AVEO PHARMACEUTICALS INC
Form 10-K
March 13, 2018

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

(Mark One)

ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the fiscal year ended: December 31, 2017

Or

TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the transition period from to

Commission file number: 001-34655

AVEO PHARMACEUTICALS, INC.

(Exact Name of Registrant as Specified in Its Charter)

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 Capital Market

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

None

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes No

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes No

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes No

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes No

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§229.405) is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K.

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company, or emerging growth company. See definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act. (Check one):

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

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act.

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

The aggregate market value of the registrant's common stock, $0.001 par value per share, held by non-affiliates of the registrant, based on the last reported sale price of the common stock on the Nasdaq Capital Market at the close of

business on June 30, 2017, was $218,171,452

The number of shares outstanding of the registrant's Common Stock as of March 8, 2018 were 118,867,471.

Documents incorporated by reference:

Portions of our definitive proxy statement for our 2018 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

Any statement contained in this Annual Report on Form 10-K or in the documents we incorporate by reference herein other than a statement of historical fact, may be a forward-looking statement, including statements regarding our and our collaborators’ future discovery, development and commercialization efforts, our strategy, future operations, future financial position, future revenue, projected costs, prospects, plans and objectives of management. In some cases, you can identify forward-looking statements by such terms as “anticipate,” “believe,” “could,” “estimate,” “expect,” “forecast,” “in “may,” “plan,” “project,” “should,” “target,” “will,” “would” or other words that convey uncertainty of future events or outcom identify these forward-looking statements. Forward-looking statements may include, but are not limited to, statements about:

- the initiation, timing, progress and results of future clinical trials, and our development programs;
- our plans to develop and commercialize our product candidates;
- our ability to secure new collaborations, maintain existing collaborations or obtain additional funding;
- the timing or likelihood of regulatory filings and approvals;
- the implementation of our business model, strategic plans for our business, product candidates and technology;
- our commercialization, marketing and manufacturing capabilities and strategy;
- the rate and degree of market acceptance and clinical utility of our products;
- our competitive position;
- our intellectual property position;
- developments and projections relating to our competitors and our industry;
- our estimates of the period in which we anticipate that existing cash, cash equivalents and investments will enable us to fund our current and planned operations;
- our estimates regarding expenses, future revenue, capital requirements and needs for additional financing; and
- our ability to continue as a going concern.

Our actual results may differ materially from those indicated by these forward-looking statements as a result of various important factors, including risks relating to:

- our ability to maintain our third-party collaboration agreements and our ability, and the ability of our licensees, to achieve development and commercialization objectives under these arrangements;
- our ability, and the ability of our licensees, to demonstrate to the satisfaction of applicable regulatory agencies the safety, efficacy and clinically meaningful benefit of our product candidates;
- our ability to successfully enroll and complete clinical trials of our product candidates, including our TIVO-3 trial;
- our ability to achieve and maintain compliance with all regulatory requirements applicable to our product candidates;
- our ability to obtain and maintain adequate protection for intellectual property rights relating to our product candidates and technologies;
- developments, expenses and outcomes related to our ongoing stockholder litigation;
- our ability to successfully implement our strategic plans;
- our ability to raise the substantial additional funds required to achieve our goals;
- unplanned capital requirements;
- adverse general economic and industry conditions;
- competitive factors;

- our ability to continue as a going concern; and
- those risks discussed under the heading "Risk Factors" in Part I, Item 1A of this report.

If one or more of these factors materialize, or if any underlying assumptions prove incorrect, our actual results, performance or achievements may vary materially from any future results, performance or achievements expressed or implied by the forward-looking statements we make.

You should consider these factors and the other cautionary statements made in this report and the documents we incorporate by reference herein as being applicable to all related forward-looking statements wherever they appear in this report or the documents incorporated by reference. While we may elect to update forward-looking statements wherever they appear in this report or the documents incorporated by reference herein, we do not assume, and specifically disclaim, any obligation to do so, whether as a result of new information, future events or otherwise, unless required by law.

PART I

ITEM 1. Business

Overview

We are a biopharmaceutical company dedicated to advancing a broad portfolio of targeted medicines for oncology and other areas of unmet medical need. Our strategy is to retain North American rights to our oncology portfolio while securing partners in development and commercialization outside of North America. We are working to develop and commercialize our lead candidate tivozanib in North America as a treatment for renal cell carcinoma, or RCC. We have entered into partnerships to fund the development and commercialization of our preclinical and clinical stage assets, including AV-203 and ficlatuzumab in oncology and AV-380 in cachexia. Tivozanib (FOTIVDA®), which we have outlicensed outside of North America, is approved in the European Union, as well as Norway and Iceland, for the first-line treatment of adult patients with advanced RCC, or aRCC, and for adult patients who are vascular endothelial growth factor receptor, or VEGFR, and mTOR pathway inhibitor-naïve following disease progression after one prior treatment with cytokine therapy for aRCC. We are currently seeking a partner to develop our AV-353 platform, a preclinical asset, worldwide for the potential treatment of pulmonary arterial hypertension, or PAH.

Going Concern

We have identified conditions and events that raise substantial doubt about our ability to continue as a going concern. To continue as a going concern, we must secure additional funding to support our current operating plan. As of December 31, 2017, we had approximately $33.5 million in existing cash, cash equivalents and marketable securities. In the first quarter of 2018 to-date, we have raised an additional approximate $1.9 million in net funding. Based on these available cash resources, we do not have sufficient cash on hand to support current operations for at least the next twelve months from the date of filing this Annual Report on Form 10-K. This condition raises substantial doubt about our ability to continue as a going concern. For a further discussion of our liquidity, please refer to Part II, Item 7 of this report under the heading “Management’s Discussion and Analysis of Financial Condition and Results of Operations—Liquidity and Capital Resources—Operating Capital Requirements and Going Concern” and Note 1 to our consolidated financial statements included elsewhere in this Annual Report on Form 10-K.

Tivozanib

Our pipeline includes our lead candidate tivozanib, an oral, once-daily, vascular endothelial growth factor receptor tyrosine kinase inhibitor, or VEGFR TKI. Tivozanib is a potent, selective and long half-life inhibitor of all three VEGF receptors and is designed to optimize VEGF blockade while minimizing off-target toxicities, potentially resulting in improved efficacy and minimal dose modifications. Tivozanib has been investigated in several tumor types, including renal cell, hepatocellular, colorectal and breast cancers, as well as in non-oncologic ocular conditions. In 2006, we acquired the exclusive rights to develop and commercialize tivozanib in all countries outside of Asia and the Middle East under a license from Kyowa Hakko Kirin Co., Ltd. (formerly Kirin Brewery Co. Ltd.), or KHK. In 2015, we entered into a license agreement with EUSA Pharma (UK) Limited, or EUSA, under which we granted EUSA the right to develop and commercialize tivozanib for all diseases and conditions in humans, excluding non-oncologic eye conditions, in Europe (excluding Russia, Ukraine and the Commonwealth of Independent States), Latin America (excluding Mexico), Africa, Australasia and New Zealand.

Clinical and Regulatory Development in RCC

RCC First-line Phase 3 Trial (TIVO-1): We conducted a global phase 3 clinical trial, which we refer to as the TIVO-1 trial, comparing the efficacy and safety of tivozanib with sorafenib (Nexavar®), an approved therapy, for first-line treatment of RCC. The trial met its primary endpoint for progression-free survival, or PFS, with a median PFS in the tivozanib arm of 11.9 months compared with 9.1 months in the sorafenib arm. The trial also showed significant improvement in overall response rate, or ORR, of 33.1% for tivozanib and 23.3% for sorafenib. The trial showed a

favorable tolerability profile for tivozanib, as evidenced by fewer dose interruptions and dose reductions than sorafenib. However, the trial showed a non-statistically significant trend favoring the sorafenib treatment group in overall survival, or OS, with a final median OS for the tivozanib treatment arm of 28.2 months and a final median OS for the sorafenib arm of 30.8 months. We believe that the imbalance in subsequent therapy combined with the significant activity seen with tivozanib treatment following sorafenib contributed to the discordance in the efficacy results in the TIVO-1 trial between the PFS and ORR benefit, which significantly favored tivozanib, and the OS, which trended in favor of sorafenib.

In 2012, we submitted a NDA to the U.S. Food and Drug Administration, or FDA, seeking U.S. marketing approval for tivozanib. In June 2013, the FDA issued a complete response letter informing us that it would not approve tivozanib for the first-line treatment of aRCC based solely on the data from this single pivotal trial (TIVO-1), and recommended that we perform an additional clinical trial adequately sized to assure the FDA that tivozanib does not adversely affect OS.

TIVO-1 Extension Study - One-way crossover from sorafenib to tivozanib (Study 902): We completed a TIVO-1 extension study in which patients with aRCC received tivozanib as second-line treatment subsequent to disease progression on the sorafenib arm in the TIVO-1 first-line RCC trial. The final results showed a median PFS of 11.0 months, a median OS of 21.6 months and an ORR of 18%, demonstrating the clinically meaningful activity of tivozanib in a VEGFR treatment refractory population. We presented the final results at the 2015 American Society of Clinical Oncology, or ASCO, Annual Meeting.

European Marketing Approval: Our licensee EUSA submitted a marketing authorization application, or MAA, for tivozanib for the treatment of RCC to the European Medicines Agency, or EMA, in February 2016. The MAA was based primarily on the results from the TIVO-1 clinical trial of tivozanib in the first-line treatment of RCC, combined with the TIVO-1 extension trial, and one phase 1 and two phase 2 trials in RCC. On May 17, 2017, EUSA completed an oral explanation to the Committee for Medicinal Products for Human Use, or CHMP, which is the scientific committee of the EMA. On June 23, 2017, the CHMP issued an opinion recommending tivozanib for approval as a first-line treatment of adult patients with aRCC and for adult patients who are VEGFR and mTOR pathway inhibitor-naive following disease progression after one prior treatment with cytokine therapy for aRCC.

In August 2017, the European Commission granted marketing authorization to EUSA for tivozanib in all 28 countries of the European Union, Norway and Iceland. Tivozanib is sold under the brand name FOTIVDA. FOTIVDA is approved for the first-line treatment of adult patients with aRCC and for adult patients who are VEGFR and mTOR pathway inhibitor-naïve following disease progression after one prior treatment with cytokine therapy for aRCC.

In November 2017, EUSA commercially launched FOTIVDA with the initiation of product sales in Germany. In February 2018, the United Kingdom's National Institute for Health and Care Excellence, or the NICE, published a Final Appraisal Determination recommending FOTIVDA for the first-line treatment of adult patients with aRCC. This positive recommendation allows for reimbursement approval of FOTIVDA in the UK. EUSA is in the process of applying for reimbursement approval in additional European countries.

RCC Third Line Phase 3 Trial (TIVO-3): In May 2016, we initiated enrollment and treatment of patients in a phase 3 trial of tivozanib in the third-line treatment of patients with aRCC, which we refer to as the TIVO-3 trial. The TIVO-3 clinical trial was designed to address the FDA's concern about the negative OS trend expressed in the complete response letter from June 2013. Our intention is to seek regulatory approval in the United States for tivozanib based on results from the TIVO-3 study as a third-line treatment for RCC. In addition, we plan to seek approval in the first-line using these data together with the results from the TIVO-1 trial. Our TIVO-3 trial design, which we reviewed with the FDA, provided for a randomized, controlled, multi-center, open-label phase 3 clinical trial randomized 1:1 to receive either tivozanib or sorafenib. Subjects enrolled in the trial must have failed two systemic therapies, including a VEGFR TKI. Patients may have received prior immunotherapy, including immune checkpoint (PD-1) inhibitors, reflecting the evolving treatment landscape. The primary objective of the TIVO-3 trial is to show improved PFS. Secondary endpoints include OS, safety and ORR. The trial's sites are located in North America and Europe. The TIVO-3 trial does not include a crossover design; accordingly, patients who progress in one therapy are not offered the opportunity to cross over to the other therapy.

The TIVO-3 trial has enrolled a total of 351 patients and has passed three semi-annual safety data assessments. In October 2017, we successfully passed a pre-planned interim futility analysis for TIVO-3. Based on the results of the futility analysis, which were reviewed by an independent statistician, the trial continued as planned without modification. We expect to receive and report topline data from the TIVO-3 trial (including PFS and preliminary OS data) in the second quarter of 2018, approximately 8-10 weeks after the 255th event (progression determined by an independent radiology committee or death) is reported.

RCC PD-1 Combination Trial with Opdivo® (TiNivo): In recent clinical trials, VEGFR TKI and immune checkpoint (PD-1) inhibitor combinations have shown promising efficacy in treating aRCC. However, several combinations of non-specific VEGFR TKIs with anti-PD-1 antibodies have encountered toxicity levels that we believe have challenged or prohibited such VEGFR TKIs from safely combining with PD-1 inhibitors for RCC treatment, or required them to combine at reduced doses, which can potentially reduce efficacy. In our clinical trials, tivozanib has demonstrated lower rates of key potential overlapping toxicities with PD-1 inhibitors. Based on this data, we believe that tivozanib's tolerability profile may allow tivozanib to combine with PD-1 inhibitors with improved tolerability.

In March 2017, we initiated enrollment in a phase 1b/2 clinical trial of tivozanib in combination with Opdivo (nivolumab), an immune checkpoint (PD-1) inhibitor, for the treatment of aRCC, which we refer to as the TiNivo

trial. The phase 1b/2 trial enrolled a total of 28 patients. We are sponsoring the trial, for which Bristol-Myers Squibb, or BMS, has supplied nivolumab. The TiNivo trial is being led by the Institut Gustave Roussy in Paris under the direction of Professor Bernard Escudier, MD, Chairman of the Genitourinary Oncology Committee. The phase 1b portion of the trial enrolled six patients. In June 2017, we successfully completed the phase 1 dose escalation portion of the trial, where oral tivozanib was administered in two escalating dose cohorts in combination with intravenous nivolumab at a constant 240 mg every two weeks. The full dose tivozanib regimen of 1.5 mg daily for 21 days, followed by a 7-day rest period, was selected as the recommended phase 2 dose for the expansion portion of the trial. On November 3, 2017, the results from the phase 1b portion of the phase 1b/2 TiNivo trial were presented at the 16th International Kidney Cancer Symposium of the Kidney Cancer Association. The phase 1b portion of the trial demonstrated that the combination of tivozanib and nivolumab was well tolerated to the full dose and schedule of single agent tivozanib, with no dose limiting toxicities.

The phase 2 portion of the trial, which enrolled an additional 22 patients, was designed to assess the safety, tolerability, and anti-tumor activity of the combination of tivozanib and nivolumab. On February 10, 2018, we presented the preliminary results from the phase 2 portion of the trial on 27 of the 28 patients with available data at the 2018 ASCO Genitourinary Cancers Symposium. The combination was generally well tolerated. Treatment-related Grade 3/4 adverse events occurred in 44% of patients, the most common of which was hypertension. Preliminary efficacy was assessed in 14 patients treated with the full dose and schedule of oral tivozanib in combination with intravenous nivolumab and enrolled at least four months prior to the data cutoff date. Of these, seven had received at least one prior systemic therapy and seven were treatment naive. An ORR was observed in 64% of patients (partial responses), and a disease control rate (partial response + stable disease) was observed in 100% of patients. At the time of data collection, 11 of 14 evaluable patients remained on study.

Following the receipt of these preliminary results in the TiNivo trial, we and our development partner EUSA intend to explore further development of tivozanib as a combination therapy with immune checkpoint inhibitors.

Clinical Development in HCC

NCCN-AVEO Phase 1b/2 Trial. In January 2018, Dr. Renuka Iyer from the Roswell Park Cancer Institute presented data from a multicenter, investigator-sponsored phase 1b/2 trial of tivozanib in previously untreated patients with advanced, unresectable hepatocellular carcinoma (HCC). The data were presented at the 2018 ASCO Gastrointestinal Cancers Symposium. The phase 1b/2 trial was one of several studies funded by a grant provided to the National Comprehensive Cancer Network by AVEO.

The trial, designed to evaluate the safety and efficacy of tivozanib in advanced HCC, enrolled a total of 21 patients at three trial sites. In the phase 1b portion of the trial, which used a modified 3+3 dose escalation design, 8 patients were dosed with tivozanib starting at 1.0 mg daily for 21 days followed by 7 days off drug, with inter-patient escalation to 1.5 mg daily or de-escalation to 0.5 mg daily based on cumulative dose-limiting toxicities (DLT). Tivozanib at 1.0 mg daily had no DLTs and was selected for the phase 2 expansion portion.

Of 19 evaluable patients in the phase 2 portion of the trial, at a median follow up of 16.9 months, the trial's primary endpoint of median PFS and PFS at week 24 were 5.5 months and 47%, respectively. A partial response was seen in 4 of 19 patients (21%) and stable disease (SD) in 8 of 19 patients (42%), for a disease control rate of 63%. OS at 6 and 12 months was 58% and 25%, respectively, with a median OS of 7.5 months. Notably, four patients have maintained SD for over two years. There were no significant changes in hepatitis B or hepatitis C viral load during study treatment. Tivozanib was generally well tolerated at 1.0 mg daily, with adverse events consistent with those observed in previous tivozanib trials.

We plan to explore the further development of tivozanib in HCC, both as a monotherapy and potentially as a combination therapy.

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. In April 2014, we and Biodesix, Inc., or Biodesix, entered into a worldwide Co-Development and Collaboration Agreement, or the Biodesix Agreement, to develop and commercialize ficlatuzumab. The Biodesix Agreement was amended in October 2016 to provide, among other things, for equal cost sharing in the development of ficlatuzumab.

Development in HNSCC. We and Biodesix are funding an investigator-sponsored clinical trial of ficlatuzumab in combination with ERBITUX® (cetuximab) in squamous cell carcinoma of the head and neck, or HNSCC. In June 2017, preliminary results from the phase 1 trial were presented at the 2017 ASCO Annual Meeting. The trial of ficlatuzumab in combination with the EGFR inhibitor cetuximab in patients with cetuximab-resistant, metastatic

HNSCC demonstrated activity with an overall response rate of 17% (two partial responses out of 12 patients), a disease control rate of 67% and prolonged PFS and OS compared to historical controls, in addition to being well tolerated. A randomized, phase 2, multicenter, investigator-initiated trial to confirm these findings was initiated in the fourth quarter of 2017 under the direction of Julie E. Bauman, MD, MPH, Chief, Division of Hematology/Oncology at the University of Arizona Cancer Center. The phase 2 trial is expected to enroll approximately 60 patients randomized to receive either ficlatuzumab alone or ficlatuzumab and cetuximab.

Development in AML. We and Biodesix are funding an investigator-sponsored clinical trial of ficlatuzumab in combination with Cytosar® (cytarabine) in acute myeloid leukemia, or AML. In June 2017, preliminary results from the phase 1 trial were presented at the 2017 ASCO Annual Meeting. This trial, exploring ficlatuzumab in combination with high-dose cytarabine in patients with high risk relapsed or refractory AML, demonstrated early signs of tolerability and activity, including a 50% complete response rate in the eight evaluable patients. The phase 2 portion is ongoing and expected to enroll ten additional patients.

Development in pancreatic cancer. We and Biodesix are funding an investigator-sponsored clinical trial of ficlatuzumab in combination with nab-paclitaxel and gemcitabine in pancreatic cancer. The trial was initiated in December 2017 to test the safety and tolerability of ficlatuzumab when combined with nab-paclitaxel and gemcitabine in previously untreated metastatic pancreatic ductal cancer (PDAC). The goal of the trial, which is based on preclinical findings demonstrating a synergistic effect of these drugs in a preclinical model of PDAC, is designed to determine maximum tolerated dose of ficlatuzumab when combined with gemcitabine and nab-paclitaxel. Secondary outcome measures include response rate and progression free survival. The trial, which is being conducted under the direction of Kimberly Perez, M.D. at the Dana-Farber Cancer Institute, is expected to enroll approximately 30 patients.

We continue to evaluate additional opportunities for the further clinical development of ficlatuzumab. The expansion of the ficlatuzamab clinical program would require the manufacturing of additional clinical supplies.

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. We have completed a phase 1 dose escalation trial of AV-203, which established a recommended phase 2 dose, demonstrated good tolerability and promising early signs of activity, and reached the maximum planned dose of AV-203 monotherapy. In 2014, the expansion cohort of this trial was discontinued to conserve capital resources.

In March 2016, we entered into a collaboration and license agreement with CANbridge Life Sciences Ltd., or CANbridge, under which we granted CANbridge the exclusive right to develop, manufacture and commercialize AV-203 in all countries other than the United States, Canada and Mexico. CANbridge has completed work to optimize the manufacturing of AV-203, and in December 2017, CANbridge filed an IND application in China in order to initiate clinical trials of AV-203. Subject to the decision by the Chinese regulatory authorities regarding CANbridge's IND application, CANbridge expects that AV-203 will reenter the clinic in 2018.

AV-380

AV-380 is a potent humanized IgG1 inhibitory monoclonal antibody targeting growth differentiation 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 chronic kidney disease, congestive heart failure, chronic obstructive pulmonary disease, or COPD, anorexia nervosa and other diseases. We believe that AV-380 represents a unique approach to treating cachexia because it addresses key underlying mechanisms of the syndrome. AV-380 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).

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 OS benefit. We have demonstrated preclinical proof-of-concept for AV-380 in multiple cancer cachexia models and have completed cell line development.

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 our related 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. Novartis has informed us that the AV-380 program development continues, but that timelines for development are uncertain. In connection with the AV-380 program, we have in-licensed certain patents and patent applications from St. Vincent's Hospital Sydney Limited in Sydney, Australia, which we refer to as St. Vincent's.

AV-353 Platform

The AV-353 platform includes a number of potent inhibitory antibody candidates specific to Notch 3. The Notch 3 pathway is important in cell-to-cell communication involving gene regulation mechanisms that control multiple cell differentiation processes during the entire life cycle. Scientific literature has implicated the Notch 3 receptor pathway in multiple diseases, including cancer, cardiovascular diseases and neurodegenerative conditions. Publications, including Nature Medicine (2009), have implicated the Notch 3 pathway in PAH, a rare and life-threatening disorder that affects approximately 250,000 people worldwide (Global Data 2016 PAH Opportunity Analyzer; 2012 Decision Resources PAH Report) and is caused by thickening of the arterial walls in small arteries between the heart and the lungs, resulting in restricted blood flow. Currently, no known cure for PAH exists. Existing treatments for PAH have focused on controlling symptoms by avoiding vasoconstriction and increasing vasodilation of blood vessels but have not reversed the underlying cause of the disease. However, the results of a preclinical research study conducted at the University of California at San Diego and presented in a poster at the November 2016 American Heart Association meeting using one of our anti-Notch3 antibody candidates generated preclinical data that supports the ability of the antibody to potentially reverse the thickening of vascular smooth muscle cells, which would represent a disease-modifying approach to treatment.

We are currently seeking a partner to develop the AV-353 platform worldwide for the potential treatment of PAH.

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, Xbiotech Inc., Novartis, BMS, Merck & Co., Merrimack Pharmaceuticals, Inc., Arqule, Inc., Exelixis, Inc., Eisai Co., Ltd., Merck KGaA and AstraZeneca plc are pursuing the development or are currently marketing pharmaceuticals that target VEGF, HGF, ErbB3, Notch 3 or other pathways that could compete with our development candidates in oncology, cachexia, age-related macular degeneration, or AMD, and PAH. 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, cachexia, AMD, and PAH 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

There are currently eleven FDA-approved drugs in oncology which target the VEGF receptors. Eight of the FDA-approved VEGF pathway inhibitors are oral small molecule receptor TKIs. Nexavar (sorafenib) and Stivarga (regorafenib) are marketed by Bayer, Sutent (sunitinib) and Inlyta (axitinib) are marketed by Pfizer, and Votrient (pazopanib) is marketed by Novartis. Most of these approved VEGF TKIs are not specific to VEGFR 1, 2 and 3. Nexavar is approved for aRCC and unresectable HCC. Stivarga is approved for refractory metastatic colorectal cancer, or mCRC, and refractory gastrointestinal stromal tumors, or GIST. Sutent is approved for aRCC, GIST, and progressive, well-differentiated pancreatic neuroendocrine tumors. Inlyta is approved for aRCC after failure of one

prior systemic therapy. Votrient is approved for aRCC and advanced soft tissue sarcoma after prior chemotherapy. Caprelsa (vandetanib), marketed by Sanofi Genzyme is approved for advanced medullary thyroid cancer, Lenvima (lenvatinib) marketed by Eisai is approved for differentiated thyroid cancer, and RCC following one prior anti-angiogenic therapy in combination with everolimus, and Cabometyx (cabozantinib), marketed by Exelixis, is approved for RCC.

Avastin (bevacizumab), marketed by Roche/Genentech, Inc., is a monoclonal antibody approved for intravenous administration in combination with other anti-cancer agents for the treatment of mCRC and ovarian cancer, cervical cancer, non-squamous non-small cell lung cancer, and metastatic RCC in combination with interferon alfa. 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 S.A. and Regeneron Pharmaceuticals, Inc., 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 VEGF-2 receptor that is approved for the treatment of advanced gastric or gastro-esophageal junction adenocarcinoma as monotherapy or in combination with paclitaxel, metastatic CRC in combination with FOLFIRI 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 anti-PD-1/PD-L1 and anti CTLA-4 antibodies present additional competition for tivozanib in aRCC. For example, Opdivo (nivolumab), marketed by BMS, is an approved anti-PD-1 for second line RCC. Additional clinical trials that are testing mono and combination therapies of PD-1/PD-L1 with other immuno-oncology targets and VEGF TKIs targeting RCC are underway. We are aware of several ongoing phase 3 registration studies evaluating PD-1/PD-L1 inhibitors in combination with anti-angiogenic agents or other immune therapies for RCC. Positive phase 3 trial results have recently been announced from CheckMate-214, a Bristol-Myers Squibb trial combining nivolumab and ipilimumab vs sunitinib in first line RCC, and also for the phase 3 IMmotion151 combination trial of bevacizumab and atezolizumab vs sunitinib in first line RCC. If approved, these combinations could present additional competition for tivozanib.

Ficlatuzumab

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 include 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. ArQule, Inc. and Daiichi Sankyo, Inc., under a collaboration agreement, completed a phase 3 trial of ARQ-197 (tivantinib) in liver cancer that failed to meet its primary endpoint.

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/Cabometyx, cabozantinib), 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 U.S. LLC's SAR-125844, EMD Serono, Inc.'s MSC2156119J, Amgen BioPharma's AMG-337 and AMG-208, Lilly's merestinib (LY2801653), Les Laboratoires Servier SAS's S-49076, AstraZeneca and Hutchison MediPharma Limited's savolitinib, Merck KGaA's tepotinib, AbbVie Inc.'s ABT-700, Deciphera Pharmaceuticals, LLC's altiratinib, Betta Pharmaceuticals Co., Ltd.'s BPI-9016 and Bristol-Myers Squibb Company's and Aslan Pharmaceuticals' BMS-777607.

AV-203

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 in heregulin positive NSCLC, and Daiichi Sankyo, Inc.'s and Amgen, Inc.'s patritumab (AMG-888), which recently entered phase 2 clinical development for head and neck cancer and metastatic breast cancer. Other clinical-stage ErbB3-specific competitors include Roche's RG-7116, Novartis's elgemtumab, Regeneron's REGN1400, GSK's GSK-2849330, Merus N.V.'s MCLA-128, AstraZeneca's sapitinib, Celldex Therapeutics Inc.'s KTN-3379 and Sihuan Pharmaceutical Holdings Group Ltd.'s pirotinib and sirotinib. Clinical stage competitors targeting ErbB3 in addition to other targets include Roche's MEHD7945A, and Merrimack Pharmaceuticals MM-111 and MM-141.

AV-380

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.

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 Biotherapeutics, Inc.'s PINTA 745. Of these, both Lilly's LY2495655 and PINTA 745 have announced failures to demonstrate clinical proof of concept in their respective phase 2 trials. 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 Biotherapeutics Inc.'s clazakizumab (ALD-518, targeting IL-6), PsiOxus Therapeutics, Ltd.'s MT-102 (dual acting catabolic/anabolic transforming agent), Acacia Pharma Group plc's APD-209 (progestin/ß2 antagonist) and Ohr Pharmaceutical, Inc.'s OHR118 (cytoprotectant/immunomodulator). PsiOxus's espindolol has completed phase 1 trials.

