determined that the lease should be classified as an operating lease.

In order to make the space usable for the Company's operations, substantial improvements were made to the space. These improvements were planned, managed and carried out by the Company and the improvements were tailored to the Company's needs. BMR agreed to reimburse the Company for up to $14.9 million of the improvements, and the Company bore all risks associated with any cost overruns that may be incurred. As such, the Company determined it

was the owner of the improvements and, as such, the Company accounted for tenant improvement reimbursements from BMR as a lease incentive. The Company recorded a deferred lease incentive (included as a component of the deferred rent balance in the accompanying consolidated balance sheets) and the incentive was amortized as an offset to rent expense over the term of the lease. Rent expense, inclusive of the escalating rent payments, was recognized on a straight-line basis over the initial term of the lease agreement. Refer to Footnote 14 for further discussion regarding the termination of this lease. The Company recognized rent expense of approximately ($9.5) million, $4.3 million and $6.7 million related to the lease during the years ended December 31, 2015, 2014 and 2013, respectively. The expense recognized during the years ended December 31, 2015 and 2014 include the recognition of deferred rent credits totaling $10.6 million and $3.8 million, respectively, following the termination of the lease agreement.

Employment Agreements

Certain key executives are covered by severance and change in control agreements. Under these agreements, if the executive’s employment is terminated without cause or if the executive terminates his employment for good reason, such executive will be entitled to receive severance equal to his base salary, benefits and prorated bonuses for a period of time equal to either 12 months or 18 months, depending on the terms of such executive’s individual agreement. In addition, in December 2007, the Company approved a key employee change in control severance benefits plan, which was amended in November 2009, and which provides for severance

and other benefits under certain qualifying termination events upon a change in control for a period of time ranging from 6 months to 18 months, depending upon the position of the key employee.

Refer to Footnote 16 for further discussion of legal contingencies.

9. Income Taxes

The Company accounts for income taxes under the provisions of ASC 740. For the years ended December 31, 2015, 2014 and 2013, the Company did not have any federal, state, or foreign income tax expense as it generated taxable losses in all filing jurisdictions.

A reconciliation of the expected income tax benefit computed using the federal statutory income tax rate to the Company's effective income tax rate is as follows for the years ended December 31, 2015, 2014 and 2013:

	December 31, 2015	December 31, 2014	December 31, 2013
Income tax computed at federal statutory tax rate	34.0 %	34.0 %	34.0 %
State taxes, net of federal benefit	5.3 %	5.3 %	5.1 %
Research and development credits	2.0 %	2.6 %	2.0 %
Other permanent differences	(2.0)%	(0.8)%	(0.9)%
Foreign rate differential	(0.1)%	0.0 %	(0.2)%
Permanent difference – estimated settlement liability	(9.1)%	0.0 %	0.0 %
Other	(3.8)%	(5.7)%	(0.5)%
Change in valuation allowance	(26.3)%	(35.4)%	(39.5)%
Total	0.0 %	0.0 %	0.0 %

Prior to 2011, the Company had incurred net operating losses from inception. At December 31, 2015, the Company had domestic federal, state, and UK net operating loss carryforwards of approximately $444.5 million, $338.7 million, and $6.6 million respectively, available to reduce future taxable income. The federal net operating loss carryforwards expire beginning in 2024 through 2035 and the state loss carryforwards begin to expire in 2030 and continue through 2035. The foreign net operating loss carryforwards in the UK do not expire. The Company also had federal and state research and development tax credit carryforwards of approximately $10.1 million and $4.0 million, respectively, available to reduce future tax liabilities and which expire at various dates. The federal credits expire beginning in 2022 through 2035 and the state credits begin to expire in 2019. The net operating loss and research and development carryforwards are subject to review and possible adjustment by the Internal Revenue Service and may be limited in the event of certain changes in the ownership interest of significant stockholders.

The Company's net deferred tax assets as of December 31, 2015, 2014 and 2013 are as follows:

	December 31,	December 31,	December 31,

	2015	2014	2013
NOL carryforwards	$170,200	$ 162,248	$134,023
Research and development credits	12,721	12,721	11,357
Deferred revenue	1,451	302	7,224
Other temporary differences	5,935	11,135	15,158
Valuation allowance	(190,307)	(186,406)	(167,762)
Total	—	—	—

A full valuation allowance has been recorded in the accompanying consolidated financial statements to offset these deferred tax assets because the future realizability of such assets is uncertain. This determination is based primarily on the Company's historical losses. Accordingly, future favorable adjustments to the valuation allowance may be required, if and when circumstances change. The valuation allowance increased by $3.9 million, $18.6 million and $42.3 million during the years ended December 31, 2015, 2014, and 2013, respectively, primarily due to the generation of net operating loss carryforwards.

As of December 31, 2015, the Company had federal and state net operating losses of approximately $4.1 million related to excess tax deductions that have been excluded from the above table. The benefit of these net operating losses will be recognized as an increase in additional paid in capital when it results in a reduction of taxes payable.

The Company applies FASB Interpretation No. 48, "Accounting for Uncertainty in Income Taxes, an interpretation of FAS 109" (codified within ASC 740, Income Taxes), for the financial statement recognition, measurement, presentation and disclosure of uncertain tax positions taken or expected to be taken in income tax returns. Unrecognized tax benefits represent tax positions for which reserves have been established. A full valuation allowance has been provided against the Company's deferred tax assets, so that the effect of the unrecognized tax benefits is to reduce the gross amount of the deferred tax asset and the corresponding valuation allowance. Since the Company has incurred net operating losses since inception, it has never been subject to a revenue agent review. The Company is currently open to examination under the statute of limitations by the Internal Revenue Service and state jurisdictions for the tax years ended 2012 through 2015. Carryforward tax attributes generated in years past may still be adjusted upon future examination if they have or will be used in a future period. The Company is currently not under examination by the Internal Revenue Service or any other jurisdictions for any tax years.