AV-353 Platform

There are currently no Notch 3-specific inhibitors approved or in clinical trials in oncology or PAH indications. Pfizer recently stopped development of PF-06650808, a Notch 3-specific antibody drug conjugate which was in phase 1 trials in multiple oncology indications. However, a number of agents for applications in oncology are being explored which target the Notch 3 receptor and may inhibit other Notch receptors including Notch 1, Notch 2 and Notch 4, including BMS-906024, BMS-986115, BMS-871 and Tarextumab (OMP-59R5).

There are multiple treatments approved for PAH through various other mechanisms apart from Notch 3 inhibition. These include treatments such as epithelial receptor antagonists, phosphodiesterase type 5 inhibitors, and prostacyclin analogues. We do not believe that any of these approved therapies has demonstrated disease modifying effects.

Strategic Partnerships

CANbridge

In March 2016, we entered into a collaboration and license agreement with CANbridge, or the CANbridge Agreement, under which we granted CANbridge the exclusive right to develop, manufacture and commercialize AV-203, our proprietary ErbB3 (HER3) inhibitory antibody, for the diagnosis, treatment and prevention of disease in humans and animals in all countries other than the United States, Canada and Mexico. Under the terms of the CANbridge Agreement, if we determine to grant a license to any ErbB3 inhibitory antibody in the United States, Canada or Mexico, we are obligated to first negotiate with CANbridge for the grant to CANbridge of a license to such rights. The parties have both agreed not to directly or indirectly develop or commercialize any other ErbB3 inhibitory antibody product during the term of the CANbridge Agreement other than pursuant to the CANbridge Agreement.

CANbridge has responsibility for all activities and costs associated with the further development, manufacture, regulatory filings and commercialization of AV-203 throughout its licensed territory. CANbridge is obligated to use commercially reasonable efforts to develop and obtain regulatory approval for AV-203 in each of China, Japan, the United Kingdom, France, Italy, Spain, and Germany. CANbridge will bear all costs for development of AV-203 through proof-of-concept in Esophageal Squamous Cell Carcinoma, after which we would expect to contribute to certain worldwide development costs.

Pursuant to the CANbridge Agreement, CANbridge paid us an upfront fee of $1.0 million in April 2016. CANbridge also agreed to reimburse us $1.0 million for certain manufacturing costs and expenses that we previously incurred. CANbridge paid this manufacturing reimbursement in two installments of $0.5 million each, including one in March 2017 and one in September 2017, net of foreign withholding taxes. We are also eligible to receive up to $42.0 million in potential development and regulatory milestone payments and up to $90.0 million in potential sales based milestone payments based on annual net sales of licensed products. Upon commercialization, we are eligible to receive a tiered royalty, with a percentage range in the low double-digits, on net sales of approved licensed products. CANbridge's obligation to pay royalties for each licensed product expires on a country-by-country basis on the later of the expiration of patent rights covering such licensed product in such country, the expiration of regulatory data exclusivity in such country and ten years after the first commercial sale of such licensed product in such country. A percentage of any milestone and royalty payments received by us, excluding upfront and reimbursement payments, is due to Biogen Idec International GmbH, or Biogen Idec, as a sublicensing fee under our option and license agreement, up to $50 million, with Biogen dated March 18, 2009, as amended.

The term of the CANbridge Agreement commenced on the effective date and will continue until the last to expire royalty term applicable to licensed products. Either party may terminate the CANbridge Agreement in the event of a material breach of the CANbridge Agreement by the other party that remains uncured for a period of 45 days, in the case of a material breach of a payment obligation, and 90 days in the case of any other material breach. CANbridge may terminate the CANbridge Agreement without cause at any time upon 180 days' prior written notice to us. We may

terminate the CANbridge Agreement upon thirty days' prior written notice if CANbridge challenges any of the patent rights licensed to CANbridge under the CANbridge Agreement.

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 eye conditions. EUSA is obligated to use commercially reasonable efforts to seek regulatory approval for and commercialize tivozanib throughout its licensed territories for RCC. EUSA has responsibility for all activities and costs associated with the further development, manufacture, regulatory filings and commercialization of tivozanib in its licensed territories. In September 2017, EUSA elected to exercise an opt-in right under the license agreement to co-develop the TiNivo trial, and we and EUSA have announced our intention to further collaborate in future development activities for tivozanib across our territories.

Under the license agreement, EUSA made research and development reimbursement payments to us of $2.5 million upon the execution of the license agreement in 2015 and $4.0 million in September 2017 upon its receipt of marketing approval from the EMA for tivozanib (FOTIVDA) for the treatment of RCC. In September 2017, EUSA elected to opt-in to co-develop the TiNivo trial. As a result of EUSA's exercise of its opt-in right, it became an active participant in the ongoing conduct of the TiNivo trial and is able to utilize the resulting data from the TiNivo trial for regulatory and commercial purposes in its territories. EUSA made an additional research and development reimbursement payment to us of $2.0 million upon its exercise of its opt-in right. This payment was received in October 2017, in advance of the completion of the TiNivo trial, and represents EUSA's approximate 50% share of the total estimated costs of the TiNivo trial. We are also eligible to receive an additional research and development reimbursement payment from EUSA of fifty percent (50%) of our total costs for our TIVO-3 trial, up to $20.0 million, if EUSA elects to opt-in to that trial.

We are entitled to receive milestone payments of $2.0 million per country upon reimbursement approval, if any, for RCC in each of France, Germany, Italy, Spain and the United Kingdom, and an additional $2.0 million for the grant of marketing approval, if any, in three of the following five countries: Argentina, Australia, Brazil, South Africa and Venezuela. In February 2018, EUSA obtained reimbursement approval from the NICE in the United Kingdom in first line RCC. Accordingly, we earned a $2.0 million milestone payment that was received from EUSA in March 2018. We are also eligible to receive a payment of $2.0 million in connection with a filing by EUSA with the EMA for marketing approval, if any, 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 up to $335.0 million upon EUSA's achievement of certain sales thresholds. Upon commercialization, we are eligible to receive tiered double-digit royalties on net sales, if any, of licensed products in its licensed territories ranging from a low double digit up to mid-twenty percent depending on the level of annual net sales. In November 2017, we began earning sales royalties upon EUSA's commencement of the first commercial launch of tivozanib (FOTIVDA) with the initiation of product sales in Germany.

The research and development reimbursement payments under the EUSA license agreement are not subject to the 30% sublicensing fee to KHK, subject to certain limitations. We would, however, owe KHK 30% of other, non-research and development payments we may receive from EUSA pursuant to our license agreement, including EU reimbursement approval milestones in up to five specified EU countries, EU marketing approvals for up to three additional indications beyond RCC, marketing approvals in up to three specified licensed territories outside of the EU, sales-based milestones and royalties, as set forth above. The $2.0 million milestone we earned in February 2018 upon EUSA's reimbursement approval from the NICE in the UK in first line RCC is subject to the 30% KHK sub-license fee, or $0.6 million.

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 worldwide license agreement with Novartis, under which we granted Novartis the exclusive right to develop and commercialize AV-380 and our related antibodies that bind to GDF15. 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 in September 2015. In December 2015, Novartis also exercised its right under the license agreement to acquire our inventory of clinical quality drug substance, reimbursing us approximately $3.5 million for such existing inventory. We are also eligible to receive (a) up to $51.2 million in potential clinical 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 sales based milestone payments based on annual net sales of such products. If the product is commercialized, we would be 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. Certain milestones achieved by Novartis would trigger milestone payment obligations from us to St. Vincent’s, under our amended and restated license agreement with St. Vincent’s. In addition, royalties on approved products, if any, will be payable to St. Vincent’s, and we and Novartis will share that obligation equally.

In February 2017, Novartis paid $1.8 million out of its future payment obligations to us under the license agreement. The funds were used to satisfy a $1.8 million time-based milestone obligation that we owed to St. Vincent's on March 2, 2017. Novartis will reduce any subsequent payment obligations to us, if any, by the $1.8 million. We recognized the $1.8 million of consideration as revenue during the three months ended March 31, 2017, as the amount was fixed and determinable and non-refundable, and we do not have any further performance obligations to Novartis in connection with the license agreement. This payment reduces the aggregate future amounts potentially payable by Novartis to us under the license agreement by the $1.8 million, but does not amend any other terms of the Novartis license agreement.

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.

Biodesix

In April 2014, we and Biodesix entered into the Biodesix Agreement to develop and commercialize ficlatuzumab. Under the Biodesix 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 VeriStrat®, Biodesix's proprietary companion diagnostic test. Biodesix granted us perpetual, non-exclusive rights to certain intellectual property, including diagnostic data related to VeriStrat, with respect to the development and commercialization of ficlatuzumab; each license includes the right to sublicense, subject to certain exceptions.

Under the Biodesix Agreement, we and Biodesix are each required to contribute 50% of all clinical, regulatory, manufacturing and other costs to develop ficlatuzumab. Pending marketing approval or the sublicense of ficlatuzumab, and subject to the negotiation of a commercialization agreement, each party would share equally in commercialization profits and losses, subject to our right to be the lead commercialization party. Prior to the first commercial sale of ficlatuzumab, 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. 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. 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. 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 remains in effect until the expiration of all payment obligations between the parties related to development and commercialization of ficlatuzumab, unless earlier terminated.

In September 2016, we and Biodesix announced the termination of the FOCAL trial, a phase 2 proof-of-concept clinical trial of ficlatuzumab in which VeriStrat was used to select clinical trial subjects. We and Biodesix are currently funding investigator sponsored trials of ficlatuzumab, alone and in combination, in HCCN, AML and pancreatic cancer.

In addition, we and Biodesix are funding investigator-sponsored clinical trials, including ficlatuzumab in combination with ERBITUX® (cetuximab) in squamous cell carcinoma of the head and neck, ficlatuzumab in combination with Cytosar (cytarabine) in acute myeloid leukemia and ficlatuzumab in combination with nab-paclitaxel and gemcitabine in pancreatic cancer.

St. Vincent's Hospital

In July 2012, we entered into a license agreement with St. Vincent's, under which we obtained an exclusive, worldwide license to 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.

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. 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 a $1.5 million upfront payment to St. Vincent's. Under our license agreement with St. Vincent's, we are obligated to use diligent efforts to conduct research and clinical development and commercially launch at least one licensed therapeutic product. We are required to make milestone payments, up to an aggregate total of $16.7 million, upon the earlier of achievement of specified development and regulatory milestones or a specified date for the first indication, and upon the achievement of specified development and regulatory milestones for the second and third 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. In February 2017, Novartis paid $1.8 million out of its future payment obligations to us under the license agreement. The funds were used to satisfy a $1.8 million time-based milestone obligation that we owed to St. Vincent's on March 2, 2017.

In addition, we will be required to 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.

The license agreement remains 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.

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 preclinical 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.

Biogen Idec

In March 2009, we entered into an exclusive option and license agreement with Biogen Idec regarding the development and commercialization of our discovery-stage ErbB3-targeted antibodies for the potential treatment and diagnosis of cancer and other diseases in humans outside of North America. In March 2014, we amended our agreement with Biogen Idec, and regained worldwide rights to AV-203. Pursuant to the amendment, we were obligated to in good faith use reasonable efforts to seek a collaboration partner to fund further development and commercialization of ErbB3-targeted antibodies. We satisfied this obligation in March 2016 upon entering into our license agreement with CANbridge. We are obligated to pay Biogen Idec a percentage of milestone payments we receive under the CANbridge agreement and single-digit royalty payments on net sales related to the sale of AV-203, up to cumulative maximum amount of $50.0 million.

Kyowa Hakko Kirin

In December 2006, we entered into a license agreement with KHK under which we obtained an exclusive license, with the right to grant sublicenses subject to certain restrictions, to research, develop, manufacture and commercialize tivozanib, pharmaceutical compositions thereof and associated biomarkers in all potential indications. Our exclusive

license covers all territories in the world except for Asia and the Middle East, where KHK has retained the rights to tivozanib. 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. 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 a VEGF receptor.

We have upfront, milestone and royalty payment obligations to KHK under our license agreement. Upon entering into the license agreement with KHK, we made an upfront payment in the amount of $5.0 million. In March 2010, we made a milestone payment to KHK in the amount of $10.0 million in connection with the dosing of the first patient in our first phase 3 clinical trial of tivozanib (TIVO-1). In December 2012, we made a $12.0 million milestone payment to KHK in connection with the acceptance by the FDA of our 2012 new drug application, or NDA, filing for tivozanib. Each milestone under the KHK agreement is a one-time only payment obligation. Accordingly, we did not owe KHK another milestone payment in connection with the dosing of the first patient in our TIVO-3 trial, and would not owe a milestone payment to KHK if we file an NDA with the FDA following the completion of our TIVO-3 clinical trial. If we obtain approval for tivozanib in the U.S., we would owe KHK a one-time milestone payment of $18.0 million, provided that we do not sublicense U.S. rights for tivozanib prior to obtaining a U.S. regulatory approval. If we were to sublicense the U.S. rights, the associated U.S. regulatory milestone would be replaced by a specified percentage of sublicensing revenue, as set forth below.

If we sublicense any of our rights to tivozanib to a third party, as we have done with EUSA pursuant to our license agreement, the sublicense defines the payment obligations of the sublicensee, which may vary from the milestone and royalty payment obligations under our KHK license relating to rights we retain. We are required to pay KHK a fixed 30% of amounts we receive from our sublicensees, including upfront license fees, milestone payments and royalties, but excluding amounts we receive in respect of research and development reimbursement payments or equity investments, subject to certain limitations.

Certain research and development reimbursement payments by EUSA, including the $2.5 million upfront payment in December 2015, the $4.0 million in September 2017 upon the approval from the EMA of tivozanib (FOTIVDA) and the $2.0 million upon EUSA's election in September 2017 to opt-in to co-develop the TiNivo trial were not subject to sublicense revenue payments to KHK. In addition, if EUSA elects to opt-in to the TIVO-3 trial, the additional research and development reimbursement payment from EUSA of fifty percent (50%) of the total trial costs, up to $20.0 million, would also not be subject to a sublicense revenue payment to KHK, subject to certain limitations. We would, however, owe KHK 30% of other, non-research and development payments we may receive from EUSA pursuant to our license agreement, including EU reimbursement approval milestones in up to five specified EU countries, EU marketing approvals for up to three additional indications beyond RCC, marketing approvals in up to three specified licensed territories outside of the EU, sales-based milestones and royalties. The $2.0 million milestone we earned in February 2018 upon EUSA's reimbursement approval from the NICE in the UK in first line RCC is subject to the 30% KHK sub-license fee, or $0.6 million.

We are also required to pay tiered royalty payments on net sales we make of tivozanib in our North American 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.

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 continue to build a strong intellectual property portfolio, and, whenever possible, we seek to have multiple tiers of patent protection for our product candidates.

Tivozanib

With respect to tivozanib, we have exclusively licensed from KHK its patents that cover the molecule and its therapeutic use, a key step in manufacturing the molecule, and a crystal form of the molecule.

With respect to tivozanib, we have the following in-licensed patents:

- U.S.: 3 granted patents with expirations ranging from 2018 to 2023
- Europe: 3 granted patents with expirations ranging from 2018 to 2023
- Canada: 1 granted patent expiring in 2022
- Australia: 1 granted patent expiring in 2022

The U.S. patent covering the tivozanib molecule and its therapeutic use is expected to expire in 2022. However, in view of the length of time that tivozanib has been under regulatory review at the FDA, a patent term extension of up to five years may be available under The Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Act, which, if a five-year extension were to be granted, would extend the term of this patent to 2027. In addition, Supplementary Protection Certificates (SPCs) have been filed in over 15 European countries, including, Belgium, Denmark, France, Germany, Great Britain, Italy, Netherlands, Spain, and Switzerland, for the corresponding patent in those countries that cover the tivozanib molecule, which, if granted, could extend the term of the patent in each of those countries up to 2027.

KHK has filed an International (PCT) patent application directed to a new invention corresponding to a formulation for tivozanib with ophthalmologic applications. Pursuant to the KHK license agreement, we have exclusive, sub-licensable rights to this new invention and the corresponding know-how outside of Asia and the Middle East.

Ficlatuzumab

With respect to our anti-HGF platform, including ficlatuzumab, we have six 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 platform we have:

- U.S.: 6 granted patents with expirations ranging from 2027 to 2028
- Europe: 1 granted patent expiring in 2027
- Japan: 2 granted patents expiring in 2027
- Canada: 1 granted patent expiring in 2027
- Australia: 1 granted patent expiring in 2027

AV-203

With respect to our anti-ErbB3 platform, including AV-203, we have four U.S. patents and two pending U.S. patent applications covering our anti-ErbB3 antibodies, nucleic acids and expression vectors encoding the antibodies, host cells, methods of making the antibodies, and methods of treatment using our anti-ErbB3 antibodies, which are expected to expire from 2031 to 2032. With respect to our anti-ErbB3 platform we have:

- U.S.: 4 granted patents, and 2 pending patent applications, if granted, with expirations ranging from 2031 to 2032
- Europe: 1 granted patent, and 1 pending patent application, if granted, with expirations ranging from 2031 to 2032
- Japan: 2 granted patents, and 1 pending patent application, if granted, with expirations ranging from 2031 to 2032
- Canada: 2 pending patent applications, if granted, with expirations ranging from 2031 to 2032
- Australia: 1 granted patent, and 1 pending patent application, if granted, with expirations ranging from 2031 to 2032

Anti-GDF15 Antibodies

With respect to our anti-GDF15 platform, we have exclusively licensed certain patent rights from St. Vincent’s, which include a granted U.S. patent directed to a method of increasing appetite and/or body weight upon administering an effective amount of an anti-GDF15 antibody (patent expiration 2029).

With respect to the licensed patent rights, we have:

- U.S.: 1 granted patent, and 1 pending patent application, if granted, with expirations ranging from 2025 to 2029
- Europe: 1 granted patent, and 1 pending patent application, if granted, expiring in 2025
- Japan: 2 granted patents expiring in 2025
- Canada: 1 granted patent expiring in 2025
- Australia: 1 granted patent expiring in 2025

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In addition, we also own two issued U.S. patents and a pending U.S. patent application covering our anti-GDF15 antibodies and methods of treating cachexia and inhibiting loss of muscle mass associated with cachexia using our anti-GDF15 antibodies. These patents and patent application, if granted, would be expected to expire in 2033. We also have three pending U.S. patent applications directed to methods of treating or preventing congestive heart failure or chronic kidney disease using an anti-GDF15 antibody, and methods of treating a subject with cancer anorexia-cachexia syndrome with an anti-cancer agent and an anti-GDF antibody. These patent applications, if granted, would be expected to expire in 2035.

With respect to our GDF15 platform, we have:

- U.S.: 2 granted patents, and 4 pending patent applications, if granted, with expirations ranging from 2033 to 2035
- Europe: 4 pending patent applications with expirations, if granted, ranging from 2033 to 2035
- Japan: 3 pending patent applications with expirations, if granted, ranging from 2033 to 2035
- Canada: 2 pending patent applications with expirations, if granted, ranging from 2033 to 2035
- Australia: 2 pending patent applications with expirations, if granted, ranging from 2033 to 2035

AV-353 Platform

With respect to our AV-353 platform, we own an issued U.S. patent, a non-provisional U.S. patent application, and an International (PCT) patent application covering our anti-Notch3 antibodies, nucleic acids and expression vectors encoding the antibodies, host cells, methods of making the antibodies, and methods of treatment using the antibodies. The issued U.S. patent and non-provisional U.S. patent application, if granted, would be expected to expire in 2033, whereas the International (PCT) patent application, if nationalized in the U.S. and granted, would be expected to expire in 2037.

With respect to our AV-353 platform, we have:

- U.S.: 1 granted patent, and 1 pending patent application, if granted, expiring in 2033
- Europe: 1 pending patent application expiring, if granted, in 2033
- International (PCT): 1 pending patent application, which if nationalized and granted, will expire in 2037

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 our pharmaceutical products receive FDA approval, we expect to apply for patent term extensions on patents covering those products. For example, SPCs have been filed in over 15 European countries for the patent covering the tivozanib molecule, which, if granted, could extend the term of the patent in each of those European countries up to 2027.

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 that contains 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 patent owners indicating that they believe we may need a license from them in order to avoid infringing their patent rights. With regard to ficlatuzumab, we are aware of two separate families of United States patents 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. 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 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.

Trademarks

We seek trademark protection in the U.S. and other jurisdictions where available and when appropriate. We have filed applications and obtained registrations for several trademarks intended for potential use in the marketing of tivozanib, including the trademark FOTIVDA, which we have registered in the United States and over 20 other jurisdictions, and for which we have filed applications in additional countries. We own U.S. and European Union registrations for a logo containing FOTIVDA in combination with a flame design. We own a U.S. registration for HUMAN RESPONSE PLATFORM, a trademark that we use in connection with our research and development. We own U.S. registrations for AVEO, AVEO (in stylized letters), THE HUMAN RESPONSE and AVEO ONCOLOGY THE HUMAN RESPONSE (in stylized letters), trademarks that we use in connection with our business in general. We have also registered AVEO as a trademark in over 20 other jurisdictions.

Manufacturing

We or our partners 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, or CMOs.

One of our contract manufacturers has manufactured what we believe to be sufficient quantities of tivozanib 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. The same manufacturer is currently manufacturing sufficient quantities of drug product (capsules) potentially needed for launch of tivozanib. We also engaged another packager to bottle, label and serialize potential commercial launch supply. We believe that we currently have adequate supplies of tivozanib to support current and projected clinical trials. In addition, we have initiated manufacturing activities for additional tivozanib drug product to support potential commercial launch in the United States in 2019.

To date, third-party manufacturers have met the needs for manufacturing clinical trial supplies for all our pipeline products. There are alternate manufacturers with capability to supply for current clinical or potential future commercial needs. Contracting with additional CMOs may require significant lead-times and result in 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. The failure of an applicant to comply with the applicable regulatory requirements at any time during the product development process, including non-clinical testing, clinical testing, the approval process or post-approval process, may result in delays to the conduct of a study, regulatory review and approval and/or administrative or judicial sanctions. These sanctions may include, but are not limited to, the FDA's refusal to allow an applicant to proceed with clinical trials, refusal to approve pending applications, license suspension or revocation, withdrawal of an approval, warning letters, adverse publicity, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines and civil or criminal investigations and penalties brought by the FDA or Department of Justice, or DOJ, or other government entities, including state agencies.

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 investigational new drug application, or 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 an 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 similar foreign standards, which we refer to as cGMPs, 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.

Following commencement of a clinical trial under an IND, the FDA may also place a clinical hold or partial clinical hold on that trial. A clinical hold is an order issued by the FDA to the sponsor to delay a proposed clinical investigation or to suspend an ongoing investigation. A partial clinical hold is a delay or suspension of only part of the clinical work requested under the IND. For example, a specific protocol or part of a protocol is not allowed to proceed, while other protocols may do so. No more than 30 days after imposition of a clinical hold or partial clinical hold, the FDA will provide the sponsor a written explanation of the basis for the hold. Following issuance of a clinical hold or partial clinical hold, an investigation may only resume after the FDA has notified the sponsor that the investigation may proceed. The FDA will base that determination on information provided by the sponsor correcting the deficiencies previously cited or otherwise satisfying the FDA that the investigation can proceed.

A sponsor may choose, but is not required, to conduct a foreign clinical study under an IND. When a foreign clinical study is conducted under an IND, all FDA IND requirements must be met unless waived. When a foreign clinical study is not conducted under an IND, the sponsor must ensure that the study complies with certain regulatory requirements of the FDA in order to use the study as support for an IND or application for marketing approval. Specifically, on April 28, 2008, the FDA amended its regulations governing the acceptance of foreign clinical studies not conducted under an investigational new drug application as support for an IND or a new drug application. The final rule provides that such studies must be conducted in accordance with good clinical practice, or GCP, including review and approval by an independent ethics committee, or IEC, and informed consent from subjects. The GCP requirements in the final rule encompass both ethical and data integrity standards for clinical studies. The FDA's regulations are intended to help ensure the protection of human subjects enrolled in non-IND foreign clinical studies, as well as the quality and integrity of the resulting data. They further help ensure that non-IND foreign studies are conducted in a manner comparable to that required for IND studies.

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 trial at least annually. The IRB must review and approve, among other things, the trial protocol and informed consent information to be provided to trial 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 DSMB, 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 trial. 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.

Information about clinical trials must be submitted within specific timeframes to the National Institutes of Health, or NIH, for public dissemination on its ClinicalTrials.gov website.

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 trial protocols detailing, among other things, the inclusion and exclusion criteria, the objectives of the trial, 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 studies include the initial introduction of an investigational new drug or biological product into humans. 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.
- 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 trial, 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.
- 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 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. Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, or at all. Furthermore, 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 is a vehicle 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 drug product candidate must be the subject of an approved NDA before it may be commercialized in the United States. Under federal law, the submission of most NDAs is subject to an application user fee, which for federal fiscal year 2018 is $2,421,495 for an application requiring clinical data. The sponsor of an approved NDA is also subject to an annual program fee, which for fiscal year 2018 is $304,162. Certain exceptions and waivers are available for some of these fees, such as an exception from the application fee for products with orphan designation and a waiver for certain small businesses.

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. Under the FDA Reauthorization Act of 2017, the FDA must implement a protocol to expedite review of responses to inspection reports pertaining to certain applications, including applications for products in shortage or those for which approval is dependent on remediation of conditions identified in the inspection report.

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, Priority Review and Regenerative Advanced Therapy 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 referred to as fast track designation, breakthrough therapy designation, priority review designation and regenerative advanced therapy 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 products, 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 application 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 application 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, a product may be designated as a Breakthrough Therapy if it is intended, either alone or in combination with one or more other products, 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 product 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 product 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 product 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.

Finally, with passage of the 21st Century Cures Act, or the Cures Act, in December 2016, Congress authorized the FDA to accelerate review and approval of products designated as regenerative advanced therapies. A product is eligible for this designation if it is a regenerative medicine therapy that is intended to treat, modify, reverse or cure a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the drug has the potential to address unmet medical needs for such disease or condition. The benefits of a regenerative advanced therapy designation include early interactions with FDA to expedite development and review, benefits available to breakthrough therapies, potential eligibility for priority review and accelerated approval based on surrogate or intermediate endpoints.

Accelerated Approval Pathway

The FDA may grant accelerated approval to a product for a serious or life threatening condition that provides meaningful therapeutic advantage to patients over existing treatments based upon a determination that the product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit. The FDA may also grant accelerated approval for such a condition when the product has an effect on an intermediate clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality, or IMM, and that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity or prevalence of the condition and the availability or lack of alternative treatments. Products granted accelerated approval must meet the same statutory standards for safety and effectiveness as those granted traditional approval.

For the purposes of accelerated approval, a surrogate endpoint is a marker, such as a laboratory measurement, radiographic image, physical sign or other measure that is thought to predict clinical benefit, but is not itself a measure of clinical benefit. Surrogate endpoints can often be measured more easily or more rapidly than clinical endpoints. An intermediate clinical endpoint is a measurement of a therapeutic effect that is considered reasonably likely to predict the clinical benefit of a drug, such as an effect on IMM. The FDA has limited experience with accelerated approvals based on intermediate clinical endpoints, but has indicated that such endpoints generally may support accelerated approval where the therapeutic effect measured by the endpoint is not itself a clinical benefit and basis for traditional approval, if there is a basis for concluding that the therapeutic effect is reasonably likely to predict the ultimate clinical benefit of a product.

The accelerated approval pathway is most often used in settings in which the course of a disease is long and an extended period of time is required to measure the intended clinical benefit of a product, even if the effect on the surrogate or intermediate clinical endpoint occurs rapidly. Thus, accelerated approval has been used extensively in the development and approval of products for treatment of a variety of cancers in which the goal of therapy is generally to improve survival or decrease morbidity and the duration of the typical disease course requires lengthy and sometimes large trials to demonstrate a clinical or survival benefit. Thus, the benefit of accelerated approval derives from the potential to receive approval based on surrogate endpoints sooner than possible for trials with clinical or survival endpoints, rather than deriving from any explicit shortening of the FDA approval timeline, as is the case with priority review.

The accelerated approval pathway is usually contingent on a sponsor's agreement to conduct, in a diligent manner, additional post approval confirmatory studies to verify and describe the product's clinical benefit. As a result, a product candidate approved on this basis is subject to rigorous post marketing compliance requirements, including the completion of Phase 4 or post approval clinical trials to confirm the effect on the clinical endpoint. Failure to conduct required post approval studies, or confirm a clinical benefit during post marketing studies, would allow the FDA to initiate expedited proceedings to withdraw approval of the product. All promotional materials for product candidates approved under accelerated regulations are subject to prior review by the FDA.

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. If a company is found to have promoted off-label uses, it may become subject to adverse public relations and administrative and judicial enforcement by the FDA, the Department of Justice, or the Office of the Inspector General of the Department of Health and Human Services, as well as state authorities. This could subject a company to a range of penalties that could have a significant commercial impact, including civil and criminal fines and agreements that

materially restrict the manner in which a company promotes or distributes drug products.

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 Act, 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.

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. This three-year exclusivity period often protects changes to a previously approved drug product, such as a new dosage form, route of administration, combination or indication. Three-year exclusivity would be available for a drug product that contains a previously approved active moiety, provided the statutory requirement for a new clinical investigation is satisfied. Unlike five-year NCE exclusivity, an award of three-year exclusivity does not block the FDA from accepting ANDAs seeking approval for generic versions of the drug as of the date of approval of the original drug product. The FDA typically makes decisions about awards of data exclusivity shortly before a product is approved.

The FDA must establish a priority review track for certain generic drugs, requiring the FDA to review a drug application within eight (8) months for a drug that has three (3) or fewer approved drugs listed in the Orange Book and is no longer protected by any patent or regulatory exclusivities, or is on the FDA's drug shortage list. The new

legislation also authorizes FDA to expedite review of ‘‘competitor generic therapies’’ or drugs with inadequate generic competition, including holding meetings with or providing advice to the drug sponsor prior to submission of the application.

Hatch-Waxman Patent Certification and the 30-Month Stay

Upon approval of an NDA or a supplement thereto, NDA sponsors are required to list with the FDA each patent with claims that cover the applicant’s product or an approved method of using the product. Each of the patents listed by the NDA sponsor is published in the Orange Book. When an ANDA applicant files its application with the FDA, the applicant is required to certify to the FDA concerning any patents listed for the reference product in the Orange Book, except for patents covering methods of use for which the ANDA applicant is not seeking approval. To the extent that the Section 505(b)(2) applicant is relying on studies conducted for an already approved product, the applicant is required to certify to the FDA concerning any patents listed for the approved product in the Orange Book to the same extent that an ANDA applicant would.

Specifically, the applicant must certify with respect to each patent that:

- the required patent information has not been filed;
- the listed patent has expired;
- the listed patent has not expired, but will expire on a particular date and approval is sought after patent expiration; or
- the listed patent is invalid, unenforceable or will not be infringed by the new product.

A certification that the new product will not infringe the already approved product's listed patents or that such patents are invalid or unenforceable is called a Paragraph IV certification. If the applicant does not challenge the listed patents or indicates that it is not seeking approval of a patented method of use, the application will not be approved until all the listed patents claiming the referenced product have expired (other than method of use patents involving indications for which the applicant is not seeking approval).

If the ANDA applicant has provided a Paragraph IV certification to the FDA, the applicant must also send notice of the Paragraph IV certification to the NDA and patent holders once the ANDA has been accepted for filing by the FDA. The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice of the Paragraph IV certification. The filing of a patent infringement lawsuit within 45 days after the receipt of a Paragraph IV certification automatically prevents the FDA from approving the ANDA until the earlier of 30 months after the receipt of the Paragraph IV notice, expiration of the patent, or a decision in the infringement case that is favorable to the ANDA applicant.

To the extent that the Section 505(b)(2) applicant is relying on studies conducted for an already approved product, the applicant is required to certify to the FDA concerning any patents listed for the approved product in the Orange Book to the same extent that an ANDA applicant would. As a result, approval of a Section 505(b)(2) NDA can be stalled until all the listed patents claiming the referenced product have expired, until any non-patent exclusivity, such as exclusivity for obtaining approval of a new chemical entity, listed in the Orange Book for the referenced product has expired, and, in the case of a Paragraph IV certification and subsequent patent infringement suit, until the earlier of 30 months, settlement of the lawsuit or a decision in the infringement case that is favorable to the Section 505(b)(2) applicant.

Patent Term Restoration and Extension

A patent claiming a new drug product may be eligible for a limited patent term extension under the Hatch-Waxman Act, which permits a patent restoration of up to five years for patent term lost during product development and the FDA regulatory review. The restoration period granted on a patent covering a product is typically one-half the time between the effective date of a clinical investigation involving human beings is begun and the submission date of an application, plus the time between the submission date of an application and the ultimate approval date. Patent term restoration cannot be used to extend the remaining term of a patent past a total of 14 years from the product's approval date. Only one patent applicable to an approved product is eligible for the extension, and the application for the extension must be submitted prior to the expiration of the patent in question. A patent that covers multiple products for which approval is sought can only be extended in connection with one of the approvals. The United States Patent and Trademark Office reviews and approves the application for any patent term extension or restoration in consultation with the FDA.

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. As of January 1, 2018, the FDA has approved nine biosimilar products 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 Prescription Drug User Fee Act, or 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 Studies and Exclusivity

Under the Pediatric Research Equity Act of 2003, an NDA or supplement thereto must contain data that are adequate to assess the safety and effectiveness of the product for the claimed indications in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. Sponsors must also submit pediatric study plans prior to the assessment data. Those plans must contain an outline of the proposed pediatric study or studies the applicant plans to conduct, including study objectives and design, any deferral or waiver requests and other information required by regulation. The applicant, the FDA, and the FDA's internal review committee must then review the information submitted, consult with each other and agree upon a final plan. The FDA or the applicant may request an amendment to the plan at any time.

For drugs intended to treat a serious or life-threatening disease or condition, the FDA must, upon the request of an applicant, meet to discuss preparation of the initial pediatric study plan or to discuss deferral or waiver of pediatric assessments. In addition, FDA will meet early in the development process to discuss pediatric study plans with sponsors and FDA must meet with sponsors by no later than the end-of-phase 1 meeting for serious or life-threatening diseases and by no later than ninety (90) days after FDA's receipt of the study plan.

The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements. Additional requirements and procedures relating to deferral requests and requests for extension of deferrals are contained in FDASIA. Unless otherwise required by regulation, the pediatric data requirements do not apply to products with orphan designation.

The FDA Reauthorization Act of 2017 established new requirements to govern certain molecularly targeted cancer indications. Any company that submits an NDA three years after the date of enactment of that statute must submit pediatric assessments with the NDA if the drug is intended for the treatment of an adult cancer and is directed at a molecular target that FDA determines to be substantially relevant to the growth or progression of a pediatric cancer. The investigation must be designed to yield clinically meaningful pediatric study data regarding the dosing, safety and preliminary efficacy to inform pediatric labeling for the product.

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.

FDA Approval and Regulation of Companion Diagnostics

If safe and effective use of a therapeutic depends on an in vitro diagnostic, then the FDA generally will require approval or clearance of that diagnostic, known as a companion diagnostic, at the same time that the FDA approves the therapeutic product. In August 2014, the FDA issued final guidance clarifying the requirements that will apply to approval of therapeutic products and in vitro companion diagnostics. According to the guidance, if FDA determines that a companion diagnostic device is essential to the safe and effective use of a novel therapeutic product or indication, FDA generally will not approve the therapeutic product or new therapeutic product indication if the companion diagnostic device is not approved or cleared for that indication. Approval or clearance of the companion diagnostic device will ensure that the device has been adequately evaluated and has adequate performance characteristics in the intended population. The review of in vitro companion diagnostics in conjunction with the review of our therapeutic treatments for cancer will, therefore, likely involve coordination of review by the FDA's Center for Drug Evaluation and Research and the FDA's Center for Devices and Radiological Health Office of In Vitro Diagnostics Device Evaluation and Safety.

Under the FDCA, in vitro diagnostics, including companion diagnostics, are regulated as medical devices. In the United States, the FDCA and its implementing regulations, and other federal and state statutes and regulations govern, among other things, medical device design and development, preclinical and clinical testing, premarket clearance or approval, registration and listing, manufacturing, labeling, storage, advertising and promotion, sales and distribution, export and import, and post market surveillance. Unless an exemption applies, diagnostic tests require marketing clearance or approval from the FDA prior to commercial distribution.

The FDA previously has required in vitro companion diagnostics intended to select the patients who will respond to the product candidate to obtain pre-market approval, or PMA, simultaneously with approval of the therapeutic product candidate. The PMA process, including the gathering of clinical and preclinical data and the submission to and review by the FDA, can take several years or longer. It involves a rigorous premarket review during which the applicant must prepare and provide the FDA with reasonable assurance of the device's safety and effectiveness and information about the device and its components regarding, among other things, device design, manufacturing and labeling. PMA applications are subject to an application fee, which exceeds $250,000 for most PMAs fees for medical device product review; for federal fiscal year 2018, the standard fee for review of a PMA is $310,764 and the small business fee is $77,691.

After a device is placed on the market, it remains subject to significant regulatory requirements. Medical devices may be marketed only for the uses and indications for which they are cleared or approved. Device manufacturers must also establish registration and device listings with the FDA. A medical device manufacturer's manufacturing processes and those of its suppliers are required to comply with the applicable portions of the QSR, which cover the methods and documentation of the design, testing, production, processes, controls, quality assurance, labeling, packaging and shipping of medical devices. Domestic facility records and manufacturing processes are subject to periodic unscheduled inspections by the FDA. The FDA also may inspect foreign facilities that export products to the U.S.

The 21st Century Cures Act

On December 13, 2016, President Obama signed the Cures Act into law. The Cures Act is designed to modernize and personalize healthcare, spur innovation and research, and streamline the discovery and development of new therapies through increased federal funding of particular programs. It authorizes increased funding for the FDA to spend on innovation projects. The new law also amends the Public Health Service Act to reauthorize and expand funding for the National Institutes of Health. The Act establishes the NIH Innovation Fund to pay for the cost of development and implementation of a strategic plan, early stage investigators and research. It also charges NIH with leading and coordinating expanded pediatric research. Further, the Cures Act directs the Centers for Disease Control and Prevention to expand surveillance of neurological diseases.

With amendments to the FDCA and the Public Health Service Act, or PHSA, Title III of the Cures Act seeks to accelerate the discovery, development, and delivery of new medicines and medical technologies. To that end, and among other provisions, the Cures Act reauthorizes the existing priority review voucher program for certain drugs intended to treat rare pediatric diseases until 2020; creates a new priority review voucher program for drug applications determined to be material national security threat medical countermeasure applications; revises the FDCA to streamline review of combination product applications; requires FDA to evaluate the potential use of “real world evidence” to help support approval of new indications for approved drugs; provides a new “limited population” approval pathway for antibiotic and antifungal drugs intended to treat serious or life-threatening infections; and authorizes FDA to designate a drug as a “regenerative advanced therapy,” thereby making it eligible for certain expedited review and approval designations.

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 GCP, a system for the approval of clinical trials in the European Union has been implemented through national legislation of the member states. Under this system, an applicant must obtain approval from the competent national authority of a European Union member state in which the clinical trial is to be conducted, or in multiple member states if the clinical trial is to be conducted in a number of member states. Furthermore, the applicant may only start a clinical trial at a specific study site after the competent ethics committee has issued a favorable opinion. The clinical trial application ("CTA") must be accompanied by an investigational medicinal product dossier with supporting information prescribed by Directive 2001/20/EC and Directive 2005/28/EC and corresponding national laws of the member states and further detailed in applicable guidance documents.

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 become 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 2019. 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.

PRIME Designation in the EU

In March 2016, the European Medicines Agency, or EMA, launched an initiative to facilitate development of product candidates in indications, often rare, for which few or no therapies currently exist. The PRIority MEdicines, or PRIME, scheme is intended to encourage drug development in areas of unmet medical need and provides accelerated assessment of products representing substantial innovation reviewed under the centralized procedure. Products from small- and medium-sized enterprises, or SMEs, may qualify for earlier entry into the PRIME scheme than larger companies. Many benefits accrue to sponsors of product candidates with PRIME designation, including but not limited to, early and proactive regulatory dialogue with the EMA, frequent discussions on clinical trial designs and other development program elements, and accelerated marketing authorization application assessment once a dossier has been submitted. Importantly, a dedicated Agency contact and rapporteur from the Committee for Human Medicinal Products (CHMP) or Committee for Advanced Therapies (CAT) are appointed early in PRIME scheme facilitating increased understanding of the product at EMA's Committee level. A kick-off meeting initiates these relationships and includes a team of multidisciplinary experts at the EMA to provide guidance on the overall

development and regulatory strategies.

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 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.

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.

Regulatory Data Protection in the European Union

In the European Union, new chemical entities approved on the basis of a complete independent data package qualify for eight years of data exclusivity upon marketing authorization and an additional two years of market exclusivity pursuant to Regulation (EC) No 726/2004, as amended, and Directive 2001/83/EC, as amended. Data exclusivity prevents regulatory authorities in the European Union from referencing the innovator's data to assess a generic (abbreviated) application for a period of eight years. During the additional two year period of market exclusivity, a generic marketing authorization application can be submitted, and the innovator's data may be referenced, but no generic medicinal product can be marketed until the expiration of the market exclusivity. The overall ten year period will be extended to a maximum of eleven years if, during the first eight years of those ten years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to authorization, is held to bring a significant clinical benefit in comparison with existing therapies. Even if a compound is considered to be a new chemical entity so that the innovator gains the prescribed period of data exclusivity, another company may market another version of the product if such company obtained marketing authorization based on an MAA with a complete independent data package of pharmaceutical tests, preclinical tests and clinical trials.

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 trial 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.

Orphan drug 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. This is the case despite an earlier court opinion holding that the Orphan Drug Act unambiguously required the FDA to recognize orphan exclusivity regardless of a showing of clinical superiority.

Brexit and the Regulatory Framework in the United Kingdom

On June 23, 2016, the electorate in the United Kingdom voted in favor of leaving the European Union (commonly referred to as “Brexit”). Thereafter, on March 29, 2017, the country formally notified the European Union of its intention to withdraw pursuant to

Article 50 of the Lisbon Treaty. The withdrawal of the United Kingdom from the European Union will take effect either on the effective date of the withdrawal agreement or, in the absence of agreement, two years after the United Kingdom provides a notice of withdrawal pursuant to the EU Treaty. Since the regulatory framework for pharmaceutical products in the United Kingdom. covering quality, safety and efficacy of pharmaceutical products, clinical trials, marketing authorization, commercial sales and distribution of pharmaceutical products is derived from European Union directives and regulations, Brexit could materially impact the future regulatory regime which applies to products and the approval of product candidates in the United Kingdom. It remains to be seen how, if at all, Brexit will impact regulatory requirements for product candidates and products in the United Kingdom.

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.

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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:

- 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 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 and transfers of value to other health care providers and health care entities, 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 U.S. 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 ACA, which, among other things, includes changes to the coverage and payment for products under government health care programs. Among the provisions of the ACA of importance to our potential product 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 products 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 products to eligible beneficiaries during their coverage gap period as a condition for the manufacturers' outpatient products 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 ("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. However, the IPAB implementation has been not been clearly defined. The 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 product 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 PPACA 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.

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 we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used. Further, there have been several recent U.S. congressional inquiries and proposed state and federal legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products.

Further, since enactment of the ACA, there have been numerous legal challenges and Congressional actions to repeal and replace provisions of the law. For example, with enactment of the Tax Cuts and Jobs Act of 2017, which was signed by the President on December 22, 2017, Congress repealed the "individual mandate." The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, will become effective in 2019. According to the Congressional Budget Office, the repeal of the individual mandate will cause 13 million fewer Americans to be insured in 2027 and premiums in insurance markets may rise. Additionally, on January 22, 2018, President Trump signed a continuing resolution on appropriations for fiscal year 2018 that delayed the implementation of certain ACA-mandated fees, including the so-called "Cadillac" tax on certain high cost employer-sponsored insurance plans, the annual fee imposed on certain health insurance providers based on market share, and the medical device excise tax on non-exempt medical devices. The Congress will likely consider other legislation to replace elements of the ACA, during the next Congressional session.

The Trump Administration has also taken executive actions to undermine or delay implementation of the ACA. In January 2017, President Trump signed an Executive Order directing federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. In October 2017, the President signed a second Executive Order allowing for the use of association health plans and short-term health insurance, which may provide fewer health benefits than the plans sold through the ACA exchanges. At the same time, the Trump Administration announced that it will discontinue the payment of cost-sharing reduction (CSR) payments to insurance companies until Congress approves the appropriation of funds for such CSR payments. The loss of the CSR payments is expected to increase premiums on certain policies issued by qualified health plans under the ACA. A bipartisan bill to appropriate funds for CSR payments was introduced in the Senate, but the future of that bill is uncertain.

There have been, and likely will continue to be, additional legislative and regulatory proposals at the foreign, federal, and state levels directed at broadening the availability of healthcare and containing or lowering the cost of healthcare. Such reforms could have an adverse effect on anticipated revenues from product candidates that we may successfully develop and for which we may obtain marketing approval and may affect our overall financial condition and ability to develop product candidates.

Further, there have been several recent U.S. congressional inquiries and proposed federal and proposed and enacted state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products. At the federal level, Congress and the Trump administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. At the state level, individual states are increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, regional health care authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other health care programs. These measures could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing.

Employees

As of December 31, 2017, we had 19 employees. 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 $25.2 million, $23.7 million and $12.9 million for the years ended December 31, 2017, 2016 and 2015, respectively. 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 internal costs for salaries, bonuses, benefits, stock-based compensation, facilities, and research-related overhead, and external costs for clinical trials, drug manufacturing and distribution, license fees, consultants and other contracted services

Segment and Geographic Information

We view our operations and manage our business in one operating segment. As of December 31, 2017, we operate only in the United States.

Executive Officers of the Registrant

The following table lists the positions, names and ages of our executive officers as of March 13, 2018:

Executive Officers

Michael P. Bailey	52	Chief Executive Officer, President and Director
Matthew Dallas	42	Chief Financial Officer
Michael N. Needle	58	Chief Medical Officer
Nikhil Mehta	59	SVP Regulatory and Quality Assurance
Karuna Rubin	41	SVP and General Counsel

Michael P. Bailey was appointed President and Chief Executive Officer and a member of our Board of Directors in January 2015. Mr. Bailey joined our company in September 2010 as Chief Commercial Officer and was named 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 Corp., 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 PORTRAZZA® (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 SmithKline 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.

Matthew Dallas was appointed Chief Financial Officer in June 2017. From February 2015 to March 2017, Mr. Dallas served as Chief Financial Officer and Treasurer of CoLucid Pharmaceuticals, Inc., a position he held through that biopharmaceutical company's initial public offering and subsequent acquisition, for approximately $960 million, by Eli Lilly and Company. From 2011 to February 2015, he served as Vice President of Finance and Treasurer of

AVEO. Mr. Dallas previously worked at Genzyme Corporation from 2000 to 2011, NEN Life Sciences from 1999 to 2000, and Kimberly-Clark Corporation from 1997 to 1999 where he held various positions of increasing responsibility in finance and accounting. Mr. Dallas holds a B.S. in Finance from the University of Tennessee, Knoxville.

Michael N. Needle, M.D. was appointed Chief Medical Officer in January 2015. Dr. Needle has played central roles in the development of oncology and hematology drugs including Erbitux® (cetuximab), Revlimid® (lenalidomide) and Pomalyst® (pomolidimide). Dr. Needle served as Chief Medical Officer for Array BioPharma Inc., a biopharmaceutical company, from April 2013 to September 2014. From April 2012 to April 2013, Dr. Needle was Chief Medical Officer of the Multiple Myeloma Research Foundation and Consortium (MMRF), a research organization. From 2010 to 2012, Dr. Needle was Assistant Professor of Pediatrics at the College of Physicians and Surgeons of Columbia University. From 2004 to 2010, 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. Dr. Needle also served as the Vice President of Clinical Affairs at ImClone from 2000 to 2004. Dr. Needle performed 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.

Nikhil Mehta, Ph.D. was appointed Senior Vice President Regulatory and Quality Assurance in November 2017. From June 2016 to September 2017, Dr. Mehta served as Executive Vice President and Chief Regulatory Strategist at Tang Capital Management, where he worked on the establishment of two biopharmaceutical companies, Odonate Therapeutics and Sentier Therapeutics. From April 2015 to June 2016, Dr. Mehta served as Global Head of Regulatory Affairs at Baxalta, a period during which the company gained approval for ADYNOVATE®, VONVENDI®, and OBIZUR. From 2010 to 2015, he was Vice President, Global Regulatory Affairs, Oncology, Hematology, Immunology and Diagnostics, at Merck & Company, where he played a key role in the development and first approval of Merck's checkpoint inhibitor KEYTRUDA. Prior to Merck, Dr. Mehta held positions of increasing responsibility within regulatory affairs at Shire HGT, ImClone Systems, Bristol-Myers Squibb and Hoffmann-La Roche, where he played key roles in the approvals of ELAPRASE®, VPRIV®, FIRAZYR® and ERBITUX. Dr. Mehta holds a Ph.D. in Chemical and Biochemical Engineering from Rutgers University.

Karuna Rubin was appointed Senior Vice President and General Counsel in February 2018. Ms. Rubin served as our Vice President, Legal Affairs and Corporate Secretary from July 2016 to January 2018, and as our Senior Corporate Counsel from July 2015 to July 2016. Prior to joining our company, Ms. Rubin was an associate at Arnold & Porter LLP from 2001 to 2006, and then again from 2008 to August 2013. From 2006 to 2008, Ms. Rubin served as Assistant General Counsel of Cenveo, Inc. Ms. Rubin received her J.D. from Columbia Law School and A.B. in International Relations from Brown University.

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 have identified conditions and events that raise substantial doubt about our ability to continue as a going concern.

We may be forced to delay or reduce the scope of our development programs and/or limit or cease our operations if we are unable to obtain additional funding to support our current operating plan. We have identified conditions and events that raise substantial doubt about our ability to continue as a going concern. As of December 31, 2017, we had approximately $33.5 million in existing cash, cash equivalents and marketable securities. In the first quarter of 2018 to-date, we have raised an additional approximate $1.9 million in net funding, including approximately $ 0.5 million received in January 2018 related to the exercise of warrants to purchase 0.5 million shares of common stock issued in connection with our 2016 private placement, which we refer to as the PIPE Warrants and $1.4 million in net partnership-related funding in connection with the $2.0 million milestone payment by EUSA for the February 2018 reimbursement approval by the NICE for RCC in the UK that was received in March 2018, net of the corresponding 30% sub-license fee due to KHK. Based on these available cash resources, we believe we do not have sufficient cash on hand to support current operations for at least the next twelve months from the date of filing this Annual Report on Form 10-K. This condition raises substantial doubt about our ability to continue as a going concern within one year after the date these financial statements are issued. Management’s plans in this regard are described in Note 1 of the consolidated financial statements included elsewhere in this Annual Report on Form 10-K However, we cannot guarantee that we will be able to obtain sufficient additional funding when needed or that such funding, if available, will be obtainable on terms satisfactory to us. In the event that these plans cannot be effectively realized, there can be no assurance that we will be able to continue as a going concern.

We have incurred significant losses since inception and 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 $65.0 million, $26.9 million and $15.0 million for the years ended December 31, 2017, 2016 and 2015, respectively, and, as of December 31, 2017, had an accumulated deficit of $587.0 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. As noted above, we and our auditors have identified conditions and events that raise substantial doubt about our ability to continue as a going concern.

If we do not successfully develop and obtain and maintain 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.

We will require substantial additional funding, 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 additional 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 development and commercialization activities for tivozanib beyond our cash runway. For example, we estimate that the aggregate remaining costs for the TIVO-3 trial, including drug supply and distribution, could be in the range of $9 million to $12 million through 2019. We estimate that the overall cost for the TIVO-3 trial, including drug supply and distribution, could be in the range of $44 million to $47 million. Our aggregate remaining costs for the TiNivo trial in collaboration with BMS and EUSA, including tivozanib drug supply and distribution, could be in the range of $1.5 million to $2.0 million through 2019. We estimate that the overall cost for the TiNivo trial, including drug supply and distribution, could be in the range of $4.0 million to $4.5 million, of which EUSA is responsible for approximately 50% of these costs up to a maximum of $2.0 million. BMS is providing nivolumab for the study.

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 portion of sublicense revenue in certain instances.

We believe that our approximately $33.5 million in cash, cash equivalents and marketable securities at December 31, 2017, along with the additional approximately $1.9 million in net funding raised in the first quarter of 2018 to-date, as described above, would allow us to fund our planned operations into the first quarter of 2019. This estimate assumes no receipt of additional milestone payments from our partners or additional related payments of potential licensing milestones to third parties, no funding from new partnership agreements, no equity financings, no debt financings, no sales of equity under our at-the-market-sales agreement with Leerink, which we refer to as the Leerink Sales Agreement, and no additional sales of equity through the exercise of our PIPE Warrants. Accordingly, the timing and nature of activities contemplated for the remainder of 2018 and thereafter will be conducted subject to the availability of sufficient financial resources.

Furthermore, there are numerous risks and uncertainties associated with research, development and commercialization of pharmaceutical products. Accordingly, our future capital requirements may vary from our current expectations and 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 of 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, which we refer to as the Hercules Loan Agreement, or under any other agreements with third parties;
- the outcome of legal actions against us, including the current lawsuits described in Part II, Item 1 of this report under the heading "Legal Proceedings";
- 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;
- the timing, receipt and amount of sales of, or royalties on, our future products, if any; and
- our ability to continue as a going concern.

We will require additional funding to extend our planned operations. 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. 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.

If we are unable to raise substantial additional capital in the near term, whether on terms that are acceptable to us, or at all, Hercules may accelerate payments if we were to default under the Hercules Loan Agreement and we may be required to:

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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.

We are a development stage company, which may make it difficult for you to evaluate the success of our business to date and to assess our future viability.

Other than the European marketing approval for tivozanib (FOTIVDA) received by our partner EUSA in August 2017, all of our product candidates are in the development stage. 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 a development 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.

Risks Related to our Litigation

We and certain of our former officers were defendants in a lawsuit that has been settled, subject to the court's final approval.

We and certain of our former officers were named as defendants in a consolidated class action lawsuit initiated in 2013 that generally alleged that we and those individuals violated federal securities laws by making allegedly false and/or misleading statements in 2012 and 2013, concerning the development of our drug tivozanib and its prospects for FDA approval at that time. The lawsuit sought 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 appealed the District Court's decision to the United States Court of Appeals for the First Circuit and also filed a motion to vacate and reconsider the District Court's judgment, which we opposed. On January 3, 2017, the District Court granted the plaintiffs' motion to vacate the dismissal and judgment and the plaintiffs filed a motion to dismiss their appeal on February 8, 2017. On February 2, 2017, the plaintiffs filed a third amended complaint alleging claims similar to those alleged in the prior complaints, namely that we and certain of our former officers violated Sections 10(b) and/or 20(a) of the Exchange Act 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 clinical trial in an effort to lead investors to believe that the drug would receive approval from the FDA. On March 2, 2017, we filed an answer to the third amended complaint, and the parties initiated discovery. On June 29, 2017, the plaintiffs filed a motion for class certification and on July 27, 2017, we filed our response. On July 18, 2017, the District Court entered an order referring the case to alternative dispute resolution. The parties mediated on September 12 and 13, 2017, and again on October 23, 2017. On December 26, 2017, the parties entered into a binding memorandum of understanding, or MOU, regarding the settlement of the lawsuit. On January 29, 2018, the parties entered into a Stipulation of Settlement, or the Stipulation, which was filed with District Court on February 2, 2018. Under the terms of the MOU and Stipulation, we agreed with counsel for the lead plaintiffs to cause certain of our and the individual defendants' insurance carriers to provide the class with a cash payment of $15,000,000, which includes the cash amount of any attorneys' fees or litigation expenses that the District Court may award lead plaintiffs' counsel and costs lead plaintiffs incur in administering and providing notice of the settlement. Additionally, we agreed to issue to the class warrants for the purchase of 2,000,000 shares of our common stock exercisable from the date of issue until the expiration of a one-year period after the date of issue at an exercise price equal to the closing price on December 22, 2017, the trading day prior to the execution of the MOU, which was $3.00 per share. On February 8, 2018, the District Court issued an order preliminarily approving the terms of the Stipulation. The

Stipulation is subject to final approval by the District Court. The District Court set a final approval hearing for May 30, 2018. There can be no guarantee that the District Court will grant final approval.