The Company may from time to time be assessed interest or penalties by major tax jurisdictions. The Company recognizes interest and penalties related to uncertain tax positions in income tax expense. No interest and penalties have been recognized by the Company to date.

The Company anticipates that the amount of unrecognized tax benefits recorded will not change in the next twelve months.

The following is a reconciliation of the Company's gross uncertain tax positions at December 31, 2015, 2014 and 2013:

	Year ended December 31, 2015	Year ended December 31, 2014	Year ended December 31, 2013
	(in thousands)		
Amount established upon adoption	$ 1,200	$ 1,200	$1,200
Additions for current year tax positions	—	—	—
Additions for prior year tax positions	—	—	—
Reductions of prior year tax positions	—	—	—
Balance as of end of year	$ 1,200	$ 1,200	$1,200

10. Common Stock and Warrants

As of December 31, 2015, the Company had 200,000,000 authorized shares of common stock, $0.001 par value, of which 58,181,715 shares were issued and outstanding. The number of authorized shares of common stock was increased from 100,000,000 at the Company's 2015 annual shareholders meeting.

As part of the Amended Loan Agreement with Hercules Technology II, L.P. and Hercules Technology III, L.P., affiliates of Hercules Technology Growth (collectively, "Hercules"), on September 24, 2014, the Company issued warrants to the lenders to purchase up to 608,696 shares of the Company's common stock at an exercise price equal to $1.15 per share to Hercules. All warrants issued during the year remain outstanding as of December 31, 2015.

ATM Sales Agreement

In February 2015, the Company entered into an at-the-market issuance sales agreement with FBR & Co. (formerly MLV & Co. LLC ("FBR"), pursuant to which the Company could issue and sell shares of its common stock from time to time up to an aggregate amount of $17.9 million, at the Company's option, through FBR as its sales agent. Sales of common stock through FBR may be made by any method that is deemed an "at-the-market" offering as defined in Rule 415 promulgated under the Securities Act of 1933, as amended, including by means of ordinary brokers' transactions at market prices, in block transactions or as otherwise agreed by the Company and FBR. Subject to the terms and conditions of the sales agreement between the Company and FBR (the "Sales Agreement"), FBR will use commercially reasonable efforts to sell the common stock based upon the Company's instructions (including any price, time or size limits or other customary parameters or conditions the Company may impose). The Company is not obligated to make any sales of its common stock under the Sales Agreement. Any shares sold will be sold pursuant to an effective shelf registration statement on Form S-3. The Company will pay FBR a commission of up to 3% of the gross proceeds. The Sales Agreement may be terminated by the Company at any time.

On May 7, 2015, the Company filed a shelf registration statement on Form S-3 with the SEC, which covers the offering, issuance and sale by the Company of up to $100.0 million of its common stock, preferred stock, debt securities, warrants and/or units (the "2015 Shelf"). The 2015 Shelf was filed to replace the Company's existing $250.0 million shelf registration statement (the "2012 Shelf"). On May 7, 2015, the Company amended its Sales Agreement with FBR to provide for the offering, issuance and sale by the Company of up to $15.0 million of its common stock under the 2015 Shelf, which replaced the Company's existing $17.9 million

offering that expired along with the expired 2012 Shelf. As of December 31, 2015, the Company has sold approximately 5.9 million shares pursuant to the Sales Agreement, resulting in proceeds of approximately $10.2 million, net of commissions and issuance costs.

Approximately $9.0 million remains available for sale under the Sales Agreement.

11. Stock-Based Compensation

Stock Incentive Plan—Overview

The Company maintains the 2010 Stock Incentive Plan (the "Plan") for employees, consultants, advisors, and directors. The Plan provides for the grant of equity awards such as stock options and restricted stock. The Plan has been amended at various times since its approval. In March 2013, the Company's board of directors amended the Plan to increase the number of shares of common stock reserved for issuance to 7,875,000 shares, plus the number of shares of common stock subject to awards granted under the Company's 2002 Incentive Plan which expire, terminate or are otherwise surrendered, cancelled, forfeited or repurchased by us, up to a maximum of 625,000 shares. This amendment also adopted a fungible share pool whereby any award that is a full-value award (i.e. any restricted stock award, restricted stock unit award, or other stock-based award with a per share price or per unit purchase price lower than 100% of fair market value on the date of the grant) is counted against the share limits under the Plan as 1.5 shares for each one share of common stock subject to such full-value award. In June 2014, the Company's stockholders approved an amendment to the Plan, which increased the annual per participant share limit under the Plan from 250,000 to 1,000,000 shares per fiscal year. No other amendments to the Plan were made.

The Company has reserved 8,500,000 shares of common stock under the Plan, and at December 31, 2015, the Company has 3,413,353 shares available for future issuance under the Plan. Shares issued upon exercise of options are generally issued from new shares of the Company. The Plan provides that the exercise price of incentive stock options cannot be less than 100% of the fair market value of the common stock on the date of the award for participants who own less than 10% of the total combined voting power of stock of the Company and not less than 110% for participants who own more than 10% of the total combined voting power of the stock of the Company. Options and restricted stock granted under the Plan vest over periods as determined by the Board, which generally are equal to four years. Options generally expire ten years from the date of grant.