We have concluded a settlement with the SEC, but the SEC is still pursuing an action against our former officer.

We paid $4.0 million to settle a lawsuit filed by the SEC in federal court alleging that we violated federal securities laws by omitting to disclose the recommendation of the staff of the FDA, on May 11, 2012, that we conduct an additional clinical trial with respect to tivozanib. See Part I, Item 3 of this Annual Report on Form 10-K under the heading “Legal Proceedings” for a further discussion of these claims. The SEC also named three of our former officers as defendants in the same lawsuit. The SEC and two of our former officers have settled. The lawsuit against the remaining officer is still pending. We are not a party to the continuing litigation between the SEC and the former officer. However, that individual has and may continue to 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 substantially dependent on the success of tivozanib. If we are unable to complete the clinical development of, obtain and maintain 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.

Other than the European marketing approval for tivozanib received by our partner EUSA in August 2017, 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 for marketing approval in North America. Our prospects are substantially dependent on our ability to develop, obtain marketing approval for and successfully commercialize tivozanib in North America in one or more disease indications.

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

- our ability to secure the substantial additional capital required to complete our clinical trials of tivozanib, including the TIVO-3 trial and the TiNivo trial;
- successful enrollment and completion of clinical trials;
    - a safety, tolerability and efficacy profile that is satisfactory to the FDA, EMA or any other comparable foreign regulatory authority for marketing approval;
- timely receipt of marketing approvals from applicable regulatory authorities;
- the performance of our collaborators and third-party contractors;
- the extent of any required post-marketing approval commitments to applicable regulatory authorities;
- maintenance of existing or establishment of new supply arrangements with third-party raw materials suppliers and manufacturers including with respect to the supply of active pharmaceutical ingredient for tivozanib and 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 KHK;
- protection of our rights in our intellectual property portfolio, including our ability to maintain our license agreement with KHK;
- 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 trial results, the regulatory approval process, potential threats to our intellectual property rights and the development, 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 we fail to develop and commercialize other product candidates, we may be unable to grow our business.

Although the development and commercialization of tivozanib is our primary focus, as part of our growth strategy, we are developing a pipeline of product candidates. These other product candidates will require additional, time-consuming and costly development efforts, by us or by our collaborators, prior to commercial sale, including preclinical studies, clinical trials and approval by the FDA and/or applicable foreign regulatory authorities. All product candidates are prone to the risks of failure that are inherent in pharmaceutical product development, including the possibility that the product candidate will not be shown to be sufficiently safe and effective for approval by regulatory authorities. In addition, we cannot assure you that any such products that are approved will be manufactured or produced economically. Successfully commercialized or widely accepted in the marketplace or be

more effective than other commercially available alternatives.

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

We, and any collaborators, including our partners and sublicensees, 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 EMA, impose similar requirements. We and our collaborators must complete extensive preclinical development and clinical trials that demonstrate the safety and efficacy of our product candidates in humans before we can obtain these approvals.

Preclinical and clinical testing is expensive, is difficult to design and implement, and can take many years to complete. It 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 preclinical and clinical development of our product candidates is susceptible to the risk of failure inherent at any stage of product development, as well as failure to demonstrate efficacy at all in a clinical trial or across a broad population of patients, the occurrence of adverse events that are medically severe or commercially unacceptable, failure to comply with protocols or regulatory requirements and determination by the applicable regulatory authority that a product candidate may not continue development or is not approvable. Even if a product candidate has a beneficial effect, that effect may not be detected during preclinical or clinical evaluation due to a variety of factors, including the size, duration, design, measurements, conduct or analysis of our preclinical and clinical trials. Conversely, as a result of the same factors, our preclinical or 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 preclinical or clinical trials we may fail to detect toxicity or intolerability of 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 timely or successfully complete preclinical and clinical development could result in additional unplanned costs 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 those planned, or if the results of these trials or tests are unfavorable, uncertain, only modestly favorable or indicate safety concerns, we or our collaborators, may:

- 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 complete clinical trials of our product candidates and to demonstrate the efficacy and safety necessary to obtain regulatory approval would significantly harm our business.

Adverse events or undesirable side effects caused by, or other unexpected properties of, tivozanib or our other product candidates 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 our other product candidates could cause us, any collaborators, an institutional review board or regulatory authorities to interrupt, delay or halt preclinical or 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 side effects that prevented further development of the compound.

If we or our collaborators experience any of a number of possible complications in connection with preclinical or clinical trials of our product candidates, potential clinical development, marketing approval or commercialization of our product candidates could be delayed or prevented.

We or our collaborators may experience numerous complications in connection with preclinical or clinical trials that could delay or prevent clinical development, marketing approval or commercialization of our product candidates 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;
- delay or failure to reach agreement on clinical trial contracts or clinical trial protocols with prospective trial sites;
- unfavorable or inconclusive clinical trial results;
- our decision or a regulatory order to conduct additional clinical trials or abandon product development programs;
- the number of patients required for our clinical trials may be larger than anticipated, patient enrollment may be slower than anticipated or participants may drop out of these clinical trials at a higher rate than anticipated;
- the costs of our clinical trials may be greater than we anticipate;
- our third-party contractors, including those manufacturing our product candidates, or conducting clinical trials on our behalf, may fail to successfully comply with regulatory requirements or meet their contractual obligations 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 may decide, or regulators or institutional review boards may require that we 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 our collaborators' clinical trial designs or 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 and our collaborators will increase if we experience delays in testing or pursuing marketing approvals, and we 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 may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do could impair our ability 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 our collaborators experience delays or difficulties in the enrollment of patients in clinical trials, receipt of necessary regulatory approvals could be delayed or prevented.

We or our collaborators may not be able to initiate or continue clinical trials for our product candidates if we 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 and the drug being provided as a control in relation to other available therapies, including any new drugs that may be approved for the indications we are investigating.

Our inability to enroll a sufficient number of patients for our clinical trials could result in significant delays or may require us to abandon one or more clinical trials altogether. Enrollment delays in our 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 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.

We are conducting, and intend in the future to conduct, clinical trials for certain of our product candidates at sites outside the United States. The FDA may not accept data from trials conducted in such locations and the conduct of trials outside the United States could subject us to additional delays and expense.

We are conducting, and intend in the future to conduct, one or more of our clinical trials with one or more trial sites that are located outside the United States. Although the FDA may accept data from clinical trials conducted outside the United States, acceptance of these data is subject to certain conditions imposed by the FDA. For example, the clinical trial must be well designed and conducted and performed by qualified investigators in accordance with good clinical practice. The FDA must be able to validate the data from the trial through an onsite inspection if necessary. The trial population must also have a similar profile to the U.S. population, and the data must be applicable to the U.S. population and U.S. medical practice in ways that the FDA deems clinically meaningful, except to the extent the disease being studied does not typically occur in the United States. In addition, while these clinical trials are subject to the applicable local laws, FDA acceptance of the data will be dependent upon its determination that the trials also complied with all applicable U.S. laws and regulations. There can be no assurance that the FDA will accept data from trials conducted outside of the United States. If the FDA does not accept the data from any trial that we conduct outside the United States, it would likely result in the need for additional trials, which would be costly and time-consuming and delay or permanently halt our development of our product candidates.

In addition, the conduct of clinical trials outside the United States could have a significant adverse impact on us. Risks inherent in conducting international clinical trials include:

- clinical practice patterns and standards of care that vary widely among countries;
- non-U.S. regulatory authority requirements that could restrict or limit our ability to conduct our clinical trials;
- administrative burdens of conducting clinical trials under multiple non-U.S. regulatory authority schema;
- foreign exchange fluctuations; and
- diminished protection of intellectual property in some countries.

Results of early clinical trials may not be predictive of results of later clinical trials.

The outcome of early clinical trials, such as our phase 1b/2 TiNivo trial, may not be predictive of the success of later clinical trials. In addition, interim results and analyses of clinical trials, such as the analysis performed in our TIVO-3 trial, do not necessarily predict success once the trial is complete. 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.

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. For example, in June 2013, the FDA issued a complete response letter informing us that it would not approve tivozanib for the first-line treatment of aRCC based solely on the data from the TIVO-1 trial, and recommended that we perform an additional clinical trial adequately sized to assure the FDA that tivozanib does not adversely affect OS. Our current TIVO-3 clinical trial was designed to address the FDA's concern about the negative OS trend expressed in the complete response letter from June 2013. However, the TIVO-3 trial could fail to achieve its endpoints, or could otherwise be rejected by the FDA as a basis for marketing approval for another reason.

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 may not obtain marketing approvals for our product candidates.

We may not obtain marketing approval for our product candidates. It is possible that the FDA or comparable foreign regulatory agencies may refuse to accept for substantive review any future application that we or a collaborator may submit to market and sell our product candidates, or that any such agency may conclude after review of our or our collaborator's data that such application is insufficient to obtain marketing approval of our product candidate. In June 2013, for example, the FDA issued a complete response letter informing us that it would not approve tivozanib for the first-line treatment of aRCC based solely on the data from the TIVO-1 trial, and recommended that we perform an additional clinical trial adequately sized to assure the FDA that tivozanib does not adversely affect OS. Our current TIVO-3 clinical trial was designed to address the FDA's concern about the negative OS trend expressed in the complete response letter from June 2013. However, the TIVO-3 trial could fail to achieve its endpoints, or could otherwise be rejected by the FDA as a basis for marketing approval for another reason.

If the FDA or other comparable foreign regulatory agency does not accept or approve any application to market and sell any of our product candidates, such regulators may require that we conduct additional clinical trials, preclinical studies or manufacturing validation studies and submit that data before it will reconsider our application. Depending on the extent of these or any other required trials or studies, approval of any application that we submit may be delayed by several years, or may require us or our collaborator to expend more resources than we or they have available. It is also possible that additional trials or studies, if performed and completed, may not be considered sufficient by the FDA or other Foreign regulatory agency to approve our applications for marketing and commercialization.

Any delay in obtaining, or an inability to obtain, marketing approvals would prevent us or our collaborators from commercializing our product candidates and generating revenues. If any of these outcomes occur, we would not be eligible for certain milestone and royalty revenue under our partnership agreements, our collaborators could terminate our partnership agreements, and we may be forced to abandon our development efforts for our product candidates, any of which could significantly harm our business.

Even if a product candidate receives 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 our product candidates will be conducted in carefully defined subsets of patients who have agreed to participate in these. Consequently, it is possible that our clinical trials 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 of our 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, or any of our collaborators, 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 of our collaborators, may be required to create a Medication Guide outlining the risks of the previously unidentified side effects for distribution to patients;
- we could be sued and held liable for harm caused to patients;
- physicians and patients may stop using our product; 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 product candidates receive marketing approval, they 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. There are already a number of competitive therapies on the market to tivozanib, as well as our other product candidates, in indications we intend to target.

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 advantages of the product compared to competitive therapies;
- the number of competitors approved for similar uses;
- the relative promotional effort of us as compared with our competitors;
- 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 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;
- the timing of market introduction of our approved products as well as competitive products;
- adverse publicity about the product or favorable publicity about competitive products;
- potential product liability claims;
- 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.

We may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

Because we have limited financial and managerial resources, we intend to focus on developing product candidates for specific indications that we identify as most likely to succeed, in terms of both their potential for marketing approval and commercialization. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that may prove to have greater commercial potential.

Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable product candidates. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to the product candidate.

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 sales, marketing or distribution infrastructure and have limited experience as an organization in the sales, marketing, and distribution of pharmaceutical products. Our licensee EUSA has been responsible for the sales, marketing, and distribution efforts associated with the commercial launch of tivozanib in certain European countries. To achieve commercial success for any approved product, we must either develop a sales and marketing organization or outsource these functions to third parties. The development of sales, marketing and distribution capabilities will require substantial resources, will be time consuming and, if not initiated sufficiently in advance of marketing approval, could delay any product launch. Conversely, 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 incur substantial costs 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 we enter into arrangements with third parties to perform sales, marketing and distribution services such as our collaboration with EUSA, our product revenues or the profitability of these products may be 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.

We may 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. 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.

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, we or our collaborators 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. 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. We expect to rely in part on third parties for the design, development and manufacture of any companion diagnostic. 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 from existing approved products. Our competitors may also discover, develop or commercialize new competing products before, or more successfully, than we do.

The biotechnology and pharmaceutical industries are highly competitive. 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.

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, Actelion Pharmaceuticals Ltd., Amgen, Inc., Arqule, Inc., AstraZeneca, Bayer HealthCare AG, Bristol-Myers Squibb, Eisai Co., Ltd., Eli Lilly and Company, Exelixis, Inc., Gilead Sciences, Inc., GlaxoSmithKline plc, GTx, Inc., Helsinn and XBiotech, Incyte Corporation, Janssen Pharmaceuticals, Inc. (a division of Johnson and Johnson), Jazz Pharmaceuticals plc, Merck, Merrimack Pharmaceuticals, Inc., Novartis, OncoMed Pharmaceuticals, Inc., Pfizer Inc. and Roche Laboratories, Inc. are pursuing development in diseases we focus on or are currently developing or marketing pharmaceuticals that target VEGFR, HGF, ErbB3, Notch 3 or other pathways on which we may focus. It is probable that the number of companies seeking to develop competing products and therapies 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 product discovery and development, obtaining FDA and other regulatory approvals, and commercialization. Many 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 renal cell carcinoma. 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, develop and commercialize products that are superior to other products in the market in terms of, among other things, safety, efficacy, convenience, or price;
- 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 our products.

Established competitors may invest heavily to 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, our business will not grow and our financial condition and operations will suffer.

There are currently 11 FDA-approved drugs in oncology which, like tivozanib, target the VEGFR pathway as a part or all of their inhibitory mechanism. Eight of the FDA-approved VEGFR pathway inhibitors are oral small molecule receptor TKIs. Many of the approved VEGFR pathway inhibitors 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 VEGFR pathway. The emergence of PD-1/PD-L1 inhibitor and other immune system-targeted therapies, both alone and in combination, present additional competition for tivozanib in aRCC. We are aware of several phase 3 registration studies evaluating PD-1/PD-L1 inhibitors in combination with VEGFR TKIs in RCC, as well as combinations of PD-1 agents with other immune therapies for RCC. Positive phase 3 study results have recently been announced from CheckMate-214, a Bristol-Myers Squibb study combining nivolumab and ipilimumab vs sunitinib in first line RCC, and also for the phase 3 IMmotion151 combination study of bevacizumab and atezolizumab vs sunitinib in first line RCC. If approved, these products could

present additional competition for tivozanib.

We believe the products that are considered competitive with ficlatuzumab include those agents targeting the HGF/c-Met pathway. We believe the most direct competitors to our AV-203 program are monoclonal antibodies that specifically target the ErbB3 receptor. There are also other agents that target ErbB3 as a part or all of their inhibitory mechanism. Only a limited number of agents have been approved for the treatment or prevention of cachexia caused by any disease. A number of agents with different mechanisms of action, however, have completed or are currently being studied in phase 2 trials in cachexia or muscle wasting. Currently, there are no ongoing clinical trials of Notch 3-specific inhibitors or any approved Notch 3-specific inhibitors in PAH patients; however, there are multiple treatments approved for PAH through various mechanisms.

Even if we or our collaborators are able to commercialize any product candidate, 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. For example, our European licensee for tivozanib, EUSA Pharma, is currently in the process of seeking reimbursement approval for tivozanib in the countries in which tivozanib has been approved. 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 our collaborators to establish or maintain pricing sufficient to realize a sufficient return on our 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 time consuming and costly and 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 obtained or applied consistently.

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 our 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 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 to sell our product candidates profitably. These payors may not view our products, even if approved, as cost-effective, and coverage and reimbursement may not be available to our customers or may not be sufficient to allow our products to be marketed on a competitive basis. Cost-control initiatives could cause us or our collaborators to decrease the price we 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, for 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 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 clinical 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;
- withdrawal of clinical trial participants;
- delay or termination of our clinical trial;
- significant 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;
- injury to our reputation and negative media attention; and
- a decline in our stock price.

Our inability to maintain 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. We will need to increase our insurance coverage if we commercialize any product that receives marketing approval. 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. The cost of any such product liability litigation or other proceeding, even if resolved in our favor, could be substantial. In addition, insurance coverage is becoming increasingly expensive. If we are unable to maintain sufficient insurance coverage at an acceptable cost or to otherwise protect against potential product liability claims, it could prevent or inhibit the development and commercial production and sale of our product candidates, which could harm our business, financial condition, results of operations and prospects.

Risks Related to Our Dependence on Third Parties

We rely on third parties, such as contract 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 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 and 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 product candidates or to 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. Other risks of our reliance on third-party manufacturers include the possible mislabeling of clinical supplies, potentially resulting in the wrong dose amounts being supplied or active drug or placebo not being properly identified; the possibility of clinical supplies not being delivered to clinical sites on time, leading to clinical trial interruptions, or of drug supplies not being distributed to commercial vendors in a timely manner, resulting in lost sales; and the possible misappropriation of our proprietary information, including our trade secrets and know-how. In addition, the FDA and other regulatory authorities require that our product candidates be manufactured according to cGMPs. 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 and potential commercial manufacturing. There are a small number of suppliers raw and starting materials that we use to manufacture our product candidates. Such suppliers may not sell these materials to our manufacturers at the times we need them or on commercially reasonable terms. We do not have any control over the process or timing of the acquisition of these materials by our manufacturers. Any significant delay in the supply of a product candidate or the raw material components thereof for an ongoing clinical trial or potential commercial launch 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

there could 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, quantity or timeframe 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 matures, we will have a greater need for 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 may need to increase their scale of production or we may need to secure alternate suppliers.

We may not be successful in establishing or maintaining strategic partnerships to further the development of our therapeutic programs. Additionally, if any of our current or future strategic partners fails to perform its obligations or terminates the

partnership, the development and commercialization of the product candidates under such agreement could be delayed or terminated. Such failures could have a material adverse effect on our operations and business.

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 our product candidates. In these partnerships, we would expect our strategic partner to provide capabilities in research, development, marketing and sales, in addition to funding.

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 product candidates 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 as having the requisite potential.

Any delay in entering into new strategic partnership agreements related to our product candidates could have an adverse effect on our business, including delaying the development and commercialization of our product candidates. If we are not able to establish and maintain strategic partnerships:

- we will have fewer resources with which to continue to operate our business;
- the development of certain of our product candidates may be terminated or delayed; and
- our cash expenditures needed to develop such product candidates would increase significantly and we do not have the cash resources to develop our product candidates on our own.

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. Furthermore, we may not be able to maintain such strategic partnerships if, for example, development or approval of a product candidate is delayed, sales of an approved product are disappointing or the partner experiences its own financial or operational constraints or a change in business strategy. If any current or future strategic partners do not devote sufficient time and resources to their 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 our own. Our current partners and licensees can terminate their agreements with us under various conditions, including without cause, at which point they would no longer continue to develop our products.

Much of the potential revenue from any of our strategic partnerships will likely consist of contingent payments, such as development milestones and 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 are not involved in these processes, and we depend entirely on our strategic partners. Any of our 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 or maintaining adequate patent protection for one or more of our product candidates, or the scope of our patient protection could be insufficiently broad, 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, or USPTO, 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 USPTO will grant with respect to the antibodies in our antibody product pipeline is uncertain. It is possible that the USPTO 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.

If we do not obtain patent term extensions under the Hatch-Waxman Act and similar non-U.S. legislation to extend the term of patents covering each of our product candidates, our business may be materially harmed.

Patents have a limited duration. The term of a U.S. patent, if granted from an application filed on or after June 8, 1995, is generally 20 years from its earliest U.S. non-provisional filing date. Even if patents covering our product candidates are obtained, once the patents expire, we may be open to competition from competitive medications. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our owned or in-licensed patent rights may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

Depending upon the circumstances, the term of our owned and in-licensed patent rights that cover our product candidates may be extended in the U.S. under the Hatch-Waxman Act, by Supplementary Protection Certificates, or SPCs, in certain European countries, and by similar legislation in other countries for delays incurred when seeking marketing approval for a drug candidate. For example, the Hatch-Waxman Act permits a patent term extension of up to five years for a patent covering an approved product as compensation for effective patent term lost during product development and the FDA regulatory review process. However, we may not receive an extension if we fail to apply within the applicable deadline, fail to apply prior to expiration of relevant patents or otherwise fail to satisfy applicable requirements. Moreover, the length of the extension could be less than we request. If we are unable to obtain patent term extension or the term of any such extension is less than we request, the period during which we can enforce our patent rights for that product will be shortened and our competitors may obtain approval to market competing products sooner. As a result, our revenue from applicable products could be materially reduced.

The U.S. patent rights that we exclusively license covering tivozanib are scheduled to expire from 2018 to 2023. The U.S. patent covering the molecule and its therapeutic use is scheduled to expire in 2022. In view of the length of time tivozanib has been under regulatory review at the FDA, however, a patent term extension of up to 5 years may be available, which, if granted, could extend the term of this patent until 2027. However, the length of the extension could be less than we request, or no extension may be granted at all. In addition, SPCs have been filed in over 15 European countries for the corresponding patents covering the tivozanib molecule, which, if granted, could extend the term of the such patents in each of those European countries until 2027. If we are unable to obtain a patent term extension or the term of any such extension is less than we request, the period of time during which the patent rights covering tivozanib or its use can be enforced will be shortened, and our competitors may obtain approval to market a competing product sooner. As a result, our potential revenue from tivozanib could be materially reduced, causing material harm to our business.

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 strategic 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 Office, 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 USPTO, 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 USPTO 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. 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 that contains 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 patent owners indicating that they believe we may need a license from them in order to avoid infringing their patent rights. With regard to ficlatuzumab, we are aware of two separate families of United States patents 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. 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.

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 commercially 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, 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 which we have licensed and on which our business depends or may prosecute them in a manner not in the best interests of our business. 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 EUSA, 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 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 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 may not 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.
- Our pending patent applications might 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.
- 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 biopharmaceutical industry involves both technological complexity and legal complexity. Therefore, obtaining and enforcing biopharmaceutical 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 in the U.S. 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 biopharmaceutical industry will be affected by such changes in the patent system. In addition, the U.S. 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 USPTO, 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 regulatory 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 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 EMA 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 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. For example, in June 2013, the FDA issued a complete response letter informing us that it would not approve tivozanib for the first-line treatment of aRCC based solely on the data from the TIVO-1 trial.

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 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 collaborators must obtain 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 must be approved for reimbursement before the product can be approved for sale in that country. We or our 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.

Additionally, on June 23, 2016, the electorate in the United Kingdom voted in favor of leaving the European Union, commonly referred to as Brexit. On March 29, 2017, the country formally notified the European Union of its intention to withdraw pursuant to Article 50 of the Lisbon Treaty. Since a significant proportion of the regulatory framework in the United Kingdom is derived from European Union directives and regulations, the referendum could materially impact the regulatory regime with respect to the approval of our product candidates in the United Kingdom or the European Union. Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of Brexit or otherwise, would prevent us from commercializing our product candidates in the United Kingdom and/or the European Union and restrict our ability to generate revenue and achieve and sustain profitability. If any of these

outcomes occur, we may be forced to restrict or delay efforts to seek regulatory approval in the United Kingdom and/or European Union for our product candidates, which could significantly and materially harm our business.

We 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 our collaborators may seek orphan drug designations for other product candidates and may be unable to obtain such designations.

Even if we obtain orphan drug designation for a product candidate, we 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 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, to be more effective or to make a major contribution to patient care.

On August 3, 2017, the Congress passed the FDA Reauthorization Act of 2017, or FDARA. FDARA, among other things, codified the FDA's pre-existing regulatory interpretation, to require that a drug sponsor demonstrate the clinical superiority of an orphan drug that is otherwise the same as a previously approved drug for the same rare disease in order to receive orphan drug exclusivity. The new legislation reverses prior precedent holding that the Orphan Drug Act unambiguously requires that the FDA recognize the orphan exclusivity period regardless of a showing of clinical superiority. The FDA may further reevaluate the Orphan Drug Act and its regulations and policies. We do not know if, when, or how the FDA may change the orphan drug regulations and policies in the future, and it is uncertain how any changes might affect our business. Depending on what changes the FDA may make to its orphan drug regulations and policies, our business could be adversely impacted.

Even if we or our collaborators obtain marketing approvals for our product candidates, the terms of approvals and ongoing regulation of our products may limit how we 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 our collaborators must therefore comply with requirements concerning advertising and promotion for any of our product candidates for which we 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 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 and our collaborators and our contract manufacturers could be subject to periodic unannounced inspections by the FDA to monitor and ensure compliance with cGMPs.

Accordingly, assuming we receive marketing approval for one or more of our product candidates, we 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 our collaborators are not able to comply with post-approval regulatory requirements, we could have the marketing approvals for our products withdrawn by regulatory authorities and our 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 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.

The efforts of the Trump Administration to pursue regulatory reform may limit the FDA's ability to engage in oversight and implementation activities in the normal course, and that could negatively impact our business.

The Trump Administration has taken several executive actions, including the issuance of a number of executive orders, that could impose significant burdens on, or otherwise materially delay, the FDA's ability to engage in routine regulatory and oversight activities such as implementing statutes through rulemaking, issuance of guidance, and review and approval of marketing applications. On January 30, 2017, President Trump issued an executive order, applicable to all executive agencies, including the FDA, that requires that for each notice of proposed rulemaking or final regulation to be issued in fiscal year 2017, the agency shall identify at least two existing regulations to be repealed, unless prohibited by law. These requirements are referred to as the "two-for-one" provisions. This executive order includes a budget neutrality provision that requires the total incremental cost of all new regulations in the 2017 fiscal year, including repealed regulations, to be no greater than zero, except in limited circumstances. For fiscal years 2018 and beyond, the executive order requires agencies to identify regulations to offset any incremental cost of a new regulation. In interim guidance issued by the Office of Information and Regulatory Affairs within the Office of Management and on February 2, 2017, the administration indicates that the "two-for-one" provisions may apply not only to agency regulations, but also to significant agency guidance documents. It is difficult to predict how these requirements will be implemented, and the extent to which they will impact the FDA's ability to exercise its regulatory authority. If these executive actions impose constraints on FDA's ability to engage in oversight and implementation

activities in the normal course, our business may be negatively impacted.

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 $10,781 to $21,563 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 annually report to Centers for Medicare and Medicaid Services, or CMS, (i) payments and other transfers of value to physicians and teaching hospitals, and (ii) certain physician ownership or investment interests; 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 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 manufacturers to report information related to payments and other transfers of value to other healthcare providers and healthcare entities, 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, individual imprisonment, integrity obligations, exclusion from funded healthcare programs and the curtailment or restructuring of our operations. Any such penalties 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, individual imprisonment, integrity obligations, exclusion 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 exclusion 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 and commercialize our product candidates and affect the prices we, or they, may obtain.

In the United States and foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability to profitably sell any product candidates for which we 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.

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 ACA. Among the provisions of the ACA 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.

In addition, other legislative changes have been proposed and adopted since the ACA was enacted. 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 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. These changes included aggregate reductions to 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. 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 we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used.

With the new Administration and Congress, there will likely be additional administrative or legislative changes, including modification, repeal, or replacement of all, or certain provisions of, the ACA. For example, with enactment of the Tax Cuts and Jobs Act of 2017, which was signed by the President on December 22, 2017, Congress repealed the “individual mandate.” The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, will become effective in 2019. According

to the Congressional Budget Office, the repeal of the individual mandate will cause 13 million fewer Americans to be insured in 2027 and premiums in insurance markets may rise. Further, each chamber of the Congress has put forth multiple bills designed to repeal or repeal and replace portions of the ACA. Although none of these measures has been enacted by Congress to date, Congress may consider other legislation to repeal and replace elements of the ACA. The Congress will likely consider other legislation to replace elements of the ACA, during the next Congressional session.

The Trump Administration has also taken executive actions to undermine or delay implementation of the ACA. In January 2017, President Trump signed an Executive Order directing federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. In October 2017, the President signed a second Executive Order allowing for the use of association health plans and short-term health insurance, which may provide fewer health benefits than the plans sold through the ACA exchanges. At the same time, the Trump Administration announced that it will discontinue the payment of cost-sharing reduction, or CSR, payments to insurance companies until Congress approves the appropriation of funds for such CSR payments. The loss of the CSR payments is expected to increase premiums on certain policies issued by qualified health plans under the ACA. A bipartisan bill to appropriate funds for CSR payments was introduced in the Senate, but the future of that bill is uncertain.

The costs of prescription pharmaceuticals in the United States has also been the subject of considerable discussion in the United States, and members of Congress and the Trump Administration have stated that they will address such costs through new legislative and administrative measures. To date, there have been several recent U.S. congressional inquiries and proposed state and federal legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products. The pricing of prescription pharmaceuticals is also subject to governmental control outside the United States. 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 may be required to conduct a clinical trial that compares the cost effectiveness of our product candidates 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 ability to generate revenues and become profitable could be impaired.

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 our 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, our competition position could be harmed, and our product development and commercialization efforts could be delayed.

Risks Related to Employee Matters and Managing Potential 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. We have completed several reductions in force related to restructurings we have completed in the past, which 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 Capital 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 Capital Market. We are required to meet specified requirements to maintain our listing on the Nasdaq Capital Market, including, among other things, a minimum bid price of $1.00 per share. If we fail to satisfy the Nasdaq Capital Market’s continued listing requirements, we may transfer to the OTC Bulletin Board. Having our common stock trade on the OTC Bulletin Board could adversely affect the liquidity of our common stock. Any such transfer could make it more difficult to dispose of, or obtain accurate quotations for the price of, our common stock, and there also would likely be a reduction in our coverage by securities analysts and the news media, which could cause the price of our common stock to decline further. We may also face other material adverse consequences in such event, such as negative publicity, a decreased ability to obtain additional financing, diminished investor and/or employee confidence, and the loss of business development opportunities, some or all of which may contribute to a further decline in our stock price.

The market price of our common stock has been, and is likely 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 our product candidates;
- the results of our efforts to 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 in Part I, Item 3 of this report under the heading "Legal Proceedings". 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 and our collaborators 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 statements we have made about the initiation and completion of clinical trials, filing and approval of regulatory applications and other developments and milestones under our research and development programs and those of our partners and collaborators for tivozanib, ficlatuzumab, AV-203, AV-380 and the AV-353 platform. The actual timing of these events can vary significantly due to a number of factors, including, without limitation, delays or failures in our preclinical studies or clinical trials, the amount of time, effort and resources committed to our programs and the uncertainties inherent in the regulatory approval process. As a result, there can be no assurance that our preclinical studies and clinical trials will advance or be completed in the time frames we expect or announce, that we will make regulatory submissions or receive regulatory approvals as planned or that we will be able to adhere to our current schedule for the achievement of key milestones under any of our programs. If we 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 and 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 clinical development programs;
- the level of expenses incurred in connection with our clinical development programs, including development and manufacturing costs relating to our clinical development candidates;
- the implementation of restructuring and cost-savings strategies;
- the implementation or termination of collaboration, licensing, manufacturing or other material agreements with third parties, and non-recurring revenue or expenses under any such agreement;
    - costs associated with lawsuits against us or other litigation in which we may become involved, including the current class action described in Part I, Item 3 of this report under the heading “Legal Proceedings”;
- changes in our Hercules Loan Agreement, including the existence of any event of default that may accelerate payments due thereunder;
- non-cash changes in fair value related to re-valuations of our PIPE Warrant liability and warrants we intend to issue in connection with the proposed settlement of the current class action, which we refer to as the Settlement Warrants, as a result of fluctuations in our stock price; 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. 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, 2017, we had approximately $33.5 million of cash, cash equivalents and marketable securities consisting of cash on deposit with banks, a U. S. government money market fund, corporate debt securities, including commercial paper, and U.S. government agency securities. 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 and warrants, could negatively affect our stock price.

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

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 stockholders.

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 stockholders 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 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.

If we are unable to successfully remediate any material weaknesses in our internal control, the accuracy and timing of our financial reporting may be adversely affected, we may be unable to maintain compliance with securities law requirements regarding timely filing of periodic reports in addition to applicable stock exchange listing requirements, investors may lose confidence in our financial reporting, and our stock price may decline as a result. We also could become subject to investigations by Nasdaq, the SEC, or other regulatory authorities.

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.

We have incurred significant net losses since our inception and cannot guarantee when, if ever, we will become profitable. To the extent that we continue to generate federal and state taxable losses, unused net operating loss and tax credit carryforwards will carry forward to offset future taxable income, subject to applicable limitations on the use of those losses. Losses incurred in taxable years ending on or before December 31, 2017, are eligible to be carried forward for up to 20 years, and to be deducted in full against income for the years to which they may be carried. Losses incurred in taxable years ending after December 31, 2017, are eligible to be carried forward indefinitely, but may offset no more than 80% of the taxable income for the years to which they are carried (computed without regard to the deduction for carryovers of net operating losses). Net operating loss carryovers from periods ending on or before December 31, 2017, and tax credit carryovers from all periods 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 and credit carryovers to reduce its tax liability for post-change periods may be limited. We may experience ownership changes as a result of shifts in our stock ownership, some of which may be outside of our control. In addition, we have not conducted a detailed study to document whether our historical activities qualify to support the research and development credits currently claimed as a carryover. A detailed study could result in adjustment to our research and development credit carryovers. If we determine that an ownership change has occurred and our ability to

use our historical net operating loss and tax credit carryovers is materially limited, or if our research and development carryforwards are adjusted, our use of those attributes to offset future income tax liabilities would be limited.

The recently passed comprehensive tax reform bill could adversely affect our business and financial condition.

On December 22, 2017, President Trump signed into law new legislation that significantly revised the Internal Revenue Code of 1986, as amended. The newly enacted federal income tax law, among other things, contains significant changes to corporate taxation, including reduction of the corporate tax rate from a top marginal rate of 35% to a flat rate of 21%, limitation of the tax deduction for interest expense to 30% of adjusted earnings (except for certain small businesses), limitation of the deduction for net operating losses to 80% of current year taxable income and elimination of net operating loss carrybacks, one time taxation of offshore earnings at reduced rates regardless of whether they are repatriated, elimination of U.S. tax on foreign earnings (subject to certain important exceptions), immediate deductions for certain new investments instead of deductions for depreciation expense over time, and modifying or repealing many business deductions and credits. Notwithstanding the reduction in the corporate income tax rate, the overall impact of the new federal tax law is uncertain and our business and financial condition could be adversely affected. In addition, it is uncertain how various states will respond to the newly enacted federal tax law. The impact of this tax reform on holders of our common stock is also uncertain and could be adverse. We urge our stockholders to consult with their legal and tax advisors with respect to this legislation and the potential tax consequences of investing in or holding our common stock.

ITEM 1B. Unresolved Staff Comments

None.

ITEM 2. Properties

We sublease our principal facilities, which consist of approximately 3,000 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 and for the foreseeable future.

ITEM 3. Legal Proceedings

Two class action lawsuits have been filed against us and certain of our former officers and directors, (Tuan Ha-Ngoc, David N. Johnston, William Slichenmyer, and Ronald DePinho), in the United States District Court for the District of Massachusetts, or the District Court, 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 a class of stockholders who purchased our common stock between January 3, 2012 and May 1, 2013, or the Class. This consolidated amended complaint was dismissed without prejudice on March 20, 2015, and the lead plaintiffs then filed a second amended complaint bringing similar allegations, and which no longer named Mr. DePinho as a defendant. We moved to dismiss again, and after a second round of briefing and oral argument, the District Court ruled in our favor and dismissed the second amended complaint with prejudice on November 18, 2015. The lead plaintiffs appealed the District Court's decision to the United States Court of Appeals for the First Circuit. They also filed a motion to vacate and reconsider the District Court's judgment, which we opposed. On January 3, 2017, the District Court granted the plaintiffs' motion to vacate the dismissal and judgment, and the plaintiffs filed a motion to dismiss their appeal on February 8, 2017. On February 2, 2017, the plaintiffs filed a third amended complaint, on behalf of stockholders who purchased common stock between May 16, 2012 and May 1, 2013, alleging claims similar to those alleged in the prior complaints, namely that we and certain of our former officers and directors violated Sections 10(b) and/or 20(a) of the Exchange Act 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 clinical trial in an effort to lead investors to believe that the drug would receive approval from the FDA. On March 2, 2017, we filed an answer

to the third amended complaint, and the parties initiated discovery. On June 29, 2017, the plaintiffs filed a motion for class certification and on July 27, 2017, we fled our response. On July 18, 2017, the District Court entered an order referring the case to alternative dispute resolution. The parties mediated on September 12 and 13, 2017. On December 26, 2017, the parties entered into a binding MOU regarding the settlement of the lawsuit. On January 29, 2018, the parties entered into a Stipulation of Settlement which was filed with District Court on February 2, 2018. Under the terms of the MOU and Stipulation, we agreed with counsel for the lead plaintiffs to cause certain of our and the individual defendants' insurance carriers to provide the Class with a cash payment of $15.0 million, which includes the cash amount of any attorneys' fees or litigation expenses that the District Court may award lead plaintiffs' counsel and costs lead plaintiffs incur in administering and providing notice of the settlement. Additionally, we agreed to issue to the Class warrants for the purchase of 2.0 million shares of our common stock exercisable from the date of issue until the expiration of a one-year period after the date of issue at an exercise price equal to the closing price on December 22, 2017, the trading day prior to the execution of the MOU, which was $3.00 per share. On February 8, 2018, the District Court issued an order preliminarily approving the terms of the Stipulation. The Stipulation is subject to final approval by the District Court. The District Court set a final approval hearing for May 30, 2018. We have agreed to use our best efforts to issue and deliver the Settlement Warrants within ten business days following the effective date of the final approval of the Stipulation.

On July 3, 2013, the staff, or SEC Staff, of the SEC served a subpoena on us for documents and information concerning tivozanib, including related communications with the FDA, investors and others. In September 2015, the SEC Staff invited us to

discuss the settlement of potential claims asserting that we violated federal securities laws by omitting to disclose to investors the recommendation by the staff of the FDA on May 11, 2012, that we conduct an additional clinical trial with respect to tivozanib. On March 29, 2016, the SEC filed a complaint against us and three of our former officers in the U.S. District Court for the District of Massachusetts alleging that we misled investors about our efforts to obtain FDA approval for tivozanib. Without admitting or denying the allegations in the SEC's complaint, we consented to the entry of a final judgment pursuant to which we paid the SEC a $4.0 million civil penalty to settle the SEC's claims against us. On March 31, 2016, the District Court entered a final judgment which (i) approved the settlement; (ii) permanently enjoined us from violating Section 17(a) of the Securities Act of 1933, as amended, or the Securities Act, Sections 10(b) and 13(a) of the Exchange Act and rules 10b-5, 12b-20, 13a-1, 13a-11 and 13a-13 promulgated thereunder; and (iii) ordered us to pay the agreed-to civil penalty. On September 15, 2017 and October 31, 2017, respectively, two of our former officers consented to entry of final judgment to settle the SEC's claims against them. We are not a party to the litigation between the SEC and the remaining former officer, and we can make no assurance regarding the outcome of that action or the SEC's claims against that individual.

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 Capital 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
2016		
First Quarter	$1.27	$0.82
Second Quarter	$1.15	$0.84
Third Quarter	$1.09	$0.81
Fourth Quarter	$0.89	$0.54

	High	Low
2017		
First Quarter	$0.98	$0.50
Second Quarter	$2.42	$0.55
Third Quarter	$4.24	$2.12
Fourth Quarter	$4.15	$2.56

Holders

As of March 8, 2018, there were approximately 50 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.

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

None.

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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, “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 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 12/31/2012 to 12/31/2017.

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

	12/12	12/13	12/14	12/15	12/16	12/17
AVEO Pharmaceuticals, Inc.	100.00	22.73	10.44	15.65	6.71	34.66
Nasdaq Composite	100.00	141.63	162.09	173.33	187.19	242.29
Nasdaq Biotechnology	100.00	174.05	230.33	244.29	194.95	228.29

ITEM 6. Selected Financial Data

The following selected consolidated financial data should be read in conjunction with our Consolidated Financial Statements and the Notes thereto and Management's Discussion and Analysis of Financial Condition and Results of Operations included elsewhere in this Annual Report on Form 10-K. The Balance Sheet Data at December 31, 2017 and 2016 and the Statement of Operations Data for each of the three years in the period ended December 31, 2017 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, 2015, 2014 and 2013, and the Statement of Operations Data for each of the two years in the period ended December 31, 2014 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,				
Statement of Operations data:	2017	2016	2015	2014	2013
	(in thousands, except per share data)				
Revenue	$7,579	$2,515	$19,024	$18,123	$1,293
Operating expenses:					
Research and development	25,179	23,703	12,875	38,254	68,468
General and administrative	9,138	8,205	10,217	18,589	28,712
Settlement costs	2,073	—	4,000	—	—
Restructuring and lease exit	—	—	4,358	11,729	8,017
Total operating expenses	36,390	31,908	31,450	68,572	105,197
Loss from operations	(28,811)	(29,393)	(12,426)	(50,449)	(103,904)
Interest expense, net	(2,373)	(1,949)	(2,286)	(2,356)	(3,002)
Change in fair value of warrant liability	(33,740)	4,751	—	—	—
Other (expense) income	—	(195)	(289)	66	(123)
Net loss before income taxes	(64,924)	(26,786)	(15,001)	(52,739)	(107,029)
Provision for income taxes	(101)	(101)	—	—	—
Net loss	$(65,025)	$(26,887)	$(15,001)	$(52,739)	$(107,029)
Basic and diluted net loss per share	$(0.61)	$(0.39)	$(0.27)	$(1.01)	$(2.10)
Weighted average number of common shares outstanding	105,930	69,268	55,701	52,289	50,928

	Years Ended December 31,				
Balance sheet data:	2017	2016	2015	2014	2013
	(in thousands)				
Cash, cash equivalent, and marketable securities	$33,525	$23,348	$34,135	$52,306	$118,506
Working capital	18,059	15,966	27,978	18,773	97,511
Total assets	50,198	27,285	40,542	70,662	146,346
Loans payable, including current portion, net of discount	18,477	14,003	9,471	20,652	19,205
Accumulated deficit	(586,969)	(521,916)	(495,029)	(480,028)	(427,289)
Total stockholders' (deficit) equity	(40,763)	(1,923)	17,227	20,606	69,938

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 medicines for oncology and other areas of unmet medical need. Our strategy is to retain North American rights to our oncology portfolio while securing partners in development and commercialization outside of North America. We are working to develop and commercialize our lead candidate tivozanib in North America as a treatment for renal cell carcinoma, or RCC. We have entered into partnerships to fund the development and commercialization of our preclinical and clinical stage assets, including AV-203 and ficlatuzumab in oncology and AV-380 in cachexia. Tivozanib (FOTIVDA®), which we have outlicensed outside of North America, is approved in the European Union, as well as Norway and Iceland, for the first-line treatment of adult patients with advanced RCC, or aRCC, and for adult patients who are vascular endothelial growth factor receptor, or VEGFR, and mTOR pathway inhibitor-naïve following disease progression after one prior treatment with cytokine therapy for aRCC. We are currently seeking a partner to develop our AV-353 platform, a preclinical asset, worldwide for the potential treatment of pulmonary arterial hypertension, or PAH.

Going Concern

We have identified conditions and events that raise substantial doubt about our ability to continue as a going concern. To continue as a going concern, we must secure additional funding to support our current operating plan. As of December 31, 2017, we had approximately $33.5 million in existing cash, cash equivalents and marketable securities. In the first quarter of 2018 to-date, we have raised an additional approximate $1.9 million in net funding, including approximately $0.5 million received in January 2018 related to the exercise of 0.5 million PIPE Warrants and $1.4 million in net partnership-related funding in connection with the $2.0 million milestone payment by EUSA for the February 2018 reimbursement approval by the NICE, for RCC in the UK that was received in March 2018, net of the corresponding 30% sub-license fee due to KHK. Based on these available cash resources, we do not have sufficient cash on hand to support current operations for at least the next twelve months from the date of filing this Annual Report on Form 10-K. This condition raises substantial doubt about our ability to continue as a going concern. We expect that, in order to obtain additional funding, we will need to receive additional milestone payments from our partners and / or complete public or private financings of debt or equity. We may also seek to procure additional funds through future arrangements with collaborators, licensees or other third parties, and these arrangements would generally require us to relinquish or encumber rights to some of our technologies or drug candidates. Moreover, we may not be able receive milestone payments or complete financings or enter into such arrangements on acceptable terms, if at all. For more information, refer to "—Liquidity and Capital Resources—Operating Capital Requirements and Going Concern" below and Note 1 to our consolidated financial statements included elsewhere in this Annual Report on Form 10-K.

Recent Developments

In December 2017, we entered into a binding Memorandum of Understanding with class representatives Bob Levine and William Windham, or Plaintiffs, regarding the settlement of a securities class action lawsuit, or Class Action, filed in 2013 and pending in the United States District Court for the District of Massachusetts against us and certain of our former officers (Tuan Ha-Ngoc, David Johnston, and William Slichenmyer, who are collectively referred to as the Individual Defendants), In re AVEO Pharmaceuticals, Inc. Securities Litigation et al. , No. 1:13-cv-11157-DJC. As

previously disclosed, the Class Action was brought on behalf of stockholders who purchased our common stock between May 16, 2012 and May 1, 2013.

In January 2018, we entered into a Stipulation of Settlement with the Plaintiffs that was preliminarily approved by the District Court in February 2018. Under the terms of the MOU and the Stipulation, we agreed to cause certain of our and the Individual Defendants' insurance carriers to provide the Class with a cash payment of $15.0 million, which includes the cash amount of any attorneys' fees or litigation expenses that the District Court may award Plaintiff's counsel and costs Plaintiffs incur in administering and providing notice of the settlement. Additionally, we agreed to issue to the Class warrants for the purchase of 2.0 million shares of our common stock, which we refer to as the Settlement Warrants, exercisable from the date of issue until the expiration of a one-year period after the date of issue at an exercise price equal to the closing price on December 22, 2017, the trading day prior to the execution of the MOU, which was $3.00 per share. The settlement is subject to notice to the Class and final approval of the District Court. The settlement shall be effective on the date, or the Effective Date, on which all of the following circumstances have occurred: (a) a final judgment containing the requisite release of claims has been entered by the District Court; (b) no appeal is pending with

respect to the final judgment; (c) the final judgment has not been reversed, modified, vacated or amended; (d) the time to file any appeal from the final judgment has expired without the filing of an appeal or an order dismissing the appeal or affirming the final judgment has been entered, and any time to file a further appeal (including a writ of certiorari or for reconsideration of the appeal) has expired; and (e) the MOU and any settlement agreement with respect to the claims released in the final judgment have not expired or been terminated. We have agreed to use our best efforts to issue and deliver the Settlement Warrants within ten business days following the Effective Date. A hearing by the District Court for final approval of the Stipulation has been scheduled for May 30, 2018.

Strategic Partnerships

CANbridge

In March 2016, we entered into a collaboration and license agreement with CANbridge, or the CANbridge Agreement, under which we granted CANbridge the exclusive right to develop, manufacture and commercialize AV-203, our proprietary ErbB3 (HER3) inhibitory antibody, for the diagnosis, treatment and prevention of disease in humans and animals in all countries other than the United States, Canada and Mexico. Under the terms of the CANbridge Agreement, if we determine to grant a license to any ErbB3 inhibitory antibody in the United States, Canada or Mexico, we are obligated to first negotiate with CANbridge for the grant to CANbridge of a license to such rights. The parties have both agreed not to directly or indirectly develop or commercialize any other ErbB3 inhibitory antibody product during the term of the CANbridge Agreement other than pursuant to the CANbridge Agreement.

CANbridge has responsibility for all activities and costs associated with the further development, manufacture, regulatory filings and commercialization of AV-203 throughout its licensed territory. CANbridge is obligated to use commercially reasonable efforts to develop and obtain regulatory approval for AV-203 in each of China, Japan, the United Kingdom, France, Italy, Spain, and Germany. CANbridge will bear all costs for development of AV-203 through proof-of-concept in esophageal squamous cell carcinoma, after which we would expect to contribute to certain worldwide development costs.

Pursuant to the CANbridge Agreement, CANbridge paid us an upfront fee of $1.0 million in April 2016. CANbridge also agreed to reimburse us $1.0 million for certain manufacturing costs and expenses that we previously incurred. CANbridge paid this manufacturing reimbursement in two installments of $0.5 million each, including one in March 2017 and one in September 2017, net of foreign withholding taxes. We are also eligible to receive up to $42.0 million in potential development and regulatory milestone payments and up to $90.0 million in potential sales based milestone payments based on annual net sales of licensed products. In December 2017, CANbridge filed an IND with the China Food and Drug Administration for a Phase 1b / III clinical study of AV-203 in esophageal squamous cell cancer. Upon commercialization, we are eligible to receive a tiered royalty, with a percentage range in the low double-digits, on net sales of approved licensed products. CANbridge's obligation to pay royalties for each licensed product expires on a country-by-country basis on the later of the expiration of patent rights covering such licensed product in such country, the expiration of regulatory data exclusivity in such country and ten years after the first commercial sale of such licensed product in such country. A percentage of any milestone and royalty payments received by us, excluding upfront and reimbursement payments, are due to Biogen Idec International GmbH, or Biogen Idec, as a sublicensing fee under our option and license agreement with Biogen dated March 18, 2009, as amended.

The term of the CANbridge Agreement commenced on the effective date and will continue until the last to expire royalty term applicable to licensed products. Either party may terminate the CANbridge Agreement in the event of a material breach of the CANbridge Agreement by the other party that remains uncured for a period of 45 days, in the case of a material breach of a payment obligation, and 90 days in the case of any other material breach. CANbridge may terminate the CANbridge Agreement without cause at any time upon 180 days' prior written notice to us. We may terminate the CANbridge Agreement upon thirty days' prior written notice if CANbridge challenges any of the patent rights licensed to CANbridge under the CANbridge Agreement.

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 eye conditions. EUSA is obligated to use commercially reasonable efforts to seek regulatory approval for and commercialize tivozanib throughout its licensed territories for RCC. 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 its licensed territories.

Under the license agreement, EUSA made research and development reimbursement payments to us of $2.5 million upon the execution of the license agreement in 2015 and $4.0 million in September 2017 upon its receipt of marketing approval from the EMA for tivozanib (FOTIVDA) for the treatment of RCC. In September 2017, EUSA elected to opt-in to co-develop the TiNivo trial. As a result of EUSA's exercise of its opt-in right, it became an active participant in the ongoing conduct of the TiNivo trial and is able to utilize the resulting data from the TiNivo trial for regulatory and commercial purposes in its territories. EUSA made an additional research and development reimbursement payment to us of $2.0 million upon its exercise of its opt-in right. This payment was received in October 2017, in advance of the completion of the TiNivo trial, and represents EUSA's approximate 50% share of the total estimated costs of the TiNivo trial. We are also eligible to receive an additional research and development reimbursement payment from EUSA of fifty percent (50%) of our total costs for our TIVO-3 trial, up to $20.0 million, if EUSA elects to opt-in to that study.

We are entitled to receive milestone payments of $2.0 million per country upon reimbursement approval, if any, for RCC in each of France, Germany, Italy, Spain and the United Kingdom, and an additional $2.0 million for the grant of marketing approval, if any, in three of the following five countries: Argentina, Australia, Brazil, South Africa and Venezuela. In February 2018, EUSA obtained reimbursement approval from the NICE in the UK in first line RCC. Accordingly, we earned a $2.0 million milestone payment that was received from EUSA in March 2018. We are also eligible to receive a payment of $2.0 million in connection with a filing by EUSA with the EMA for marketing approval, if any, 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 up to $335.0 million upon EUSA's achievement of certain sales thresholds. Upon commercialization, we are eligible to receive tiered double-digit royalties on net sales, if any, of licensed products in its licensed territories ranging from a low double digit up to mid-twenty percent depending on the level of annual net sales. In November 2017, we began earning sales royalties upon EUSA's commencement of the first commercial launch of tivozanib (FOTIVDA) with the initiation of product sales in Germany.

The research and development reimbursement payments under the EUSA license agreement are not subject to the 30% sublicensing payment to KHK, subject to certain limitations. We would, however, owe KHK 30% of other, non-research and development payments we may receive from EUSA pursuant to our license agreement, including EU reimbursement approval milestones in up to five specified EU countries, EU marketing approvals for up to three additional indications beyond RCC, marketing approvals in up to three specified licensed territories outside of the EU, sales-based milestones and royalties, as set forth above. The $2.0 million milestone we earned in February 2018 upon EUSA's reimbursement approval from the NICE in the UK in first line RCC is subject to the 30% KHK sub-license fee, or $0.6 million.

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, 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.

Novartis made an upfront payment to us of $15.0 million in September 2015. We are also eligible to receive (a) up to $51.2 million in potential clinical 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 sales based milestone payments based on annual net sales of such products. If the product is commercialized, we would be 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. In December 2015, Novartis also exercised its right under the license agreement to acquire our inventory of clinical quality drug substance, reimbursing us approximately $3.5 million for such existing inventory. Certain milestones achieved by Novartis would trigger milestone payment obligations from us to St. Vincent’s, under our amended and restated license agreement with St. Vincent’s. In addition, royalties on approved products, if any, will be payable to St. Vincent’s, and we and Novartis will share that obligation equally.

In February 2017, Novartis paid $1.8 million out of its future payment obligations to us under the license agreement. The funds were used to satisfy a $1.8 million time-based milestone obligation that we owed to St. Vincent's on March 2, 2017. Novartis will reduce any subsequent payment obligations to us, if any, by the $1.8 million. We recognized the $1.8 million of consideration as revenue during the three months ended March 31, 2017, as the amount was fixed and determinable and non-refundable, and we do not have any further performance obligations to Novartis in connection with the license agreement. This payment reduces the aggregate future amounts potentially payable by Novartis to us under the license agreement, if any, by the $1.8 million, but does not amend any other terms of the Novartis license agreement.

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.

Biodesix

In April 2014, we and Biodesix entered into the Biodesix Agreement to develop and commercialize ficlatuzumab. Under the Biodesix 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 VeriStrat®, Biodesix's proprietary companion diagnostic test. Biodesix granted us perpetual, non-exclusive rights to certain intellectual property, including diagnostic data related to VeriStrat, 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, we retain primary responsibility for clinical development of ficlatuzumab. In September 2016, we and Biodesix announced the termination of the FOCAL trial, a phase 2 proof-of-concept clinical study of ficlatuzumab in which VeriStrat was used to select clinical trial subjects.

Under the Biodesix Agreement, with the exception of the costs incurred for the FOCAL trial, we and Biodesix are each required to contribute 50% of all clinical, regulatory, manufacturing and other costs to develop ficlatuzumab. Pursuant to the Biodesix Agreement, Biodesix was obligated to fund all costs of the FOCAL trial up to a cap of $15 million, following which all costs of the FOCAL trial would be shared equally. In connection with the discontinuation of the FOCAL trial on October 14, 2016, we and Biodesix amended the Biodesix Agreement. Under the amendment, we agreed to share 50% of all the program costs from August 1, 2016 forward. In return for bearing 50% of the FOCAL shutdown costs after August 1, 2016, we will be entitled to recover an agreed multiple of the additional costs borne by us out of any income Biodesix receives from the partnership in connection with the licensing, development or commercialization of ficlatuzumab. Following such recovery, the payment structure under the original Biodesix Agreement, which generally provides that the parties share equally in any costs and revenue, will resume without such modification. Pending marketing approval or the sublicense of ficlatuzumab, and subject to the negotiation of a commercialization agreement, each party would share equally in commercialization profits and losses, subject to our right to be the lead commercialization party.