Stock Incentive Plan—Employee Stock Options

The fair value of each stock option granted is estimated on the date of grant using the Black-Scholes option-pricing model using the assumptions noted in the following table:

	Years Ended December 31,		
	2015	2014	2013
Volatility	73.04%-78.7%	69.38%-77.92%	64.22%-72.65%
Expected Term (in years)	5.50-6.25	5.50-6.25	5.50-6.25
Risk-Free Interest Rates	1.54%-1.93%	1.81%-2.02%	1.01%-2.10%
Dividend Yield	—	—	—

The risk-free interest rate is determined based upon the United States Treasury's rates for U.S. Treasury zero-coupon bonds with maturities similar to those of the expected term of the options being valued. The Company does not expect to pay dividends in the foreseeable future.

The Company does not have sufficient history to support a calculation of volatility and expected term using only its historical data. As such, the Company has used a weighted-average volatility considering the Company's own volatility since March 2010, and the volatilities of several peer companies. For purposes of identifying similar entities, the Company considered characteristics such as industry, length of trading history, similar vesting terms and in-the-money option status. Due to lack of available option activity data, the Company elected to use the "simplified" method for "plain vanilla" options to estimate the expected term of the stock option grants. Under this approach, the weighted-average expected life is presumed to be the average of the vesting term and the contractual term of the option. Additionally, the Company is required to include an estimate of the value of the awards that will be forfeited in calculating compensation costs, which the Company estimates based upon actual historical forfeitures. The forfeiture estimates are recognized over the requisite service period of the awards on a straight-line basis. During the years ending December 31, 2015, 2014 and 2013 the Company estimated its forfeiture rates to be 71%, 62% and 49%, respectively. Based upon these assumptions, the weighted-average grant date fair value of stock options granted during the years ended December 31, 2015, 2014, and 2013 was $0.75, $1.15 and $4.32 per share, respectively.

During the year ended December 31, 2014 the Company issued stock options to purchase 2,250,000 shares of common stock that contain market and performance –based vesting conditions. As of December 31, 2015, there were 381,500 shares remaining

which were not deemed probable of vesting. As of December 31, 2015, there was $0.7 million of total unrecognized stock-based compensation expense related to stock options granted under the Company's 2002 Stock Incentive Plan and 2010 Stock Incentive Plan (collectively, the "Plans"). The expense is expected to be recognized over a weighted-average period of 2.9 years. The intrinsic value of options exercised was $58,000 for the years ended December 31, 2015. No options were exercised during the year ended December 31, 2014.

The following table summarizes the activity of the Plans for the year ended December 31, 2015:

	Number of Options	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Life (in years)	Aggregate Intrinsic Value
Outstanding at December 31, 2014	5,817,313	$ 4.45		
Granted	3,159,134	$ 1.11		
Exercised	(165,805)	$ 1.45		
Forfeited	(2,964,938)	$ 1.85		
Expired	(1,049,699)	$ 5.27		
Outstanding at December 31, 2015	4,796,005	$ 3.78	6.93	$ 596,660
Exercisable at December 31, 2015	3,153,440	$ 5.09	5.86	$ 325,107
Vested or expected to vest at December 31, 2015	2,276,447	$ 6.56	4.61	$ 115,704

Stock Incentive Plan—Nonemployee Stock Options

There were no stock options granted to nonemployee consultants during 2015 or 2013. During 2014, the Company granted nonqualified options to purchase 225,000 shares of common stock to nonemployee consultants, with an average exercise price of $1.47 per share. The Company valued these options using the Black-Scholes option-pricing model and recognized expense related to these awards using the accelerated attribution method. The unvested options held by consultants have been revalued using the Company's estimate of fair value at each reporting period over the vesting period. Stock-based compensation expense of approximately $0.1 million was recorded during the year ended December 31, 2014 relating to nonemployee stock option awards.

Stock Incentive Plan—Restricted Stock

The Company periodically grants awards of restricted stock to employees. These awards typically vest upon completion of the requisite service period or upon achievement of specified performance targets.

The following table summarizes the restricted stock activity for the year ended December 31, 2015:

		Weighted-

	Number of Shares	Average Price
Unvested at December 31, 2014	477,600	$ 1.81
Granted	—	—
Cancelled	(201,180)	1.87
Expired	—	—
Vested/Released	(233,670)	1.80
Unvested at December 31, 2015	42,750	$ 1.61

The fair value of restricted stock awards that vested was $0.1 million, $0.2 million, and $0.5 million for the years ended December 31, 2015, 2014, and 2013, respectively. As of December 31, 2015, there was $6,000 of total unrecognized stock-based compensation expense related to restricted stock awards granted under the Plan. The expense is expected to be recognized over a weighted-average period of 0.1 years if all performance targets are met.

Employee Stock Purchase Plan

In February 2010, the Board of Directors adopted the 2010 Employee Stock Purchase Plan (the “ESPP”) pursuant to which the Company may sell up to an aggregate of 250,000 shares of Common Stock. The ESPP was approved by the Company’s stockholders in February 2010. The plan was amended in March 2013 to increase the total number of shares available under the ESPP for the Company to sell to 764,000. The ESPP allows eligible employees to purchase common stock at a price per share equal to 85% of the

lower of the fair market value of the common stock at the beginning or end of each six month period during the term of the ESPP. The first offering period began on July 1, 2010.

Pursuant to the ESPP, the Company sold a total of 7,138 shares of common stock during the year ended December 31, 2015 at purchase prices of $0.75 and $1.07, respectively, which represent 85% of the closing price of the Company's common stock on June 30, 2015 and December 31, 2015, respectively. For the year ended December 31, 2014, the Company sold a total of 139,032 shares of common stock at purchase prices of $1.53 and $0.71, respectively, which represent 85% of the closing price of the Company's common stock on June 30, 2014 and December 31, 2014, respectively. For the year ended December 31, 2013, the Company sold a total of 109,610 shares of common stock at purchase prices of $2.13 and $1.56, respectively, which represent 85% of the closing price of the Company's common stock on June 28, 2013 and December 31, 2013, respectively. The total stock-based compensation expense recorded as a result of the ESPP was approximately $27,000, $0.2 million and $0.2 million during the years ended December 31, 2015, 2014 and 2013, respectively.