In addition, we and Biodesix are funding investigator-sponsored clinical trials, including ficlatuzumab in combination with ERBITUX® (cetuximab) in squamous cell carcinoma of the head and neck, ficlatuzumab in combination with Cytosar (cytarabine) in acute myeloid leukemia and ficlatuzumab in combination with nab-paclitaxel and gemcitabine in pancreatic cancer.

We continue to evaluate additional opportunities for the further clinical development of ficlatuzumab.

Prior to the first commercial sale of ficlatuzumab, 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. 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. 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. 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 remains 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, under which we obtained an exclusive, worldwide license to 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.

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. 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 a $1.5 million upfront payment to St. Vincent's. Under our license agreement with St. Vincent's, we are obligated to use diligent efforts to conduct research and clinical development and commercially launch at least one licensed therapeutic product. We are required to make milestone payments, up to an aggregate total of $16.7 million, upon the earlier of achievement of specified development and regulatory milestones or a specified date for the first indication, and upon the achievement of specified development and regulatory milestones for the second and third 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. In February 2017, Novartis paid $1.8 million out of its future payment obligations to us under the license agreement. The funds were used to satisfy a $1.8 million time-based milestone obligation that we owed to St. Vincent's on March 2, 2017.

In addition, we will be required to 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.

The license agreement remains 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.

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 preclinical 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.

Astellas Pharma

In February 2011, we and our wholly-owned subsidiary AVEO Pharma Limited entered into a collaboration and license agreement with Astellas Pharma Inc. and certain of its subsidiaries pursuant to which we and Astellas intended to develop and commercialize tivozanib for the treatment of a broad range of cancers. Astellas elected to terminate the agreement effective August 2014, at which time the tivozanib rights were returned to us. In accordance with the

Astellas Agreement, committed development costs, including the costs of completing certain tivozanib clinical development activities, continue to be shared equally.

Biogen Idec

In March 2009, we entered into an exclusive option and license agreement with Biogen Idec regarding the development and commercialization of our discovery-stage ErbB3-targeted antibodies for the potential treatment and diagnosis of cancer and other diseases in humans outside of North America. In March 2014, we amended our agreement with Biogen Idec, and regained worldwide rights to AV-203. Pursuant to the amendment, we were obligated to in good faith use reasonable efforts to seek a collaboration partner to fund further development and commercialization of ErbB3-targeted antibodies. We satisfied this obligation in March 2016 upon entering into our license agreement with CANbridge. We are obligated to pay Biogen Idec a percentage of milestone payments we receive under the CANbridge agreement and single-digit royalty payments on net sales related to the sale of AV-203, up to cumulative maximum amount of $50.0 million.

Kyowa Hakko Kirin

In December 2006, we entered into a license agreement with KHK under which we obtained an exclusive license, with the right to grant sublicenses subject to certain restrictions, to research, develop, manufacture and commercialize tivozanib, pharmaceutical compositions thereof and associated biomarkers in all potential indications. Our exclusive license covers all territories in the world except for Asia and the Middle East, where KHK has retained the rights to tivozanib. 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. 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 a VEGF receptor.

We have upfront, milestone and royalty payment obligations to KHK under our license agreement. Upon entering into the license agreement with KHK, we made an upfront payment in the amount of $5.0 million. In March 2010, we made a milestone payment to KHK in the amount of $10.0 million in connection with the dosing of the first patient in our first phase 3 clinical trial of tivozanib (TIVO-1). In December 2012, we made a $12.0 million milestone payment to KHK in connection with the acceptance by the FDA of our 2012 new drug application, or NDA, filing for tivozanib. Each milestone under the KHK agreement is a one-time only payment obligation. Accordingly, we did not owe KHK another milestone payment in connection with the dosing of the first patient in our TIVO-3 trial, and would not owe a milestone payment to KHK if we file an NDA with the FDA following the completion of our TIVO-3 clinical trial. If we obtain approval for tivozanib in the U.S., we would owe KHK a one-time milestone payment of $18.0 million, provided that we do not sublicense U.S. rights for tivozanib prior to obtaining a U.S. regulatory approval. If we were to sublicense the U.S. rights, the associated U.S. regulatory milestone would be replaced by a specified percentage of sublicensing revenue, as set forth below.

If we sublicense any of our rights to tivozanib to a third party, as we have done with EUSA pursuant to our license agreement, the sublicense defines the payment obligations of the sublicensee, which may vary from the milestone and royalty payment obligations under our KHK license relating to rights we retain. We are required to pay KHK a fixed 30% of amounts we receive from our sublicensees, including upfront license fees, milestone payments and royalties, but excluding amounts we receive in respect of research and development reimbursement payments or equity investments, subject to certain limitations.

Certain research and development reimbursement payments by EUSA, including the $2.5 million upfront payment in December 2015, the $4.0 million in September 2017 upon the approval from the EMA of tivozanib (FOTIVDA) and the $2.0 million upon EUSA's election in September 2017 to opt-in to co-develop the TiNivo trial were not subject to sublicense revenue payments to KHK. In addition, if EUSA elects to opt-in to the TIVO-3 trial, the additional research and development reimbursement payment from EUSA of fifty percent (50%) of the total trial costs, up to $20.0 million, would also not be subject to a sublicense revenue payment to KHK, subject to certain limitations. We would, however, owe KHK 30% of other, non-research and development payments we may receive from EUSA pursuant to our license agreement, including EU reimbursement approval milestones in up to five specified EU countries, EU marketing approvals for up to three additional indications beyond RCC, marketing approvals in up to three specified licensed territories outside of the EU, sales-based milestones and royalties, as set forth above. The $2.0 million milestone we earned in February 2018 upon EUSA's reimbursement approval from the NICE in the UK in first line RCC is subject to the 30% KHK sub-license fee, or $0.6 million.

We are also required to pay tiered royalty payments on net sales we make of tivozanib in our North American 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.

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.

Financial Overview

We do not have a history of being profitable and, as of December 31, 2017, we had an accumulated deficit of $587.0 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 funding to support our operating activities, and the timing and nature of activities contemplated for 2018 and thereafter will be conducted subject to the availability of sufficient financial resources. Refer to the "—Going Concern" and "Liquidity and Capital Resources—Operating Capital Requirements and Going Concern" sections for a further discussion of our funding requirements.

Revenue

To date, we have not generated any revenue from our product sales. All of our revenue to date has been principally 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 November 2017, we began earning royalties under our license agreement with EUSA upon their initiation of product sales in Germany.

In the future, we may generate revenue from a combination of product sales, license fees, milestone payments and research and development payments in connection with strategic partnerships, and royalties resulting from the sales of products developed under licenses of our intellectual property. We expect that any revenue we generate will fluctuate from quarter to quarter as a result of the timing and amount of license fees, research and development reimbursements, milestones, royalties and other payments received under our strategic partnerships, and the 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. We recognize research and development expenses as they are incurred. 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 drug development related materials;
- 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

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

We anticipate that research and development expenses in 2018 will decrease as we seek to complete the TIVO-3 trial and TiNivo trials. This estimate excludes possible additional Company-sponsored clinical trials and any related drug manufacturing and drug supply distribution, regulatory costs associated with a possible NDA submission for tivozanib

in RCC and pre-commercialization activities that we may undertake if the topline data results from our TIVO-3 trial support an NDA submission to the FDA for tivozanib in RCC. We expect to receive and report topline data from the TIVO-3 trial in the second quarter of 2018,

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. Below is a summary of our research and development expenses for the years ended December 31, 2017, 2016 and 2015, respectively:

	Years Ended December 31,			2017 / 2016 Comparison		2016 / 2015 Comparison	
	2017	2016	2015	$	%	$	%
	($ in thousands)						
Tivozanib	$21,594	$21,231	$8,513	$363	2 %	$12,718	149 %
AV-380 Program in Cachexia	1,850	464	2,408	1,386	299 %	(1,944)	(81)%
Ficlatuzumab	587	746	80	(159)	(21)%	666	833 %
AV-203	—	76	532	(76)	(100)%	(456)	(86)%
Other pipeline programs	156	—	11	156	100 %	(11)	(100)%
Other research and development	—	—	10	—	-%	(10)	(100)%
Overhead	992	1,186	1,321	(194)	(16)%	(135)	(10)%
Total research and development expenses	$25,179	$23,703	$12,875	$1,476	6 %	$10,828	84 %

Tivozanib

We have pursued partnering options to fund further tivozanib development in appropriate clinical settings outside of our strategic focus of developing oncology therapeutics in the U.S. Our licensee, EUSA, obtained EMA approval in August 2017 for tivozanib (FOTIVDA) in RCC and commenced commercialization in November 2017 with the initiation of product sales in Germany. EUSA is responsible for all activities and costs associated with the further development and commercialization of tivozanib within its licensed territories, excluding non-oncologic eye conditions.

The TIVO-3 trial was initiated in May 2016 and reached its enrollment target of 322 patients in June 2017. We enrolled an additional 29 patients in July 2017 and August 2017 for a total of 351 patients. We expect the total estimated remaining costs of this trial, including drug supply and distribution, to be approximately $9 million to $12 million through completion. In March 2017, we initiated the TiNivo trial in collaboration with BMS, which is providing nivolumab for the study. In addition, in September 2017, EUSA elected to opt-in to co-develop the TiNivo trial and to share in approximately 50% of the total trial costs up to a maximum of $2.0 million. We expect the total estimated remaining costs of this trial, including tivozanib drug supply and distribution, could be in the range of $1.5 million to $2.0 million.

AV-380 Program in Cachexia

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 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. 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, which comprised substantially all of the costs incurred during the year ended December 31, 2017.

Ficlatuzumab

In April 2014, we entered into the Biodesix Agreement to develop and commercialize ficlatuzumab, our potent HGF inhibitory antibody. Pursuant to the agreement, Biodesix was to provide up to $15.0 million for the phase 2 FOCAL trial of ficlatuzumab in combination with erlotinib in first-line advanced non-small cell lung cancer patients selected using Biodesix's proprietary companion diagnostic VeriStrat. In connection with the discontinuation of the FOCAL trial on October 14, 2016, we and Biodesix amended the Biodesix Agreement. Under the amendment, we agreed to fund 50% of the shutdown costs of the FOCAL trial after August 1, 2016. In return, we would be entitled to reimbursement at a multiple of such shutdown expenses out of any future revenues Biodesix receives from ficlatuzumab. All manufacturing and all non-FOCAL development, regulatory or commercial expenses for ficlatuzumab, including investigator-sponsored clinical trials, will continue to be equally shared, as provided in the original Biodesix Agreement. 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.

AV-203

In March 2014, we regained our worldwide rights from Biogen Idec to develop, manufacture and commercialize AV-203. In March 2016, we entered into a collaboration and license agreement with CANbridge, under which we granted CANbridge the exclusive right to develop and commercialize AV-203 in all countries other than the United States, Canada and Mexico. CANbridge is responsible for all costs of developing and commercializing AV-203 within its licensed territory. For a period of time following the completion of certain proof-of-concept clinical studies by CANbridge involving the use of AV-203 for the treatment of squamous cell esophagus cancer, we agreed to negotiate exclusively with CANbridge for (a) the right to co-develop ErbB3 inhibitory antibody products for the treatment of squamous cell esophagus cancer or (b) the right to include the United States, Canada and Mexico as part of the licensed territories. We do not expect to incur any significant costs related to AV-203 prior to CANbridge's completion of a proof-of-concept clinical study.

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 exact 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, information technology, legal and human resource functions. Other general and administrative expenses include facility costs not otherwise included in research and development expenses, patent filing, prosecution and defense costs and professional fees for legal, consulting, auditing and tax services. We anticipate that our general and administrative expenses in 2018 will remain at current levels, excluding

pre-commercialization activities that we may undertake if the topline data results from our TIVO-3 trial support an NDA submission for tivozanib in RCC. We expect to receive and report topline data from the TIVO-3 trial in the second quarter of 2018,

Interest Expense, Net

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 recorded a loss for the years ended December 31, 2017, 2016, and 2015, 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, 2017, 2016, and 2015, except for a $0.1 million provision recorded in each of the years ended December 31, 2016 and 2017 related to withholding taxes incurred in a foreign jurisdiction.

On December 22, 2017, President Trump signed into law The Tax Cuts and Jobs Act, or the Act. The Act, among other things, contains significant changes to corporate taxation, including reduction of the corporate tax rate from a top marginal rate of 35% to a flat rate of 21%, limitation of the tax deduction for interest expense to 30% of adjusted earnings (except for certain small businesses), limitation of the deduction for net operating losses to 80% of current year taxable income and elimination of net operating loss carrybacks, one time taxation of offshore earnings at reduced rates regardless of whether they are repatriated, elimination of U.S. tax on foreign earnings (subject to certain important exceptions), immediate deductions for certain new investments instead of deductions for depreciation expense over time, and modifying or repealing many business deductions and credits.

On December 22, 2017, the SEC issued guidance under Staff Accounting Bulletin No. 118, Income Tax Accounting Implications of the Tax Cuts and Jobs Act directing taxpayers to consider the impact of the U.S. legislation as “provisional” when it does not have the necessary information available, prepared or analyzed (including computations) in reasonable detail to complete its accounting for the change in tax law.

We are still in the process of evaluating the new law and therefore have not determined the full effect it will have on our business, including our financial statements.

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 and the notes thereto included elsewhere in this Annual Report on Form 10-K, 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.

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, upfront license fees; option exercise fees; funding of research and/or development efforts; milestone payments; and royalties on future product sales.

We analyze our collaboration arrangements to assess whether they are within the scope of ASC 808 to determine whether such arrangements involve joint operating activities performed by parties that are both active participants in the activities and exposed to significant risks and rewards dependent on the commercial success of such

activities. This assessment is performed throughout the life of the arrangement based on changes in the responsibilities of all parties in the arrangement. For collaboration arrangements that are deemed to be within the scope of ASC 808, we first determine which elements of the collaboration are deemed to be within the scope of ASC 808 and those that are more reflective of a vendor-customer relationship and therefore within the scope of ASC 605. The Company's policy is to recognized amounts received from collaborators in connection with joint operating activities that are within the scope of ASC 808 as a reduction to research and development expense.

When evaluating multiple element arrangements, under ASC 605,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 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 estimates 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 the 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 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 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 among multiple deliverables.

We typically receive non-refundable, upfront 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.

We aggregate our 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 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 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 us upon the FDA’s acceptance of a

New Drug Application, or 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.

Adoption of ASU 2014-09 (Topic 606)

In May 2014, the Financial Accounting Standard Board, or FASB, issued Accounting Standards Update, or ASU, No. 2014-09, Revenue from Contracts with Customers (Topic 606), or ASU 2014-09, which stipulates that an entity should recognize revenue to depict the transfer of promised goods or services to customers in an amount that reflects the consideration to which the entity expects to be entitled in exchange for those goods or services. This update will be effective for us beginning in the first quarter of 2018. For additional details regarding our adoption of this authoritative guidance, see Note 3 in the accompanying consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K.

Accrued Expenses and Accrued Clinical Trial Costs and Contract Research Liabilities

As part of the process of preparing our financial statements, we are required to estimate accrued expenses. This process involves identifying services which have been performed on our behalf, and estimating the level of service performed and the associated cost incurred for such service as of each balance sheet date in our financial statements. Given our current business, the primary area of uncertainty concerning accruals which could have a material effect on our operating results is with respect to service fees paid to contract manufacturers in conjunction with the production of clinical drug supplies and to contract research organizations in connection with our clinical trials. In connection with all of the foregoing service fees, our estimates are most affected by our understanding of the status and timing of services provided. The majority of our service providers, including contract research organizations, invoice us in arrears for services performed. In the event that we do not identify some costs which have begun to be incurred, or we under or overestimate the level of services performed or the costs of such services in a given period, our reported expenses for such period would be understated or overstated. We currently reflect the effects of any changes in estimates based on changes in facts and circumstances directly in our operations in the period such change becomes known.

Our arrangements with contract research organizations in connection with clinical trials often provide for payment prior to commencing the project or based upon predetermined milestones throughout the period during which services are expected to be performed. We recognize expense relating to these arrangements based on the various services provided over the estimated time to completion. The date on which services commence, the level of services performed on or before a given date, and the cost of such services are often determined based on subjective judgments. We make these judgments based upon the facts and circumstances known to us based on the terms of the contract and our ongoing monitoring of service performance. During the years ended December 31, 2017, 2016 and 2015, we had arrangements with multiple contract research organizations whereby these organizations commit to performing services for us over multiple reporting periods. We recognize the expenses associated with these arrangements based on our expectation of the timing of the performance of components under these arrangements by these organizations. Generally, these components consist of the costs of setting up the trial, monitoring the trial, closing the trial and preparing the resulting data. Costs related to patient enrollment in clinical trials are accrued as patients are enrolled in the trial.

With respect to financial reporting periods presented in this Annual Report on Form 10-K, the timing of our actual costs incurred have not differed materially from our estimated timing of such costs. In light of the foregoing, we do not believe our practices for estimating future expenses and making judgments concerning the accrual of expenses are reasonably likely to change in the future.

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 Accounting Standards Codification, or 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.

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. In 2016, we began calculating volatility using our historical data. Previously, we did not have sufficient history to support a calculation of volatility using only our historical data. As such, prior to 2016, we used a weighted-average volatility considering our own volatility since March 2010 and the volatilities of several peer companies. For purposes of identifying similar entities, we considered characteristics such as industry, length of trading history, similar vesting terms and in-the-money option status. Due to 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.

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, 2017, 2016 and 2015, respectively, the assumptions used in the Black-Scholes pricing model for new grants were as follows:

	Years Ended December 31,		
	2017	2016	2015
Volatility factor	71.82% - 80.15%	72.18% - 75.47%	73.04% - 78.70%
Expected term (in years)	5.50 - 6.25	3.00 - 6.25	5.50 - 6.25
Risk-free interest rates	1.84% - 2.22%	1.07% - 2.01%	1.54% - 1.93%
Dividend yield	—	—	—

On January 1, 2017, we adopted ASU No. 2016-09, Compensation–Stock Compensation (Topic 718): Improvements to Employee Share-Based Payment Accounting and elected to account for forfeitures as they occur. Prior to 2017, we included an estimate of the value of the awards that would be forfeited in calculating compensation costs, which we estimated based upon actual historical forfeitures. The forfeiture estimates were recognized over the requisite service period of the awards on a straight-line basis. We used forfeiture rates of 0%, 76% and 71% during the years ended December 31, 2017, 2016 and 2015, respectively.

We recognized stock-based compensation expense of approximately $1.1 million, $1.0 million and $1.1 million for the years ended December 31, 2017, 2016, and 2015, respectively. As of December 31, 2017, we had approximately $3.4 million of total unrecognized stock-based compensation expense for stock options, which we expect to recognize over a weighted-average period of approximately 2.6 years.

For years prior to 2017, we recorded 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. Forfeitures estimated each period were adjusted if actual forfeitures differed from those estimates.

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

Warrants Issued in Connection with Private Placement

We account for warrant instruments that either conditionally or unconditionally obligate the issuer to transfer assets as liabilities regardless of the timing of the redemption feature or price, even though the underlying shares may be classified as permanent or temporary equity. In May 2016, we issued warrants to purchase an aggregate of 17,642,482 shares of our common stock in connection with a private placement financing, which we refer to herein as the PIPE Warrants. See "—Liquidity and Capital Resources—Private Placement/PIPE Warrants" below. The PIPE Warrants contain a provision giving the warrant holder the option to receive cash, equal to the fair value of the remaining unexercised portion of the warrant, as cash settlement in the event that there is a fundamental transaction (contractually defined to include various merger, acquisition or stock transfer activities). Due to this provision, ASC 480, Distinguishing Liabilities from Equity requires that the PIPE Warrants be classified as a liability and not as equity. Accordingly, we recorded a warrant liability in the amount of approximately $9.3 million. The fair value of the PIPE Warrants has been determined using the Black-Scholes pricing model. The PIPE Warrants are subject to revaluation at each balance sheet date, and any changes in fair value are recorded as a non-cash gain or (loss) in the Statement of Operations as a component of other income (expense), net until the earlier of their exercise or expiration or upon the completion of a liquidation event. Upon exercise, the PIPE Warrants are subject

to revaluation just prior to the date of exercise and any changes in fair value are recorded as a non-cash gain or (loss) in the Statement of Operations as a component of other income (expense), net and the corresponding reduction in the warrant liability is recorded as additional paid-in capital in the Balance Sheet as a component of stockholder's equity. As of December 31, 2017, PIPE Warrants exercisable for 259,067 of the shares of common stock had been exercised and PIPE Warrants exercisable for 17,383,415 shares of common stock were outstanding. In January 2018, PIPE Warrants with respect to 518,134 shares of common stock underlying such PIPE Warrants were exercised, and we issued 518,134 shares of our common stock and received approximately $0.5 million in cash proceeds.

We recorded non-cash losses of approximately $33.7 million in the year ended December 31, 2017 and a non-cash gain of approximately $4.8 million in the year ended December 31, 2016 in our Statement of Operations attributable to the increases and decreases in the fair value of the warrant liability that resulted from higher stock prices as of December 31, 2017 and lower stock prices as of December 31, 2016, relative to prior periods. In the year ended December 31, 2017, we recorded a reduction in the warrant liability, with a corresponding increase to additional paid-in capital, of approximately $0.6 million attributable to warrant exercises in the third quarter of 2017.

The key assumptions used to value the PIPE Warrants were as follows:

	Original Issuance	December 31, 2016	December 31, 2017
Expected price volatility	76.25%	78.18%	84.86%
Expected term (in years)	5.00	4.50	3.50
Risk-free interest rates	1.22%	1.93%	2.09%
Stock price	$0.89	$0.54	$2.79
Dividend yield	—	—	—

Potential Class Action Settlement

In December 2017, upon entering into the MOU, this settlement became estimable and probable. Accordingly, we recorded an estimated $17.1 million contingent liability, including $15.0 million for the cash portion of the settlement with a corresponding insurance recovery for the 100% portion to be paid directly by certain of our insurance carriers, and an approximate $2.1 million estimate for the fair value on December 31, 2017 of 2.0 million warrants to purchase shares of our common stock exercisable from the date of issue until the expiration of a one-year period after the date of issue at an exercise price equal to the closing price on December 22, 2017, the trading day prior to the execution of the MOU, which was $3.00 per share, which we refer to as the Settlement Warrants, with a corresponding non-cash charge to the Statement of Operations as a component of operating expenses. In February 2018, the insurance carriers funded the settlement escrow account related to the $15.0 million cash portion of the settlement.

The settlement is subject to the execution of a definitive settlement agreement, notice to the Class, and final approval of the District Court and shall be effective on the date, or the Effective Date, on which all of the following circumstances have occurred: (a) a final judgment containing the requisite release of claims has been entered by the District Court; (b) no appeal is pending with respect to the final judgment; (c) the final judgment has not been reversed, modified, vacated or amended; (d) the time to file any appeal from the final judgment has expired without the filing of an appeal or an order dismissing the appeal or affirming the final judgment has been entered, and any time to file a further appeal (including a writ of certiorari or for reconsideration of the appeal) has expired; and (e) the MOU and any settlement agreement with respect to the claims released in the final judgment have not expired or been terminated. We have agreed to use our best efforts to issue and deliver the Settlement Warrants within ten business days following the Effective Date. In January 2018, we entered into the Stipulation, which was preliminarily approved by the District Court in February 2018. A hearing by the District Court for final approval of the Stipulation has been

scheduled for May 30, 2018.

The estimated fair value of the Settlement Warrants expected to be issued on the Effective Date has been determined using the Black-Scholes pricing model. The estimated fair value of the Settlement Warrants expected to be issued on the Effective Date are subject to revaluation at each balance sheet date and any changes in fair value are recorded as a non-cash gain or (loss) in the Statement of Operations as a component of operating expenses until the Settlement Warrants are issued, at which point they would be recorded as equity or as a liability based upon the issuance terms.

The key assumptions used to estimate the fair value the Settlement Warrants were as follows:

	December 31, 2017
Expected price volatility	101.52%
Expected term (in years)	1.00
Risk-free interest rates	1.76%
Stock price	$2.79
Dividend yield	—

Results of Operations

Comparison of Years Ended December 31, 2017, 2016 and 2015

Revenues

	Years Ended December 31,			2017 / 2016 Comparison		2016 / 2015 Comparison	
	2017	2016	2015	$	%	$	%
Strategic Partner:	($ in thousands)						
EUSA	$4,414	$395	$14	$4,019	1017%	$381	2721%
CANbridge	1,000	1,028	—	(28)	(3)%	1,028	100%
Novartis	1,800	—	18,450	1,800	100%	(18,450)	(100)%
Biogen Idec	—	38	268	(38)	(100)%	(230)	(86)%
Pharmstandard	—	939	61	(939)	(100)%	878	1439%
Ophthotech	115	115	231	0	0%	(116)	(50)%
Other	250	—	—	250	100%	—	-%
Total revenues	$7,579	$2,515	$19,024	$5,064	201%	$(16,509)	(87)%

In 2017 as compared to 2016, revenue increased by $5.1 million, principally due to a $4.0 million research and development reimbursement payment by EUSA upon the EMA approval of tivozanib (FOTIVDA) in RCC and a $1.8 million milestone payment by Novartis related to AV-380, partially offset by $0.8 million related to the acceleration of deferred revenue that was recognized upon the effective termination of our licensing agreement with Pharmstandard in September 2016.

In 2016 as compared to 2015, revenue decreased by $16.5 million principally due to $18.5 million in revenue that was recognized in 2015 related to Novartis for the $15.0 million upfront payment received in connection with our licensing agreement entered into in August 2015 and $3.5 million for the purchase of our inventory of clinical material in the fourth quarter of 2015. This decrease was partially offset by the $1.0 million upfront payment received in connection with our collaboration and license agreement with CANbridge entered into in March 2016 and $0.8 million in the acceleration of deferred revenue that was recognized upon the effective termination of our licensing agreement with Pharmstandard in September 2016 that otherwise would have been recognized over the performance period through April 2022.

Research and Development Expenses

	Years Ended December 31,			2017 / 2016 Comparison		2016 / 2015 Comparison	
	2017	2016	2015	$	%	$	%
	($ in thousands)						
Tivozanib	$21,594	$21,231	$8,513	$363	2 %	$12,718	149 %
AV-380 Program in Cachexia	1,850	464	2,408	1,386	299 %	(1,944)	(81)%
Ficlatuzumab	587	746	80	(159)	(21)%	666	833 %
AV-203	—	76	532	(76)	(100)%	(456)	(86)%
Other pipeline programs	156	—	11	156	100 %	(11)	(100)%
Other research and development	—	—	10	—	-%	(10)	(100)%
Overhead	992	1,186	1,321	(194)	(16)%	(135)	(10)%
Total research and development expenses	$25,179	$23,703	$12,875	$1,476	6 %	$10,828	84 %

In 2017 as compared to 2016, research and development expenses increased by $1.5 million principally due to a $0.4 million net increase in tivozanib expenses, primarily related to the advancement of the TIVO-3 and TiNivo trials, and a $1.4 million increase in

AV-380 expense, primarily related to the net increase in milestone payments due to St. Vincent's under our in-licensing agreement. These increases were partially offset by $0.2 million in lower ficlatuzumab expenses, primarily related to the discontinuation of the FOCAL trial in October 2016.

The $0.4 million net increase in tivozanib expenses included an increase of $1.3 million, primarily related to the advancement of the TIVO-3 and TiNivo trials, partially offset by a $0.9 million reduction related to cost sharing provided by EUSA in connection with the TiNivo trial. In September 2017, EUSA elected to opt-in to co-develop the ongoing TiNivo trial and made a research and development reimbursement payment to us of $2.0 million that was received in October 2017, in advance of the completion of the TiNivo trial, and represents EUSA's approximate 50% share of the total estimated costs of the TiNivo trial. In 2017, we recognized an approximate $0.9 million reduction in research and development expenses related to EUSA's approximate 50% share of the cumulative study-to-date costs incurred as of December 31, 2017 as the TiNivo trial was ongoing at the time EUSA made its opt-in election and EUSA paid the $2.0 million maximum amount of cost sharing per the license agreement in advance. The remaining $1.1 million in prepaid cost sharing was classified as deferred research and development reimbursements as of December 31, 2017 and will continue to be recognized as a reduction in research and development expenses as the related TiNivo trial costs are incurred over the duration of the trial.