12. Employee Benefit Plan

In 2002, the Company established the AVEO Pharmaceuticals, Inc. 401(k) Plan (the "401(k) Plan") for its employees, which is designed to be qualified under Section 401(k) of the Internal Revenue Code. Eligible employees are permitted to contribute to the 401(k) Plan within statutory and 401(k) Plan limits. The Company makes matching contributions of 50% of the first 5% of employee contributions. The Company made matching contributions of $0.1 million, $0.1 million, and $0.4 million for the years ended December 31, 2015, 2014 and 2013, respectively.

13. Strategic Restructuring

In connection with the receipt of a complete response letter from the FDA informing the Company that the FDA would not approve the Company's NDA for tivozanib for the treatment of patients with advanced RCC, the Company announced a strategic restructuring in June 2013 to refocus the Company's efforts on the then on-going clinical development of tivozanib in colorectal and breast cancer and on the advancement of key pipeline and preclinical assets. This restructuring was completed as of December 31, 2013 and resulted in costs totaling $8.0 million, which included impairment charges of $0.3 million.

On January 6, 2015, the Board of the Company approved a further strategic restructuring of the Company that eliminated the Company's internal research function and aligned the Company's resources with the Company's future strategic plans. As part of this restructuring, the Company eliminated approximately two-thirds of the Company's workforce, or 40 positions across the organization. The Company substantially completed the restructuring during the quarter-ended March 31, 2015.

The following table summarizes the components of the Company's restructuring activity recorded in operating expenses and in accrued expenses in the accompanying consolidated balance sheet:

	Restructuring expense	Restructuring amounts	Restructuring amounts

	amounts accrued at December 31, 2013	Restructuring expense incurred during the year ended December 31, 2014	Restructuring amounts paid during the year ended December 31, 2014	Restructuring amounts accrued at December 31, 2014
	(in thousands)			
Employee severance, benefits and related costs.	$587	—	$ (587)	—

	Restructuring amounts accrued at December 31, 2014	Restructuring expense incurred during the year ended December 31, 2015	Restructuring amounts paid during the year ended December 31, 2015	Restructuring amounts accrued at December 31, 2015
	(in thousands)			
Employee severance, benefits and related costs.	$—	$ 3,560	$ (3,203)	$ 357

The Company is obligated to continue to pay the remaining amounts accrued through the first quarter of 2016. The table above excludes non-cash stock-based compensation costs of approximately $0.1 million incurred as part of the restructuring during the year ended December 31, 2015.

14. Facility Lease Exit

In September 2014, the Company entered into the Lease Termination Agreement pursuant to which the Company immediately surrendered leased space at 650 East Kendall Street in Cambridge, Massachusetts that it had previously ceased using earlier in 2014. In connection with the Lease Termination Agreement, the Company agreed to pay the landlord a termination fee totaling $15.6 million. The Company also agreed to surrender its remaining leased space upon 90 days written notice prior to September 24, 2015.

The Company previously recorded liabilities totaling $15.2 million for lease exit costs when it ceased using the leased spaces during the first and second quarters of 2014. The fair value of these liabilities was determined using the credit-adjusted risk-free rate to discount the estimated future net cash outflows associated with the space that met the cease use criteria. The estimate of future net cash outflows included the Company's expected minimum rental payments and incremental operating, utility and tax payments to the landlord less the amount of sublease income that the Company estimates it could reasonably expect to obtain during the remainder of the lease period. Upon signing the Lease Termination Agreement during the quarter ended September 30, 2014, the Company recorded an additional $1.9 million of Lease Exit charges based on the fair value of the revised net cash outflows, resulting in total Lease Exit charges of $17.1 million for the year ended December 31, 2014.

In February 2015, the Company provided notice that it would surrender the remaining space on May 29, 2015. Accordingly, the Company revised the estimated useful life of its leasehold improvements related to this office space and amortized such assets through May 2015, resulting in an additional $2.9 million of depreciation expense during the year ended December 31, 2015. Similarly, the Company accelerated the amortization of its deferred rent and leasehold improvement allowance associated with this office space through May 2015, resulting in an additional $3.5 million of amortization during the year ended December 31, 2015. Upon the surrender of the remaining space, the Company had no further rights or obligations with respect to the lease. The Company has secured office space appropriate for its current needs under a cancellable arrangement that began in May 2015.

The following tables summarize the components of the Company's lease exit activity recorded in current liabilities:

	Lease Exit Expense incurred during the year ended December 31, 2014	Accretion Expense incurred during the year ended December 31, 2014	Amounts paid during the year ended December 31, 2014	Amounts offset against tenant receivable during the year ended December 31, 2014	Amounts accrued at December 31, 2014
	(in thousands)				
Lease exit costs	$17,142	$ 974	$ (5,313)	$ (7,822)	$ 4,981

In addition to the $17.1 million of expense included in the table above, lease exit expenses also include the write-off $14.0 million of deferred rent associated with the portions of the facility that met the cease use criteria under ASC

420-10 and leasehold improvements totaling $7.6 million during the year ended December 31, 2014 as the Company's estimates of sublease income would not recover the value of the leasehold improvements.

	Amounts accrued at December 31, 2014	Accretion Expense incurred during the year ended December 31, 2015	Amounts paid during the year ended December 31, 2015	Additional expense incurred during the year ended December 31, 2015	Amounts accrued at December 31, 2015
	(in thousands)				
Lease exit costs	$4,981	$ 224	$ (5,477)	$ 272	$

In addition to the $0.5 million of expense for the year ended December 31, 2015 included in the table above, lease exit expenses also include the write-off of $0.2 million of leasehold improvements.