The $1.4 million increase in AV-380 expense is principally due to $1.8 million in research and development expense that was recognized in the first quarter of 2017 in connection with a time-based milestone obligation due to St. Vincent's. In the first quarter of 2016, w.e recognized approximately $0.4 million in research and development expense in connection with a milestone obligation due to St. Vincent's related to the selection of a development candidate.

We anticipate that research and development expenses in 2018 will decrease as we seek to complete the TIVO-3 trial and TiNivo trials. This estimate excludes possible additional Company-sponsored clinical trials and any related drug manufacturing and drug supply distribution, regulatory costs associated with a possible NDA submission for tivozanib in RCC and pre-commercialization activities that we may undertake if the topline data results from our TIVO-3 trial support an NDA submission for tivozanib in RCC. We expect to receive and report topline data from the TIVO-3 trial in the second quarter of 2018,

In 2016 as compared to 2015, research and development expenses increased by $10.8 million due to a $12.7 million increase in tivozanib-related expenses, principally related to the advancement of the TIVO-3 trial that commenced patient enrollment and treatment in May 2016. This increase was partially offset by a $1.5 million decrease related to the upfront fee incurred under the amended St. Vincent's license agreement entered into in August 2015.

Included in research and development expenses were stock-based compensation expenses of approximately $0.3 million in each of 2017, 2016 and 2015.

General and Administrative Expenses

	Years Ended December 31,			2017 / 2016 Comparison		2016 / 2015 Comparison	
	2017	2016	2015	$	%	$	%
	($ in thousands)						
General and administrative	$9,138	$8,205	$10,217	$ 933	11 %	$(2,012)	(20)%

In 2017 as compared to 2016, general and administrative expenses increased by $0.9 million, principally due to an increase of $0.8 million in professional fees, including legal fees, investor relations and audit fees.

We anticipate that general and administrative expenses in 2018 will remain at current levels, excluding pre-commercialization activities that we may undertake if the topline data results from our TIVO-3 trial support an NDA submission for tivozanib in RCC. We expect to receive and report topline data from the TIVO-3 trial in the second quarter of 2018,

In 2016 as compared to 2015, general and administrative expenses decreased by $2.0 million, principally the result of a $0.8 million decrease in external costs associated with various ongoing legal matters as well as a $0.7 million decrease in employee compensation following our decreased headcount and the reduction of our utilized facility space following our 2015 restructuring.

Included in general and administrative expenses were stock-based compensation expenses of approximately $0.8 million, $0.7 million and $0.8 million in 2017, 2016 and 2015, respectively.

Settlement Costs

	Years Ended December 31,			2017 / 2016 Comparison		2016 / 2015 Comparison	
	2017	2016	2015	$	%	$	%
	($ in thousands)						
Settlement costs	2,073	—	4,000	2,073	100%	(4,000)	(100)%

In 2017 as compared to 2016, settlement costs increased by $2.1 million as a result of a non-cash charge in connection with the Settlement Warrants to purchase 2.0 million shares of our common stock that are expected to be issued in 2018 upon final approval by the District Court of the Stipulation. Refer to Note 15, “Legal Proceedings” in the financial statements included elsewhere in this Annual Report on Form 10-K for further discussion of the class action settlement.

In 2016 as compared to 2015, settlement costs decreased by $4.0 million as a result of $4.0 million in expense recognized in 2015 related to the settlement of certain SEC claims.

Restructuring and Lease Exit

	Years Ended December 31,			2017 / 2016 Comparison		2016 / 2015 Comparison	
	2017	2016	2015	$	%	$	%
	($ in thousands)						
Restructuring and lease exit	—	—	4,358	—	-%	(4,358)	(100)%

In 2016 as compared to 2015, restructuring and lease exit expenses decreased by $4.4 million as a result of the January 2015 restructuring that was substantially completed in March 2015. As part of this restructuring, we eliminated our internal research function, reducing our headcount by approximately 40 positions.

Change in Fair Value of PIPE Warrant Liability

	Years Ended December 31,			2017 / 2016 Comparison		2016 / 2015 Comparison	
	2017	2016	2015	$	%	$	%
	($ in thousands)						
Change in fair value of warrant liability	(33,740)	4,751	—	(38,491)	(810)%	4,751	100%

In May 2016, we issued the PIPE Warrants in connection with a private placement financing and recorded the warrants as a liability. The PIPE Warrants are subject to revaluation at each balance sheet date.

In 2017 as compared to 2016, the change in fair value of the PIPE Warrant liability increased by $38.5 million, principally due to higher revaluations resulting from higher stock prices. For the year ended December 31, 2017, we recorded an approximate $33.7 million non-cash loss in our Statement of Operations attributable to the increase in the fair value of the warrant liability that principally resulted from a higher stock price of $2.79 on December 31, 2017 as compared to the stock price of $0.54 on December 31, 2016. For the year ended December 31, 2016, we recorded an approximate $4.8 million non-cash gain in our Statement of Operations attributable to the decrease in the fair value of the warrant liability that principally resulted from a lower stock price of $0.54 on December 31, 2016 as compared to the stock price of $0.89 on the date of issuance of the PIPE warrants in May 2016.

Interest Expense, net

	Years Ended December 31,			2017 / 2016 Comparison		2016 / 2015 Comparison	
	2017	2016	2015	$	%	$	%
	($ in thousands)						
Interest expense, net	(2,373)	(1,949)	(2,286)	$ (424)	22 %	$ 337	(15)%

In 2017 as compared to 2016, interest expense, net increased by $0.4 million principally attributable to the increase in the balance under the loan agreement with Hercules Technology II, L.P. and Hercules Technology III, L.P., affiliates of Hercules Technology Growth, which we collectively refer to as Hercules Loan Agreement, that resulted from the $5.0 million in loan proceeds borrowed under the 2016 Amendment in each of May 2016 and June 2017.

In December 2017, we refinanced the Hercules loan, the terms of which include a reduction in the current interest rate from 11.9% to 9.45%, an extension in the interest-only period by no less than 12 months, which could be extended up to a maximum of 24 months, assuming the achievement of specified milestones relating to the development of tivozanib, and an extension in the loan maturity from December 2019 to July 2021. As a consequence, we anticipate that interest expense in 2018 will decrease.

In 2016 as compared to 2015, interest expense, net decreased by $0.3 million principally attributable to the declining average outstanding balance on our loan with Hercules.

Provision for Income Taxes

	Years Ended December 31,			2017 / 2016 Comparison		2016 / 2015 Comparison	
	2017	2016	2015	$	%	$	%
	($ in thousands)						
Provision for Income Taxes	101	101	—	—	-%	101	100 %

We recorded a $0.1 million tax provision for foreign withholding taxes in each of the years ended December 31, 2017 and 2016 in connection with partnership payments from CANbridge. In March 2016, we received the $1.0 million upfront payment upon the execution of the collaboration and license agreement. In 2017, we received a total of $1.0 million in reimbursement payments related to manufacturing development activities conducted by us prior to the Effective Date of the collaboration and license agreement.

Contractual Obligations and Commitments

The following table summarizes our non-cancellable contractual obligations at December 31, 2017 (in thousands):

	Total	Less than 1 Year	1 to 3 Years	3 to 5 Years	More than 5 Years
Hercules loan agreement (1)	$26,318	$ 2,493	$17,738	$6,087	$ —
Clinical trial costs and contract research (2)	$20,802	$ 19,287	$1,515	—	—
Operating leases (3)	66	66	—	—	—
Total contractual obligations	$47,186	$ 21,846	$19,253	$6,087	$ —

(1) Includes scheduled interest payments and end of term payments totaling $1.6 million due in connection with the 2014 Amendment, 2016 Amendment and 2017 Loan Agreement.

(2) Clinical trial costs and contract research principally include contracts for human clinical trials and clinical drug manufacturing and distribution. In the event a contract is terminated prior to the planned completion, the amount paid under such contracts may be less than the amounts presented.

(3) We sublease our principal office facility at One Broadway in Cambridge, MA. Our lease arrangement is cancellable within 30 days' notice to our landlord. As a result, our operating lease obligation as of December 31, 2017 is the January 2018 rent payable to our landlord

(4) 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 upfront 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, we are required to make certain milestone payments upon the earlier of achievement of specified development and regulatory milestones or a specified date for the first indication, and upon the achievement of specified development and regulatory milestones for the second and third indications. 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 and have not included any additional amounts in the table above. For example, we would owe KHK a one-time milestone payment of $18.0 million, provided that we do not sublicense U.S. rights for tivozanib prior to obtaining a U.S. regulatory approval. In addition, we are required to make milestone payments to St. Vincent's Hospital, up to an aggregate total of $16.7 million, upon the earlier of achievement of specified development and regulatory milestones or a specified date for the first indication, and upon the achievement of specified development and regulatory milestones for the second and third 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.

(5) As discussed in Note 4 to our consolidated financial statements included elsewhere in this Annual Report on Form 10K, 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, three of the 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, and one agreement includes a $1.0 million license payment per product.

Liquidity and Capital Resources

We have financed our operations to date primarily through private placements and public offerings of our common stock and preferred stock, license fees, milestone payments and research and development funding from strategic partners, and loan proceeds. As of December 31, 2017, we had cash, cash equivalents and marketable securities of approximately $33.5 million. See “Operating Capital Requirements and Going Concern” below and Note 1 to the consolidated financial statements included elsewhere in this Annual Report on Form 10-K for a further discussion of our liquidity and the conditions and events which raise substantial doubt regarding our ability to continue as a going concern. Currently, our funds are invested in a U.S. government money market fund, 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,		
	2017	2016	2015
	(in thousands)		
Net cash used in operating activities	$(19,164)	$(31,066)	$(18,230)
Net cash used in investing activities	(10,402)	(764)	(6,316)
Net cash provided by (used in) financing activities	29,419	20,292	(1,126)
Net decrease in cash and cash equivalents	$(147)	$(11,538)	$(25,672)

Our operating activities used cash of $19.2 million, $31.1 million and $18.2 million in 2017, 2016 and 2015, respectively. Cash used in operations was due principally to our net loss adjusted for non-cash items and changes in working capital.

Our investing activities used cash of $10.4 million, $0.8 million and $6.3 million in 2017, 2016 and 2015, respectively. Cash used in investing activities was the net result of purchases of marketable securities, partially offset by the maturities of marketable securities.

Our financing activities provided cash of $29.4 million and $20.3 million in 2017 and 2016, respectively, and used cash of $1.1 million in 2015. In 2017, we raised approximately $29.5 million in net cash proceeds, including $15.4 million from an underwritten public offering of 34.5 million shares of our common stock, $8.8 million from sales of 6.5 million shares of our common stock under our at-the-market, or ATM, facility with FBR & Co., or FBR, (formerly MLV & Co. LLC), $5.0 million from additional borrowings under our Hercules Loan Agreement and $0.3 million from the issuance of 0.3 million shares of our common stock upon the exercise of 0.3 million PIPE warrants, offset by $0.1 million in debt issuance costs related to the 2017 Loan Agreement with Hercules. In 2016, we raised approximately $20.3 million in net cash proceeds, including $15.4 million in net proceeds from a private placement of 17,642,842 units, each including one share of our common stock and a warrant to purchase one share of our common stock, and $4.9 million in net proceeds from additional borrowings under our Hercules Loan Agreement. In 2015, we raised approximately $10.5 million in net proceeds from the sale of our common stock, including $10.2 million under our Sales Agreement with FBR and $0.3 million from the issuance of stock for stock-based compensation arrangements, offset by $11.6 million in principal payments under our Hercules Loan Agreement.

At-The-Market Issuance Sales Agreement with Leerink

On November 30, 2017, we filed a shelf registration statement on Form S-3 with the SEC, which we refer to as the 2017 Shelf. The 2017 Shelf (file No. 333-221873) was declared effective by the SEC on December 15, 2017 and covers the offering, issuance and sale from time to time of up to $200 million of our common stock, preferred stock, debt securities, warrants and/or units. The 2017 Shelf was filed to replace our then existing 2015 Shelf, which was terminated upon the 2017 Shelf being declared effective by the SEC on December 15, 2017.

In February 2018, we entered into an at-the-market issuance sales agreement, which we refer to as the Leerink Sales Agreement, with Leerink Partners LLC, or Leerink, pursuant to which we may issue and sell shares of our common stock from time to time up to

an aggregate amount of $50 million, at our option, through Leerink as our sales agent, with any sales of common stock through Leerink being made by any method that is deemed an “at-the-market” offering as defined in Rule 415 promulgated under the Securities Act. Any such shares of common stock will be sold pursuant to a prospectus supplement filed under the 2017 Shelf. We agreed to pay Leerink a commission of up to 3% of the gross proceeds of any sales of common stock pursuant to the Leerink Sales Agreement. At the time of filing this Annual Report on Form 10-K, no shares of our common stock have been sold under the Leerink Sales Agreement.

Public Offering

On March 31, 2017, we closed an underwritten public offering of 34.5 million shares of our common stock, including the exercise in full by the underwriter of its option to purchase 4.5 million shares, at the public offering price of $0.50 per share for gross proceeds of approximately $17.3 million. Certain of our executive officers and a director purchased an aggregate of 420,000 shares and an entity affiliated with New Enterprise Associates, a greater than 5% stockholder, purchased 6.0 million shares in this offering at the same public offering price per share as the other investors. The net offering proceeds to us were approximately $15.4 million after deducting underwriting discounts and estimated offering expenses payable by us. We sold these shares pursuant to the 2015 Shelf (as defined below).

Private Placement / PIPE Warrants

In May 2016, we entered into a securities purchase agreement with a select group of qualified institutional buyers, institutional accredited investors and accredited investors pursuant to which we sold 17,642,482 units, at a price of $0.965 per unit, for gross proceeds of approximately $17.0 million. Each unit consisted of one share of our common stock and a warrant to purchase one share of our common stock, which we refer to as the PIPE Warrants. The PIPE Warrants have an exercise price of $1.00 per share and are exercisable in any manner at any time for a period of five years from the date of issuance. Certain of our directors and executive officers purchased an aggregate of 544,039 units in this offering at the same price as the other investors. The net offering proceeds to us were approximately $15.4 million after deducting placement agent fees and other offering expenses payable by us. In July 2017, we issued to Hercules 259,067 shares of common stock upon its exercise of all of its PIPE Warrants, and we received approximately $0.3 million in cash proceeds. As of December 31, 2017, there were PIPE Warrants outstanding and exercisable for 17,383,415 shares of common stock. In January 2018, we issued 518,134 shares of our common stock upon exercise of PIPE Warrants and received approximately $0.5 million in cash proceeds.

At-The-Market Issuance Sales Agreement with FBR

In February 2015, we entered into an at-the-market issuance sales agreement, which we refer to as the FBR Sales Agreement, with FBR & Co. and MLV & Co. LLC, or together FBR, pursuant to which we issued and sold 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, with any sales of common stock through FBR being made by any method that is deemed an “at-the-market” offering as defined in Rule 415 promulgated under the Securities Act, pursuant to an effective shelf registration statement on Form S-3. We agreed to pay FBR a commission of up to 3% of the gross proceeds of any sales of common stock pursuant to the FBR Sales Agreement.

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 covered 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 then 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 FBR Sales Agreement to provide for the offering, issuance and sale of up to $15.0 million of our common stock under the 2015 Shelf. The prior at-the-market offering initiated under the original FBR Sales Agreement expired along with the 2012 Shelf. Through August 2015, we had sold approximately 5.9 million shares pursuant to the FBR Sales Agreement, as amended, resulting in proceeds of approximately $10.2 million, net of commissions and issuance costs. In June 2017, we sold approximately 6.5 million shares pursuant to the FBR Sales

Agreement, as amended, resulting in proceeds of approximately $8.8 million, net of commissions and issuance costs. The FBR Sales Agreement has expired.

Credit Facilities

On May 28, 2010, we entered into a loan and security agreement, or the First Loan Agreement, with Hercules. The First Loan Agreement was subsequently amended in March 2012, or the 2012 Amendment; September 2014, or the 2014 Amendment; May 2016, or the 2016 Amendment; and December 2017, or the 2017 Loan Agreement. Amounts borrowed under the 2012 Amendment were repaid in full in 2015.

Pursuant to the 2014 Amendment, we received additional loan proceeds from Hercules in the amount of $10.0 million and were not required to commence principal payments until May 1, 2016. An end-of-term payment of approximately $0.5 million continued to be due on January 1, 2018. This payment was made on the first business day of 2018.

Pursuant to the 2016 Amendment, we received additional loan proceeds from Hercules in May 2016, in the amount of $5.0 million, which increased the aggregate outstanding principal balance under the First Loan Agreement to $15.0 million. We were not required to commence principal payments on the $15.0 million loan until July 1, 2017, at which time we would have been required to make 30 equal monthly payments of principal and interest through December 2019. An end-of-term payment of approximately $0.2 million is due on December 1, 2019. The 2016 Amendment included a financial covenant that required us to maintain an unrestricted cash position greater than or equal to $10.0 million through the date of completion of our TIVO-3 trial with results that were satisfactory to Hercules.

Under the 2016 Amendment, from March 1, 2017 through June 30, 2017, we could draw down an additional $5.0 million in funding upon confirmation by Hercules, in its reasonable discretion, that we achieved the following conditions: (i) satisfactory developmental progression on a minimum of two (2) clinical programs (other than the TIVO-3 trial) that are either managed directly by us or funded, in whole or in part, by us and (ii) having an unrestricted cash position greater than or equal to $25.0 million on the date of the draw down request. If we drew down the additional $5.0 million in funding, the commencement of principal payments on the aggregate $20.0 million loan balance would be deferred by six months from July 1, 2017 until January 1, 2018.

In June 2017, pursuant to the 2016 Amendment, we received the additional $5.0 million in loan proceeds from Hercules, which increased the aggregate outstanding principal balance under the First Loan Agreement to $20.0 million and a six-month deferral in the commencement of principal payments. There was no change in the loan maturity date of December 2019. We were not required to commence principal payments on the $20.0 million loan until January 1, 2018, at which time we would have been required to make 23 equal monthly payments of principal and interest, in the approximate amount of $0.8 million, through November 2019 and an approximate $5.3 million payment of principal and interest in December 2019, which represented approximately 26% of the entire $20.0 million loan. An additional end-of-term payment of approximately $0.1 million is due on December 1, 2019, which increased the total end-of-term payments under the 2016 Amendment to $0.3 million.

In December 2017, we entered into an amended and restated loan and security agreement with Hercules to refinance the First Loan Agreement, which we refer to as the 2017 Loan Agreement. The proceeds of the new loan facility were used to retire the existing $20.0 million in secured debt outstanding under the First Loan Agreement. Per the terms of the 2017 Loan Agreement, the new loan facility has a 42-month maturity from closing, no financial covenants, a lower interest rate and an interest-only period of no less than 12 months, which could be extended up to a maximum of 24 months, assuming the achievement of specified milestones relating to the development of tivozanib. Per the 2017 Loan Agreement, Hercules did not receive any additional warrants to purchase shares of our common stock and no longer has the option, subject to our written consent, to participate in our future equity financings up to $2.0 million through the purchase of our common stock either with cash or through the conversion of outstanding principal under the loan.

Pursuant to the 2017 Loan Agreement, the loan maturity date has been revised from December 2019 to July 2021. We are not required to make principal payments until February 1, 2019, at which time we will be required to make 29 equal monthly payments of principal and interest, in the approximate amount of $0.8 million through July 2021. An additional end-of-term payment of approximately $0.8 million is due on July 1, 2021, which increases the total end-of-term payments under the 2014 Amendment, 2016 Amendment and 2017 Loan Agreement to approximately $1.6 million. The end-of-term payments under the 2014 Amendment, in the approximate amount of $0.5 million, and the 2016 Amendment, in the amount of $0.3 million, continue to be due on their original due dates of January 1, 2018 and December 1, 2019, respectively. The financial covenant per the 2016 Amendment to maintain an unrestricted cash position greater than or equal to $10.0 million through the date of completion of our TIVO-3 trial with results that are satisfactory to Hercules has been removed. Per the 2017 Loan Agreement, the current interest rate has been decreased from 11.9% to 9.45%.

The interest-only period could be extended by two 6-month deferrals upon the achievement of specified milestones relating to the development of tivozanib, including (i) on or prior to September 30, 2018, we have received positive data with respect to our TIVO-3 trial for the treatment of RCC for patients in the third-line setting which positive data supports the filing for a new drug application with the Food and Drug Administration, or FDA, subject to confirmation by Hercules at its reasonable discretion, and (ii) on or prior to June 28, 2019, we have received approval from the FDA for our tivozanib product for the treatment of RCC for patients in the third-line setting, subject to confirmation by Hercules at its reasonable discretion.

We must make interest payments on the principal balance of the loan each month it remains outstanding. Per annum interest is payable on the loan balance at the greater of 9.45% and an amount equal to 9.45% plus the prime rate minus 4.75%, as determined daily, provided however, that the per annum interest rate shall not exceed 15.0%. Our annual interest rate as of December 31, 2017 was 9.45%.

We have determined that the risk of subjective acceleration under the material adverse events clause included in the 2017 Loan 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, 2017, we are in compliance with all of the loan covenants and, through

the date of this filing, the lenders have not asserted any events of default under the loan. We do not believe that there has been a material adverse change as defined in the 2017 Loan Agreement. 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 First Loan Agreement.

Operating Capital Requirements and Going Concern

We have devoted substantially all of our resources to our drug development efforts, comprised of research and development, manufacturing, conducting clinical trials for our product candidates, protecting our intellectual property and general and administrative functions relating to these operations. Our future success is dependent on our ability to develop our product candidates and ultimately upon our ability to attain profitable operations. 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 preclinical and clinical stage assets. We will require substantial additional 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 aggregate remaining costs for the TIVO-3 trial, including drug supply and distribution, could be in the range of $9.0 million to $12.0 million through 2019. We estimate that the overall cost for the TIVO-3 trial, including drug supply and distribution, could be in the range of $44.0 million to $47.0 million. Our aggregate remaining costs for the TiNivo trial, including tivozanib drug supply and distribution, could be in the range of $1.5 million to $2.0 million through 2019. We estimate that the overall cost for the TiNivo trial, including drug supply and distribution, could be in the range of $4.0 million to $4.5 million, of which EUSA is responsible for approximately 50% of these costs up to a maximum of $2.0 million. BMS is providing nivolumab for the study. 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.

During the year ended December 31, 2017, we have raised approximately $29.5 million in net cash proceeds, including $15.4 million from an underwritten public offering of 34.5 million shares of our common stock in March 2017, $8.8 million from sales of 6.5 million shares of our common stock under our Sales Agreement with FBR and $5.0 million from additional borrowings under our First Loan Agreement with Hercules in June 2017 and $0.3 million in July 2017 from the issuance of 0.3 million shares of our common stock upon the exercise of 0.3 million PIPE Warrants issued in connection with the May 2016 private placement.

As of December 31, 2017, we had approximately $33.5 million in existing cash, cash equivalents and marketable securities, working capital of $18.1 million and an accumulated deficit of $587.0 million. In the first quarter of 2018 to-date, we have raised an additional approximate $1.9 million in net funding, including approximately $0.5 million received in January 2018 related to the exercise of 0.5 million PIPE Warrants and $1.4 million in net partnership-related funding in connection with the $2.0 million milestone payment by EUSA for the February 2018 reimbursement approval by the NICE for RCC in the UK that was received in March 2018, net of the corresponding 30% sub-license fee due to KHK. Based on these available cash resources, we believe that we do not have sufficient cash on hand to support current operations for at least the next twelve months from the date of filing this Annual Report on Form 10-K. This condition raises substantial doubt about our ability to continue as a going concern.

Our plans to address this condition include pursuing one or more of the following options to secure additional funding, none of which can be guaranteed or are entirely within our control:

- Earn royalty payments pursuant to our license agreement with EUSA. In August 2017, EUSA obtained marketing approval from the EMA for tivozanib (FOTIVDA) for the treatment of RCC.
-

- Earn milestone payments pursuant to our collaboration and license agreements or restructure / monetize existing potential milestone and/or royalty payments under those collaboration and license agreements.

For example, pursuant to our license agreement with EUSA, we are entitled to receive up to an additional $8.0 million in milestone payments of $2.0 million per country upon reimbursement approval for RCC, if any, in each of France, Germany, Italy and Spain, and an additional $2.0 million milestone payment for the grant of marketing approval, if any, in three of the five following countries: Argentina, Australia, Brazil, South Africa and Venezuela. We are also eligible to receive an additional research and development reimbursement payment from EUSA of fifty percent 50% of the total costs for our TIVO-3 trial, up to $20.0 million, if EUSA elects to opt-in to that study.

- Raise funding through the possible additional sales of our common stock, including public or private equity financings and / or sales of our common stock under our Leerink Sales Agreement.
- Partner our AV-353 platform to secure potential additional non-dilutive funds and advance development of the AV-353 platform for the potential treatment of PAH.

There can be no assurance, however, that we will receive cash proceeds from any of these potential resources or to the extent cash proceeds are received those proceeds would be sufficient to support our current operating plan for at least the next twelve months from the date of filing this Annual Report on Form 10-K.

Pursuant to the requirements of Accounting Standards Codification (ASC) 205-40, Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern, management must evaluate whether there are conditions or events, considered in the aggregate, that raise substantial doubt about our ability to continue as a going concern within one year after the date that the financial statements are issued. This evaluation initially does not take into consideration the potential mitigating effect of management's plans that have not been fully implemented as of the date the financial statements are issued. When substantial doubt exists under this methodology, management evaluates whether the mitigating effect of its plans sufficiently alleviates substantial doubt about our ability to continue as a going concern. The mitigating effect of management's plans, however, is only considered if both (1) it is probable that the plans will be effectively implemented within one year after the date that the financial statements are issued, and (2) it is probable that the plans, when implemented, will mitigate the relevant conditions or events that raise substantial doubt about the entity's ability to continue as a going concern within one year after the date that the financial statements are issued.

Under ASC 205-40, the future receipt of potential funding from our collaborators and other resources cannot be considered probable at this time because none of our current plans have been finalized at the time of filing this Annual Report on Form 10-K and the implementation of any such plan is not probable of being effectively implemented as none of the plans are entirely within our control. Accordingly, substantial doubt is deemed to exist about our ability to continue as a going concern within one year after the date these financial statements are issued.

We believe that our approximate $33.5 million in cash, cash equivalents and marketable securities at December 31, 2017, along with the additional approximate $1.9 million in net funding raised in the first quarter of 2018 to-date, as described above, would allow us to fund our planned operations into the first quarter of 2019. This estimate assumes no receipt of additional milestone payments from our partners or additional related payments of potential licensing milestones to third parties, no funding from new partnership agreements, no equity financings, no debt financings, no sales of equity under our Leerink Sales Agreement and no additional sales of equity through the exercise of our PIPE Warrants. Accordingly, the timing and nature of activities contemplated for the remainder of 2018 and thereafter will be conducted subject to the availability of sufficient financial resources.

There are numerous risks and uncertainties associated with research, development and commercialization of pharmaceutical products. Accordingly, our future funding requirements may vary from our current expectations and 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 of 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 Hercules Loan Agreement or under any other agreements with third parties;
- the outcome of legal actions against us, including the current lawsuits described in Part II, Item 1 of this report under the heading "Legal Proceedings";
- 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;
- the timing, receipt and amount of sales of, or royalties on, our future products, if any; and

- our ability to continue as a going concern.

We will require additional funding to extend our planned operations. 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. 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. If we are unable to raise substantial additional capital in the near term, whether on terms that are acceptable to us, or at all then 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, 2017, we had cash, cash equivalents and marketable securities of $33.5 million. Currently, our funds are invested in a U.S. government money market fund, corporate debt securities, including commercial paper, and U. S. government agency securities. We do not hold any of these instruments for trading or speculative purposes. Our funds are invested in accordance with investment guidelines as approved by our Board of Directors.