15. Quarterly Results (Unaudited)

	Three Months Ended			
	March 31, 2015	June 30, 2015	September 30, 2015	December 31, 2015
	(in thousands, except per share data) (unaudited)			
Collaboration revenue	$134	$134	$ 15,158	$ 3,598
Restructuring	4,333	25		
Operating expenses	5,950	4,730	6,691	9,721
Loss from operations	(10,149)	(4,621)	8,467	(6,123)
Other expense, net	(725)	(835)	(553)	(462)
Net loss	$(10,874)	$(5,456)	$ 7,914	$ (6,585)
Net loss per share—basic and diluted	$(0.21)	$(0.10)	$ 0.14	$ (0.11)

	Three Months Ended			
	March 31, 2014	June 30, 2014	September 30, 2014	December 31, 2014
	(in thousands, except per share data) (unaudited)			
Collaboration revenue	$15,289	$1,846	$ 873	$ 115
Restructuring	3,859	5,165	1,403	1,302
Operating expenses	17,322	14,146	13,569	11,806
Loss from operations	(5,892)	(17,465)	(14,099)	(12,993)
Other expense, net	(558)	(494)	(337)	(901)
Net loss	$(6,450)	$(17,959)	$ (14,436)	$ (13,894)
Net loss per share—basic and diluted	$(0.12)	$(0.35)	$ (0.28)	$ (0.27)

16. Legal Actions

Two class action lawsuits have been filed against the Company and certain of its former officers and members of its board of directors, (Tuan Ha-Ngoc, David N. Johnston, William Slichenmyer and Ronald DePinho), in the United States District Court for the District of Massachusetts, one captioned Paul Sanders v. Aveo Pharmaceuticals, Inc., et al., No. 1:13-cv-11157-JLT, filed on May 9, 2013, and the other captioned Christine Krause v. AVEO Pharmaceuticals, Inc., et al., No. 1:13-cv-11320-JLT, filed on May 31, 2013. On December 4, 2013, the District Court consolidated the complaints as In re AVEO Pharmaceuticals, Inc. Securities Litigation et al., No. 1:13-cv-11157-DJC, and an amended complaint was filed on February 3, 2014. The amended complaint purported to be brought on behalf of shareholders who purchased the Company's common stock between January 3, 2012 and May 1, 2013. The amended complaint generally alleged that the Company and certain of its present and former officers and directors violated Sections 10(b) and/or 20(a) of the Securities Exchange Act of 1934 and Rule 10b-5 promulgated thereunder by making allegedly false and/or misleading statements concerning the phase 3 trial design and results for the Company's TIVO-1 study in an effort to lead investors to believe that the drug would receive approval from the FDA. The lawsuit seeks unspecified damages, interest, attorneys' fees, and other costs. The consolidated amended complaint

was dismissed without prejudice on March 20, 2015, and the lead plaintiffs then filed a second amended complaint bringing similar allegations. The Company moved to dismiss again, and after a second round of briefing and oral argument, the court ruled in the Company's favor and dismissed the second amended complaint with prejudice on November 18, 2015. The lead plaintiffs have appealed the court's decision to the United States Court of Appeals for the First Circuit. The Company denies any allegations of wrongdoing and intends to continue to vigorously defend against this lawsuit. However, there is no assurance that the Company will be successful in its defense or that insurance will be available or adequate to fund any settlement or judgment or the litigation costs of the action. Moreover, the Company is unable to predict the outcome or reasonably estimate a range of possible loss at this time.

On April 4, 2014, Karen J. van Ingen, a purported purchaser of AVEO stock, filed a derivative complaint allegedly on behalf of AVEO in the United States District Court for the District of Massachusetts, Civil Action No. 1:14-cv-11672-DJC, naming AVEO, as a nominal defendant and also naming as defendants present and former members of the Company's board of directors, including Tuan Ha-Ngoc, Henri A. Termeer, Kenneth M. Bate, Anthony B. Evnin, Robert Epstein, Raju Kucherlapati, Robert C. Young, and Kenneth E. Weg. The complaint alleged breach of fiduciary duty and abuse of control between January 2012 and May 2013 with respect to allegedly misleading statements and omissions regarding tivozanib. The lawsuit seeks, among other relief, unspecified damages, costs and expenses, including attorneys' fees, an order requiring us to implement certain corporate governance reforms, restitution from the defendants and such other relief as the court might find just and proper. The Company filed a motion to dismiss the derivative complaint, and after briefing and oral argument, on March 18, 2015 the Court ruled in the Company's favor and dismissed the case with prejudice. The plaintiff then filed a motion seeking to vacate the Court's order of dismissal and permit filing of an amended

complaint, which the Company opposed, and which the Court denied on June 30, 2015. The plaintiff has appealed the Court's decision to the United States Court of Appeals for the First Circuit. The Company denies any allegations of wrongdoing and intends to continue to vigorously defend this lawsuit. However, there is no assurance that the Company will be successful in its defense or that insurance will be available or adequate to fund any settlement or judgment or the litigation costs of this action. Moreover, the Company is unable to predict the outcome or reasonably estimate a range of possible loss at this time.

On July 3, 2013, the staff (the "SEC Staff") of the United States Securities and Exchange Commission (the "Commission") served a subpoena on the Company for documents and information concerning tivozanib, including related communications with the FDA, investors and others. The Company fully cooperated with the inquiry. In September 2015, the SEC Staff invited the Company to discuss the settlement of potential claims that the SEC Staff may recommend that the Commission bring against the Company asserting that it violated federal securities laws by omitting to disclose to investors the recommendation made to the Company by the staff of the U.S. Food and Drug Administration, on May 11, 2012, that the Company conduct an additional clinical trial with respect to tivozanib. Based on the progress in the settlement process thus far, the Company believes that it could potentially settle with the SEC for a total amount of $4,000,000 and, accordingly, the Company has accrued an estimated settlement liability, for accounting purposes, in that amount in its financial statements as of December 31, 2015. There can be no assurance, however, that a settlement will be approved by the Commission, or that any settlement on terms agreeable to the Company will be achieved, or that any settlement the Company enters into with the SEC will be within the estimated settlement liability accrued. If settlement discussions conclude without a settlement proposal that is acceptable to the Commission and the Company, the Commission may authorize the SEC Staff to pursue claims against the Company. There can be no assurance that the Company will be able to resolve any potential claims of the Commission or that any settlement will not have a material adverse impact on the Company's ability to execute on its proposed plans or on its financial position or results of operations.

The SEC Staff also invited three of the Company's former officers to discuss the settlement of potential claims that the SEC Staff may recommend that the Commission bring against them. The Company is not a party to any discussions between the SEC Staff and the former officers, and the Company can make no assurance regarding such potential claims.

ITEM 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure

None.

ITEM 9A. Controls and Procedures

Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our Chief Executive Officer and Chief Financial Officer, evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2015. In designing and evaluating our disclosure controls and procedures, management recognized that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and our management necessarily applied its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Based on this evaluation, our Chief Executive Officer and Chief Financial Officer concluded that as of December 31, 2015, our disclosure controls and procedures were (1) designed to ensure that material information relating to us is made known to our management including our principal executive officer and principal financial officer by others, particularly during the period in which this report was prepared and (2) effective, in that they provide reasonable assurance that information required to be disclosed by us in the reports the Company files or submit under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms.

Management's report on the Company's internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) appears below.

Internal Control Over Financial Reporting

(a) Management's Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting. Internal control over financial reporting is defined in Rules 13a-15(f) and 15d-15(f) promulgated under the Exchange Act as a process designed by, or under the supervision of, the company's principal executive and principal financial officers and effected by the company's board of directors, management and other personnel, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles and includes those policies and procedures that:

- Pertain to the maintenance of records that in reasonable detail accurately and fairly reflect the transactions and dispositions of the assets of the company;
- Provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and
- Provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Therefore, even those systems determined to be effective can provide only reasonable assurance with respect to financial statement preparation and presentation. Projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Our management assessed the effectiveness of our internal control over financial reporting as of December 31, 2015. In making this assessment, management used the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission (COSO) in Internal Control—Integrated Framework (2013 framework). Based on its assessment, management believes that, as of December 31, 2015, our internal control over financial reporting is effective based on those criteria.

Our independent registered public accounting firm has issued an attestation report of our internal control over financial reporting. This report appears below.

(b) Report of Independent Registered Public Accounting Firm on Internal Control over Financial Reporting

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Board of Directors and Stockholders of

AVEO Pharmaceuticals, Inc.

We have audited AVEO Pharmaceuticals, Inc.'s internal control over financial reporting as of December 31, 2015, based on criteria established in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) (the COSO criteria). AVEO Pharmaceuticals, Inc.'s management is responsible for maintaining effective internal control over financial reporting, and for its assessment of the effectiveness of internal control over financial reporting included in the accompanying management's report on internal control over financial reporting. Our responsibility is to express an opinion on AVEO Pharmaceuticals, Inc.'s internal control over financial reporting based on our audit.

We conducted our audit in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects. Our audit included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, testing and evaluating the design and operating effectiveness of internal control based on the assessed risk, and performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

In our opinion, AVEO Pharmaceuticals, Inc. maintained, in all material respects, effective internal control over financial reporting as of December 31, 2015, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the consolidated balance sheets of AVEO Pharmaceuticals, Inc. as of December 31, 2015 and 2014, and the related consolidated statements of operations, comprehensive loss, stockholders' equity, and cash flows for each of the three years in the period ended December 31, 2015 and our report dated March 15, 2016 expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP

Boston, Massachusetts

March 15, 2016

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Changes in Internal Control Over Financial Reporting

There were no changes in our internal control over financial reporting that occurred during the quarter ended December 31, 2015 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

ITEM 9B. Other Information
None.

PART III

ITEM 10. Directors, Executive Officers and Corporate Governance

The information required by this Item 10 will be contained in the sections entitled “Election of Directors,” “Corporate Governance” and “Section 16(a) Beneficial Ownership Reporting Compliance” appearing in the definitive proxy statement we will file in connection with our 2016 Annual Meeting of Stockholders and is incorporated by reference herein. The information required by this item relating to executive officers may be found in Part I, Item 1 of this report under the heading “Business—Executive Officers” and is incorporated herein by reference.

ITEM 11. Executive Compensation

The information required by this Item 11 will be contained in the sections entitled “Executive and Director Compensation,” “Executive and Director Compensation—Compensation Committee Interlocks and Insider Participation” and “Executive and Director Compensation—Compensation Committee Report” appearing in the definitive proxy statement we will file in connection with our 2016 Annual Meeting of Stockholders and is incorporated by reference herein.

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

The information required by this Item 12 will be contained in the sections entitled “Ownership of Our Common Stock” and “Executive and Director Compensation—Equity Compensation Plan Information” appearing in the definitive proxy statement we will file in connection with our 2016 Annual Meeting of Stockholders and is incorporated by reference herein.

ITEM 13. Certain Relationships and Related Person Transactions, and Director Independence

The information required by this Item 13 will be contained in the sections entitled “Certain Relationships and Related Person Transactions” appearing in the definitive proxy statement we will file in connection with our 2016 Annual Meeting of Stockholders and is incorporated by reference herein.

ITEM 14. Principal Accounting Fees and Services

The information required by this Item 14 will be contained in the section entitled “Corporate Governance—Principal Accountant Fees and Services” appearing in the definitive proxy statement we will file in connection with our 2016 Annual Meeting of Stockholders and is incorporated by reference herein.

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PART IV

ITEM 15. Exhibits and Financial Statement Schedules

(a) Documents filed as part of Form 10-K.

(1) Financial Statements

Report of Independent Registered Public Accounting Firm

Consolidated Balance Sheets

Consolidated Statements of Operations

Consolidated Statements of Comprehensive Loss) Income

Consolidated Statements of Stockholders' Equity

Consolidated Statements of Cash Flows

Notes to Consolidated Financial Statements

(2) Schedules

Schedules have been omitted as all required information has been disclosed in the financial statements and related footnotes.

(3) Exhibits

The Exhibits listed in the Exhibit Index are filed as a part of this Form 10-K.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

AVEO PHARMACEUTICALS, INC.

Date: March 15, 2016 By: /s/ MICHAEL BAILEY
Michael Bailey
President & Chief Executive Officer
(Principal Executive Officer)

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated.

Signature	Title	Date
/s/ Michael Bailey Michael Bailey	President, Chief Executive Officer and Director Principal Executive Officer	March 15, 2016
/s/ Keith S. Ehrlich Keith S. Ehrlich	Chief Financial Officer Principal Financial and Accounting Officer	March 15, 2016
/s/ Kenneth M. Bate Kenneth M. Bate	Director	March 15, 2016
/s/ Anthony B. Evnin Anthony B. Evnin	Director	March 15, 2016
/s/ Raju Kucherlapati Raju Kucherlapati	Director	March 15, 2016
/s/ Henri Termeer Henri Termeer	Director	March 15, 2016
/s/ Robert C. Young Robert C. Young	Director	March 15, 2016

Exhibit Index

Exhibit Number	Description of Exhibit	Incorporated by Reference				Filed Herewith
		Form	File Number	Date of Filing	Exhibit Number	
	Articles of Incorporation and Bylaws					
3.1	Restated Certificate of Incorporation of the Registrant	8-K	001-34655	03/18/2010	3.1	
3.2	Certificate of Amendment of Restated Certificate of Incorporation of the Registrant	8-K	001-34655	06/03/2015	3.1	
3.3	Second Amended and Restated Bylaws of the Registrant	S-1/A	333-163778	02/08/2010	3.5	
	Instruments Defining the Rights of Security Holders, Including Indentures					
4.1	Specimen Stock Certificate evidencing the shares of common stock	S-1/A	333-163778	03/09/2010	4.1	
	Material Contracts—Management Contracts and Compensatory Plans					
10.1	2002 Stock Incentive Plan, as amended	S-1/A	333-163778	02/23/2010	10.1	
10.2	Form of Incentive Stock Option Agreement under 2002 Stock Incentive Plan	S-1	333-163778	12/16/2009	10.2	
10.3	Form of Nonstatutory Stock Option Agreement under 2002 Stock Incentive Plan	S-1	333-163778	12/16/2009	10.3	
10.4	Form of Restricted Stock Agreement under 2002 Stock Incentive Plan	S-1	333-163778	12/16/2009	10.4	
10.5	Amended and Restated 2010 Stock Incentive Plan, as amended	8-K	001-34655	06/23/2014	99.1	
10.6	Form of Incentive Stock Option Agreement under 2010 Stock Incentive Plan	S-1/A	333-163778	02/08/2010	10.6	
10.7	Form of Nonqualified Stock Option Agreement under 2010 Stock Incentive Plan	S-1/A	333-163778	02/08/2010	10.7	
10.8	Form of Restricted Stock Agreement under 2010 Stock Incentive Plan	10-K	001-34655	03/30/2012	10.8	
10.9	Key Employee Change in Control Severance Benefits Plan	S-1	333-163778	12/16/2009	10.8	

10.10	2010 Employee Stock Purchase Plan, as amended	S-1/A	333-163778	02/23/2010	10.17
10.11	Amendment No. 1 to 2010 Employee Stock Purchase Plan	8-K	001-34655	06/04/2013	99.2
10.12	Offer Letter by Registrant to Michael Bailey, dated as of January 6, 2015	10-Q	001-34655	05/07/2015	10.1
10.13	Severance and Change in Control Agreement, dated as of January 9, 2015, by and between the Registrant and Michael Needle	10-Q	001-34655	05/07/2015	10.2
10.14	Transition and Separation Agreement, dated as of January 6, 2015, by and between the Registrant and Tuan Ha-Ngoc	10-Q	001-34655	05/07/2015	10.3
10.15	Offer Letter by the Registrant to Michael Needle, dated January 8, 2015	10-Q	001-34655	05/07/2015	10.4
10.16	Severance and Change in Control Agreement, dated as of December 11, 2009, by and between the Registrant and Tuan Ha-Ngoc	S-1	333-163778	12/16/2009	10.10
10.17	Severance Agreement, dated September 13, 2010, by and between the Registrant and Michael Bailey	10-Q	001-34655	11/05/2010	10.1

Exhibit Number	Description of Exhibit	Incorporated by Reference Form	File Number	Date of Filing	Exhibit Number	Filed Herewith
10.18	Letter Agreement regarding Retention Bonus Award and Severance Agreement, dated February 3, 2014, by and between the Company and Michael Bailey	10-K	001-34655	3/13/2014	10.22	
10.19	Offer Letter by and between the Registrant and Keith Ehrlich, dated April 21, 2015					X
	Material Contracts—Financing Agreements					
10.20	Loan and Security Agreement, dated May 28, 2010, by and among the Company, Hercules Technology II, L.P. and Hercules Technology III, L.P.	8-K	001-34655	06/04/2010	10.1	
10.21	Amendment No. 1 to Loan and Security Agreement, dated December 21, 2011, by and among the Company, Hercules Technology II, L.P. and Hercules Technology III, L.P.	10-K	001-34655	03/30/2012	10.25	
10.22	Amendment No. 2 to Loan and Security Agreement, dated March 31, 2012, by and among the Company, Hercules Technology II, L.P. and Hercules Technology III, L.P.	8-K	001-34655	04/04/2012	10.1	
10.23	Amendment No. 3 to Loan and Security Agreement, dated September 24, 2014, by and among the Company, Hercules Technology Growth Capital, Inc., Hercules Capital Funding Trust 2012-1 and Hercules Technology III, L.P.	10-Q	001-34655	11/05/2014	10.1	
10.24	Warrant, dated as of September 24, 2014, issued by the Registrant to Hercules Technology II, L.P. and Hercules Technology III, L.P.	10-Q	001-34655	11/05/2014	10.2	
	Material Contracts—Lease					
10.25	Sublease, dated February 28, 2011, by and between the Company and Acceleron Pharma, Inc.	10-Q	001-34655	05/12/2011	10.4	
10.26	First Amendment to Sublease, dated September 1, 2011, by and between the Company and Acceleron Pharma, Inc.	10-K	001-34655	03/30/2012	10.29	
10.27	Lease, dated May 9, 2012, by and between the Company and BMR-650 E. Kendall B LLC	10-Q	001-34655	05/09/2012	10.3	
10.28	First Amendment to Lease, dated as of April 30, 2013, by and between the Registrant and BMR-650 E Kendall	10-K	001-34655	3/06/2015	10.27	

	B LLC				
10.29	Second Amendment to Lease, dated as of August 13, 2013, by and between the Registrant and BMR-650 E Kendall B LLC	10-K	001-34655	3/06/2015	10.28
10.30	Third Amendment to Lease and Lease Termination Agreement, dated September 24, 2014, by and between the Registrant and BMR-650 E Kendall B LLC	10-Q	001-34655	11/05/2014	10.3
10.31	Fourth Amendment to Lease, dated December 1, 2014, by and between the Registrant and BMR-650 E Kendall B LLC	10-K	001-34655	3/06/2015	10.30
	Material Contracts—License and Strategic Partnership Agreements				
10.32†	License Agreement, dated as of December 21, 2006, by and between the Registrant and Kirin Brewery Co. Ltd.	S-1	333-163778	12/16/2009	10.22
10.33†	Option and License Agreement, dated as of March 18, 2009, by and between the Registrant and Biogen Idec International GmbH	S-1	333-163778	12/16/2009	10.26
10.34†	Amendment No. 1 to Option and License Agreement, dated as of March 18, 2014 by and between the Registrant and Biogen Idec MA Inc.	10-Q	001-34655	05/07/2014	10.1

Exhibit Number	Description of Exhibit	Incorporated by Reference Form	File Number	Date of Filing	Exhibit Number	Filed Herewith
10.35†	Co-Development and Collaboration Agreement, dated as of April 9, 2014 by and between the Registrant and Biodesix Inc.	10-Q	001-34655	05/07/2014	10.2	
10.36†	Research and Exclusive License Agreement, dated as of November 10, 2014, by and between the Registrant and Ophthotech Corporation	10-K	001-34655	3/06/2015	10.35	
10.37	ATM Sales Agreement, dated February 27, 2015 by and between the Company and MLV & Co. LLC	8-K	001-34655	2/27/2015	1.1	
10.38	Amendment No. 1 to ATM Sales Agreement, dated May 7, 2015 by and between the Registration and MLV & Co. LLC	10-Q	001-34655	05/07/2015	10.6	
10.39†	License Agreement, dated August 4, 2015, by and between the Registrant and JSC “Pharmstandard-Ufimskiy Vitamin Plant”	10-Q	001-34655	11/09/2015	10.1	
10.40†	License Agreement, dated August 13, 2015, by and between the Registrant and Novartis International Pharmaceutical Ltd.	10-Q	001-34655	11/09/2015	10.2	
10.41†	Amended and Restated License Agreement, dated August 13, 2015, by and between the Registrant and St. Vincent’s Hospital Sydney Limited	10-Q	001-34655	11/09/2015	10.3	
10.42*	License Agreement, dated December 18, 2015, by and between the Registrant and EUSA Pharma (UK) Limited					X
	Additional Exhibits					
21.1	Subsidiaries of the Registrant					X
23.1	Consent of Ernst & Young LLP					X
31.1	Certification of principal executive officer pursuant to Rule 13a-14(a)/15d-14(a) of the Securities Exchange Act of 1934, as amended.					X
31.2	Certification of principal financial officer pursuant to Rule 13a-14(a)/15d-14(a) of the Securities Exchange Act of 1934, as amended.					X
32.1	Certification of principal executive officer pursuant to 18 U.S.C. §1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.					X
32.2	Certification of principal financial officer pursuant to 18 U.S.C. §1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.					X
101.INS	XBRL Instance Document.					X

101.SCH	XBRL Taxonomy Extension Schema Document.	X
101.CAL	XBRL Taxonomy Calculation Linkbase Document.	X
101DEF	XBRL Taxonomy Extension Definition Linkbase Document.	X
101.LAB	XBRL Taxonomy Label Linkbase Document.	X
101.PRE	XBRL Taxonomy Presentation Linkbase Document.	X

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

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