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 and marketable securities 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 loans payable are subject to interest rate risk. As of December 31, 2017, our aggregate principal balance outstanding on our Hercules Loan Agreement was $20.0 million. Per annum interest is payable on the principal balance of the loan each month it remains outstanding at the greater of 9.45% and an amount equal to 9.45% plus the prime rate minus 4.75% as determined daily, provided however, that the per annum interest rate shall not exceed 15.0%. As of December 31, 2017, the interest rate was 9.45%. For every 1% increase in the prime rate over 4.75%, given the amount of debt outstanding under the Hercules Loan Agreement as of December 31, 2017, we would have an increase in future annual cash outflows of approximately $0.2 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.

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ITEM 8.Financial Statements and Supplementary Data

AVEO PHARMACEUTICALS, INC.

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REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Stockholders and the Board of Directors of AVEO Pharmaceuticals, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of AVEO Pharmaceuticals, Inc. (the "Company") as of December 31, 2017 and 2016, the related consolidated statements of operations, comprehensive loss, stockholders' equity (deficit), and cash flows for each of the three years in the period ended December 31, 2017, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2017 and 2016, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2017, in conformity with U.S. generally accepted accounting principles.

We have also audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the Company's internal control over financial reporting as of December 31, 2017, 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 13, 2018 expressed an unqualified opinion thereon.

The Company's Ability to Continue as a Going Concern

The accompanying consolidated financial statements have been prepared assuming that the Company will continue as a going concern. As discussed in Note 1 to the financial statements, the Company will require additional capital to fund its current operating plan, and has stated that substantial doubt exists about the Company's ability to continue as a going concern. Management's evaluation of the events and conditions and management's plans regarding these matters are also described in Note 1. The consolidated financial statements do not include any adjustments that might result from the outcome of this uncertainty.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures include examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2003.

Boston, Massachusetts

March 13, 2018

AVEO PHARMACEUTICALS, INC.

Consolidated Balance Sheets

(In thousands, except par value amounts)

	December 31, 2017	December 31, 2016
Assets		
Current assets:		
Cash and cash equivalents	$14,949	$15,096
Marketable securities	18,576	8,252
Accounts receivable	402	1,027
Insurance recovery (Note 15)	15,000	—
Clinical trial retainers	1,027	1,702
Other prepaid expenses and other current assets	229	238
Total current assets	50,183	26,315
Clinical trial retainers	—	940
Other assets	15	30
Total assets	$50,198	$27,285
Liabilities and stockholders’ deficit		
Current liabilities:		
Accounts payable	$2,436	$2,186
Accrued clinical trial costs and contract research	8,321	3,998
Other accrued liabilities	2,458	1,531
Loans payable, net of discount	—	2,124
Deferred revenue	395	510
Deferred research and development reimbursements	901	—
Estimated settlement liability (Note 15)	17,073	—
Other liabilities (Note 6)	540	—
Total current liabilities	32,124	10,349
Loans payable, net of current portion and discount	18,477	11,879
Deferred revenue	1,302	1,697
Deferred research and development reimbursements	222	—
PIPE warrant liability (Note 7)	37,746	4,593
Other liabilities (Note 6)	1,090	690
Total liabilities	90,961	29,208
Stockholders' deficit:		
Preferred stock, $.001 par value: 5,000 shares authorized at each of December 31, 2017 and 2016; no shares issued and outstanding at each of December 31, 2017 and 2016	—	—
Common stock, $.001 par value: 250,000 shares authorized and 118,325 shares issued and outstanding at December 31, 2017; 200,000 shares authorized and 75,863 shares issued and outstanding at December 31, 2016	118	76
Additional paid-in capital	546,092	519,911
Accumulated other comprehensive income (loss)	(4)	6
Accumulated deficit	(586,969)	(521,916)
Total stockholders’ deficit	(40,763)	(1,923)

Total liabilities and stockholders' deficit	$50,198	$27,285

See accompanying notes.

AVEO PHARMACEUTICALS, INC.

Consolidated Statements of Operations

(In thousands, except per share amounts)

	Year Ended December 31,		
	2017	2016	2015
Collaboration and licensing revenue	$7,579	$2,515	$19,024
Operating expenses:			
Research and development	25,179	23,703	12,875
General and administrative	9,138	8,205	10,217
Settlement costs (Note 15)	2,073	—	4,000
Restructuring and lease exit	—	—	4,358
	36,390	31,908	31,450
Loss from operations	(28,811)	(29,393)	(12,426)
Other income (expense), net:			
Interest expense, net	(2,373)	(1,949)	(2,286)
Change in fair value of warrant liability	(33,740)	4,751	—
Other (expense) income	—	(195)	(289)
Other income (expense), net	(36,113)	2,607	(2,575)
Net loss before provision for income taxes	(64,924)	(26,786)	(15,001)
Provision for income taxes	(101)	(101)	—
Net loss	$(65,025)	$(26,887)	$(15,001)
Basic and diluted net loss per share:			
Net loss per share	$(0.61)	$(0.39)	$(0.27)
Weighted average number of common shares outstanding	105,930	69,268	55,701

See accompanying notes.

AVEO PHARMACEUTICALS, INC.

Consolidated Statements of Comprehensive Loss

(In thousands)

	Year Ended December 31,		
	2017	2016	2015
Net loss	$(65,025)	$(26,887)	$(15,001)
Other comprehensive income (loss):			
Unrealized gain (loss) on available-for-sale securities	(10)	9	(3)
Comprehensive loss	$(65,035)	$(26,878)	$(15,004)

See accompanying notes.

AVEO PHARMACEUTICALS, INC.

Consolidated Statements of Stockholders' (Deficit) Equity

(In thousands)

	Common Shares					
	Shares	Par Value	Additional Paid-in Capital	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Total Stockholders' (Deficit) Equity
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 costs 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
Issuance of common stock and warrants in a private placement, excluding to related parties (net of issuance costs of $1.6 million)	17,098	17	14,829	—	—	14,846
Issuance of common stock and warrants to related parties	544	1	524	—	—	525
Stock-based compensation expense related to equity-classified awards	—	—	999	—	—	999
Issuance of warrants in connection with a private placement	—	—	(9,344)	—	—	(9,344)
Issuance of warrants in connection with loans payable	—	—	667	—	—	667
Exercise of stock options	39	—	33	—	—	33
Issuance of common stock under employee stock purchase plan	—	—	2	—	—	2
Change in unrealized gain (loss) on investments	—	—	—	9	—	9
Net loss	—	—	—	—	(26,887)	(26,887)
Balance at December 31, 2016	75,863	$ 76	$ 519,911	$ 6	$ (521,916)	$ (1,923)
	—	—	28	—	(28)	—

Retrospective adjustment related to adoption of new stock option forfeiture standard						
Issuance of common stock in a public offering, excluding to related parties (net of issuance costs of $1.8 million)	28,080	28	12,191	—	—	12,219
Issuance of common stock to related parties	6,420	6	3,204	—	—	3,210
Issuance of common stock from at-the-market sales agreement (net of issuance costs of $180)	6,470	6	8,810	—	—	8,816
Stock-based compensation expense related to equity-classified awards	—	—	1,089	—	—	1,089
Issuance of common stock in connection with warrant exercises	1,475	2	257	—	—	259
Reduction in PIPE warrant liability in connection with warrant exercises	—	—	587	—	—	587
Exercise of stock options	17	—	15	—	—	15
Change in unrealized gain (loss) on investments	—	—	—	(10)	—	(10)
Net loss	—	—	—	—	(65,025)	(65,025)
Balance at December 31, 2017	118,325	$ 118	$ 546,092	$ (4)	$ (586,969)	$ (40,763)

See accompanying notes.

AVEO PHARMACEUTICALS, INC.

Consolidated Statements of Cash Flows

(In thousands)

	Year Ended December 31,		
	2017	2016	2015
Operating activities			
Net loss	$(65,025)	$(26,887)	$(15,001)
Adjustments to reconcile net loss to net cash used in operating activities:			
Impairment of property and equipment	—	—	232
Depreciation and amortization	—	30	9,567
Net loss (gain) on disposal of fixed assets	—	—	253
Stock-based compensation	1,089	999	1,132
Non-cash interest expense	514	465	655
Non-cash change in fair value of PIPE warrant liability	33,740	(4,751)	—
Non-cash charge for settlement warrants (Note 15)	2,073	—	—
Amortization of premium and discount on investments	68	14	34
Changes in operating assets and liabilities:			
Restricted Cash	—	—	2,997
Accounts receivable	625	3,614	(2,300)
Insurance recovery (Note 15)	(15,000)	—	—
Prepaid expenses and other current assets	684	(340)	(116)
Other noncurrent assets	955	(827)	96
Accounts payable	250	760	(1,820)
Accrued clinical trial costs and contract research	4,323	2,032	(3,562)
Other accrued liabilities	927	(609)	(1,627)
Settlement liability (Note 15)	15,000	(4,000)	4,000
Deferred revenue	(510)	(1,488)	2,927
Deferred research and development reimbursements	1,123	—	—
Lease exit obligation	—	—	(5,206)
Deferred rent	—	—	(10,569)
Other liabilities	—	(78)	78
Net cash used in operating activities	(19,164)	(31,066)	(18,230)
Investing activities			
Purchases of marketable securities	(34,852)	(29,421)	(19,085)
Proceeds from maturities and sales of marketable securities	24,450	28,664	11,550
Purchases of property and equipment	—	(7)	(22)
Proceeds from sale of property and equipment	—	—	1,241
Net cash used in investing activities	(10,402)	(764)	(6,316)
Financing activities			
Proceeds from issuance of common stock and warrants, net of issuance costs	21,294	14,846	10,218
Proceeds from issuance of common stock and warrants to related parties	3,210	525	—
Proceeds from issuance of loan payable and warrants	5,000	5,000	—
Proceeds from issuance of stock for stock-based compensation arrangements	15	36	268
Payments of debt issuance costs	(100)	(115)	—
Principal payments on loans payable	—	—	(11,612)
Net cash provided by (used in) financing activities	29,419	20,292	(1,126)

Net decrease in cash and cash equivalents	(147)	(11,538)	(25,672)
Cash and cash equivalents at beginning of period	15,096	26,634	52,306
Cash and cash equivalents at end of period	$14,949	$15,096	$26,634
Supplemental cash flow information			
Cash paid for interest	$2,069	$1,539	$1,983
Non-cash financing activity			
Fair value of warrants issued in connection with long term debt	$—	$667	$—
Fair value of warrants issued in connection with private placement	$—	$9,344	$—

See accompanying notes.

AVEO Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements

December 31, 2017

(1) Organization

AVEO Pharmaceuticals, Inc. (the "Company") is a biopharmaceutical company dedicated to advancing a broad portfolio of targeted medicines for oncology and other areas of unmet medical need. The Company's strategy is to retain North American rights to its oncology portfolio while securing partners in development and commercialization outside of North America. The Company is working to develop and commercialize its lead candidate tivozanib in North America as a treatment for renal cell carcinoma ("RCC"). The Company has entered into partnerships to fund the development and commercialization of its preclinical and clinical stage assets, including AV-203 and ficlatuzumab in oncology, AV-380 in cachexia, and tivozanib in oncology outside of North America. Tivozanib (FOTIVDA®) is approved in the European Union, as well as Norway and Iceland, for the first-line treatment of adult patients with advanced RCC ("aRCC") and for adult patients who are vascular endothelial growth factor receptor ("VEGFR") and mTOR pathway inhibitor-naïve following disease progression after one prior treatment with cytokine therapy for aRCC. The Company is currently seeking a partner to develop the AV-353 platform, a preclinical asset, worldwide for the potential treatment of pulmonary arterial hypertension ("PAH").

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

Liquidity and Going Concern

The Company has financed its operations to date primarily through private placements and public offerings of its common stock and preferred stock, license fees, milestone payments and research and development funding from strategic partners, and loan proceeds. The Company has devoted substantially all of its resources to its drug development efforts, comprising research and development, manufacturing, conducting clinical trials for its product candidates, protecting its intellectual property and general and administrative functions relating to these operations. The future success of the Company is dependent on its ability to develop its product candidates and ultimately upon its ability to attain profitable operations. As of December 31, 2017, the Company had cash, cash equivalents and marketable securities totaling approximately $33.5 million, working capital of $18.1 million and an accumulated deficit of $587.0 million.

During the year ended December, 2017, the Company raised approximately $29.5 million in net cash proceeds, including $15.4 million from an underwritten public offering of 34.5 million shares of its common stock in March 2017, $8.8 million from sales of 6.5 million shares of its common stock under an at-the-market issuance sales agreement (the "Sales Agreement") with FBR & Co. and MLV & Co. LLC (together "FBR") and $5.0 million in additional borrowings under its 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") in June 2017,

and $0.3 million in July 2017 from the issuance of 0.3 million shares of its common stock upon the exercise of 0.3 million warrants issued in connection with the May 2016 private placement (the “PIPE Warrants”). Refer to Notes 6 and 7.

The Company is subject to a number of risks, including the need for substantial additional capital for clinical research and product development. As of December 31, 2017, the Company had approximately $33.5 million in existing cash, cash equivalents and marketable securities. In the first quarter of 2018 to-date, the Company has raised an additional approximate $1.9 million in net funding, including approximately $0.5 million received in January 2018 related to the exercise of 0.5 million PIPE Warrants and $1.4 million in net partnership-related funding in connection with the $2.0 million milestone payment by EUSA Pharma (UK) Limited (“EUSA”) for the February 2018 reimbursement approval by the National Institute for Health and Care Excellence (the “NICE”) for RCC in the United Kingdom that was received in March 2018, net of the corresponding 30% sub-license fee due to Kyowa Hakko Kirin Co., Ltd. (formerly Kirin Brewery Co., Ltd.) (“KHK”). Refer to Note 4. Based on these available cash resources, the Company does not have sufficient cash on hand to support current operations for at least the next twelve months from the date of filing this Annual Report on Form 10-K. This condition raises substantial doubt about the Company’s ability to continue as a going concern.

The Company's plans to address this condition include pursuing one or more of the following options to secure additional funding, none of which can be guaranteed or are entirely within our control:

- Earn royalty payments pursuant to the license agreement with EUSA. In August 2017, EUSA obtained marketing approval from the European Medicines Agency (the "EMA") for tivozanib (FOTIVDA) for the treatment of RCC.
- Earn milestone payments pursuant to the collaboration and license agreements described in Note 4 or restructure / monetize existing potential milestone and/or royalty payments under those collaboration and license agreements.

Pursuant to the Company's license agreement with EUSA, the Company is entitled to receive up to an additional $8.0 million in milestone payments of $2.0 million per country upon reimbursement approval for RCC, if any, in each of France, Germany, Italy and Spain, and an additional $2.0 million milestone payment for the grant of marketing approval, if any, in three of the five following countries: Argentina, Australia, Brazil, South Africa and Venezuela. The Company is also eligible to receive an additional research and development reimbursement payment from EUSA of fifty percent (50%) of the total costs for the Company's TIVO-3 phase 3 study in third-line RCC, up to $20.0 million, if EUSA elects to opt-in to that study

- Raise funding through the possible additional sales of the Company's common stock, including public or private equity financings and / or sales of the Company's common stock under the at-the-market-issuance sales agreement (the "Leerink Sales Agreement") with Leerink Partners LLC ("Leerink"), as discussed in Note 7.
- Partner AV-353 to secure potential additional non-dilutive funds and advance development of the AV-353 platform for the potential treatment of PAH.

There can be no assurance, however, that the Company will receive cash proceeds from any of these potential resources or to the extent cash proceeds are received those proceeds would be sufficient to support its current operating plan for at least the next twelve months from the date of filing this Annual Report on Form 10-K.

Pursuant to the requirements of Accounting Standards Codification (ASC) 205-40, Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern management must evaluate whether there are conditions or events, considered in the aggregate, that raise substantial doubt about the Company's ability to continue as a going concern within one year after the date that the financial statements are issued. This evaluation initially does not take into consideration the potential mitigating effect of management's plans that have not been fully implemented as of the date the financial statements are issued. When substantial doubt exists under this methodology, management evaluates whether the mitigating effect of its plans sufficiently alleviates substantial doubt about the Company's ability to continue as a going concern. The mitigating effect of management's plans, however, is only considered if both (1) it is probable that the plans will be effectively implemented within one year after the date that the financial statements are issued, and (2) it is probable that the plans, when implemented, will mitigate the relevant conditions or events that raise substantial doubt about the entity's ability to continue as a going concern within one year after the date that the financial statements are issued.

Under ASC 2015-40, the future receipt of potential funding from the Company's collaborators and other resources cannot be considered probable at this time because none of the Company's current plans have been finalized at the time of filing this Annual Report on Form 10-K and the implementation of any such plan is not probable of being effectively implemented as none of the plans are entirely within the Company's control. Accordingly, substantial doubt is deemed to exist about the Company's ability to continue as a going concern within one year after the date these financial statements are issued.

The Company believes that its approximate $33.5 million in cash, cash equivalents and marketable securities at December 31, 2017, along with the additional approximate $1.9 million in net funding raised in the first quarter of 2018 to-date, as described above, would allow it to fund its planned operations into the first quarter of 2019. This estimate assumes no receipt of additional milestone payments from its partners or additional related payments of potential licensing milestones to third parties, no funding from new partnership agreements, no equity financings, no debt financings, no sales of equity under its Leerink Sales Agreement and no additional sales of equity through the exercise of the PIPE Warrants. Accordingly, the timing and nature of activities contemplated for the remainder of

2018 and thereafter will be conducted subject to the availability of sufficient financial resources.

If the Company is unable to obtain sufficient capital to continue to advance its programs, the Company would be forced to delay, reduce or eliminate its research and development programs and any future commercialization efforts.

The accompanying financial statements have been prepared on a going concern basis, which contemplates the realization of assets and satisfaction of liabilities in the ordinary course of business. The financial statements do not include any adjustments relating to the recoverability and classification of recorded asset amounts or the amounts and classification of liabilities that might result from the outcome of the uncertainties described above.

(2) Basis of Presentation

These consolidated financial statements include the accounts of the Company and its wholly-owned subsidiaries, AVEO Pharma Limited and AVEO Securities Corporation. The Company has eliminated all significant intercompany accounts and transactions in consolidation.

Certain reclassifications have been made to prior periods to conform to current period presentation. Reclassification of prior year amounts have been made to separately present settlement costs from general and administrative expenses in the consolidated statements of operations. There was no impact on total operating expenses or net income (loss) resulting from these reclassifications.

(3) Significant Accounting Policies

Revenue Recognition

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

The Company analyzes its collaboration arrangements to assess whether they are within the scope of ASC 808 to determine whether such arrangements involve joint operating activities performed by parties that are both active participants in the activities and exposed to significant risks and rewards dependent on the commercial success of such activities. This assessment is performed throughout the life of the arrangement based on changes in the responsibilities of all parties in the arrangement. For collaboration arrangements that are deemed to be within the scope of ASC 808, the Company first determines which elements of the collaboration are deemed to be within the scope of ASC 808 and those that are more reflective of a vendor-customer relationship and therefore within the scope of ASC 605. The Company's policy is to recognized amounts received from collaborators in connection with joint operating activities that are within the scope of ASC 808 as a reduction to research and development expense.

When evaluating multiple element arrangements under ASC 605, 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, upfront 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 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.

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 internal costs for salaries, bonuses, benefits, stock-based compensation, facilities, and research-related overhead, and external costs for clinical trials, drug manufacturing and distribution, license fees, consultants and other contracted services.

Warrants Issued in Connection with Private Placement

In May 2016, the Company issued PIPE warrants to purchase an aggregate of 17,642,482 shares of common stock in connection with a private placement financing and recorded the warrants as a liability (the “PIPE Warrants”). The Company accounts for warrant instruments that either conditionally or unconditionally obligate the issuer to transfer assets as liabilities regardless of the timing of the redemption feature or price, even though the underlying shares may be classified as permanent or temporary equity. As of December 31, 2017, PIPE Warrants exercisable for 259,067 shares of common stock had been exercised and PIPE Warrants exercisable for 17,383,415 shares of common stock were outstanding. In January 2018, PIPE Warrants with respect to 518,134 shares of common stock underlying such PIPE Warrants were exercised, and the Company issued 518,134 shares of its common stock and received approximately $0.5 million in cash proceeds. Refer to Note 7, “Common Stock—Private Placement / PIPE Warrants” for further discussion of the private placement financing.

The PIPE Warrants contain a provision giving the warrant holder the option to receive cash, equal to the fair value of the remaining unexercised portion of the warrant, as cash settlement in the event that there is a fundamental transaction (contractually defined to include various merger, acquisition or stock transfer activities). Due to this provision, ASC 480, Distinguishing Liabilities from Equity requires that these warrants be classified as a liability and not as equity. Accordingly, the Company recorded a warrant liability in the amount of approximately $9.3 million upon issuance of the PIPE Warrants. The fair value of these warrants has been determined using the Black-Scholes pricing model. These warrants are subject to revaluation at each balance sheet date and any changes in fair value are recorded as a non-cash gain or (loss) in the Statement of Operations as a component of other income (expense), net until the earlier of their exercise or expiration or upon the completion of a liquidation event. Upon exercise, the PIPE Warrants are subject to revaluation just prior to the date of the warrant exercise and any changes in fair value are recorded as a non-cash gain or (loss) in the Statement of Operations as a component of other income (expense), net and the corresponding reduction in the warrant liability is recorded as additional paid-in capital in the Balance Sheet as a component of stockholder's equity. The Company recorded a non-cash loss of approximately $33.7 million in the year ended December 31, 2017 and a non-cash gain of approximately $4.8 million in the year ended December 31, 2016 in its Statement of Operations attributable to the increases and decreases in the fair value of the warrant liability that resulted from higher stock prices as of December 31, 2017 and lower stock prices as of December 31, 2016 relative to prior periods. In the year ended December 31, 2017, the Company recorded a reduction in the warrant liability, with a corresponding increase to additional paid-in capital, of approximately $0.6 million attributable to warrant exercises in the third quarter of 2017.

The following table rolls forward the fair value of the Company's PIPE warrant liability, the fair value of which is determined by Level 3 inputs for the year ended December 31, 2017 (in thousands):

Issuance of warrants on May 13, 2016	$9,344
Decrease in fair value	(4,751)
Fair value at December 31, 2016	$4,593
Increase in fair value	33,740
Reduction in warrant liability for PIPE Warrant exercises	(587)
Fair value at December 31, 2017	$37,746

The key assumptions used to value the PIPE Warrants were as follows:

	Original Issuance	December 31, 2016	December 31, 2017
Expected price volatility	76.25%	78.18%	84.86%
Expected term (in years)	5.00	4.50	3.50
Risk-free interest rates	1.22%	1.93%	2.09%
Stock price	$0.89	$0.54	$2.79
Dividend yield	—	—	—

Potential Class Action Settlement

In December 2017, the Company entered into a binding memorandum of understanding (the "MOU") with class representatives Bob Levine and William Windham (the "Plaintiffs"), regarding the settlement of a securities class action lawsuit (the "Class Action") filed in 2013 and pending in the United States District Court for the District of Massachusetts (the "District Court") against us and certain of our former officers (Tuan Ha-Ngoc, David Johnston, and William Slichenmyer, together, the "Individual Defendants"), In re AVEO Pharmaceuticals, Inc. Securities Litigation et al. , No. 1:13-cv-11157-DJC. As previously disclosed, the Class Action was purportedly brought on behalf of stockholders who purchased our common stock between May 16, 2012 and May 1, 2013 (the "Class").

In December 2017, upon entering into the MOU, this settlement became estimable and probable. Accordingly, the Company recorded an estimated $17.1 million contingent liability, including $15.0 million for the cash portion of the settlement with a corresponding insurance recovery for the 100% portion to be paid directly by certain of the Company's insurance carriers, and an approximate $2.1 million estimate for the fair value on December 31, 2017 of 2.0 million warrants to purchase shares of its common stock exercisable from the date of issue until the expiration of a one-year period after the date of issue at an exercise price equal to the closing price on December 22, 2017, the trading day prior to the execution of the MOU, which was $3.00 per share ("the Settlement Warrants") with a corresponding non-cash charge to the Statement of Operations as a component of operating expenses. In February 2018, the insurance carriers funded the settlement escrow account related to the $15.0 million cash portion of the settlement.

The settlement is subject to the execution of a definitive settlement agreement, notice to the Class, and final approval of the District Court and shall be effective on the date (the "Effective Date") on which all of the following circumstances have occurred:

(a) a final judgment containing the requisite release of claims has been entered by the District Court ("Final Judgment"); (b) no appeal is pending with respect to the Final Judgment; (c) the Final Judgment has not been reversed, modified, vacated or amended; (d) the time to file any appeal from the Final Judgment has expired without the filing of an appeal or an order dismissing the appeal or affirming the Final Judgment has been entered, and any time to file a further appeal (including a writ of certiorari or for reconsideration of the appeal) has expired; and (e) the MOU and any settlement agreement with respect to the claims released in the Final Judgment have not expired or been terminated. The Company as agreed to use its best efforts to issue and deliver the Settlement Warrants within ten business days following the Effective Date. In January 2018, the Company entered into a stipulation of settlement agreement (the "Stipulation") that was preliminarily approved by the District Court in February 2018. A hearing by the District Court for final approval of the Stipulation has been scheduled for May 30, 2018. Refer to Note 15, "Legal Proceedings" for further discussion of this class action settlement.

The estimated fair value of the Settlement Warrants to be issued on the Effective Date has been determined using the Black-Scholes pricing model. The estimated fair value of the Settlement Warrants to be issued on the Effective Date are subject to revaluation at each balance sheet date and any changes in fair value are recorded as a non-cash gain or (loss) in the Statement of Operations as a component of operating expenses until the Settlement Warrants are issued, at which point they will be recorded as equity or as a liability based upon the issuance terms

The key assumptions used to estimate the fair value the Settlement Warrants were as follows:

	December 31, 2017
Expected price volatility	101.52%
Expected term (in years)	1.00
Risk-free interest rates	1.76%
Stock price	$2.79
Dividend yield	—

Cash and Cash Equivalents

The Company considers all highly liquid investments with original maturities of three months or less at the date of purchase and an investment in a U.S. government money market fund to be cash equivalents. Changes in the balance of cash and cash equivalents may be affected by changes in investment portfolio maturities, as well as actual cash disbursements to fund operations.

The Company's cash is deposited in highly-rated financial institutions in the United States. The Company invests in U.S. government money market funds, high-grade, short-term commercial paper, corporate bonds and other U.S. government agency securities, which management believes are subject to minimal credit and market risk. The carrying values of the Company's cash and cash equivalents approximate fair value due to their short-term maturities.

Marketable Securities

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 invests in high-grade corporate obligations, including commercial paper, and U. S. government and government agency obligations that are classified as available-for-sale. Since these securities are available to fund current operations they are classified as current assets on the consolidated

balance sheets.

Marketable securities are stated at fair value, including accrued interest, with their unrealized gains and losses included as a component of accumulated other comprehensive income or loss, which is a separate component of stockholders' equity. The fair value of these securities is based on quoted prices and observable inputs on a recurring basis. The cost of marketable securities is adjusted for amortization of premiums and accretion of discounts to maturity, with such amortization and accretion recorded as a component of interest expense, net. Realized gains and losses are determined on the specific identification method. Unrealized gains and losses are included in other comprehensive loss until realized, at which point they would be recorded as a component of interest expense, net.

Below is a summary of cash, cash equivalents and marketable securities at December 31, 2017 and December 31, 2016:

	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
December 31, 2017				
Cash and cash equivalents:				
Cash and money market funds	$ 14,949	$ —	$ —	$ 14,949
Corporate debt securities	—	—	—	—
Total cash and cash equivalents	14,949	—	—	14,949
Marketable securities:				
Corporate debt securities due within 1 year	$ 17,074	$ 1	$ (5)	$ 17,070
US government agency securities due within 1 year	1,506	—	—	1,506
Total marketable securities	18,580	1	(5)	18,576
Total cash, cash equivalents and marketable securities	$ 33,529	$ 1	$ (5)	$ 33,525
December 31, 2016				
Cash and cash equivalents:				
Cash and money market funds	$ 14,091	$ —	$ —	$ 14,091
Corporate debt securities	1,005	—	—	1,005
Total cash and cash equivalents	15,096	—	—	15,096
Marketable securities:				
Corporate debt securities due within 1 year	8,246	6	—	8,252
Total marketable securities	8,246	6	—	8,252
Total cash, cash equivalents and marketable securities	$ 23,342	$ 6	$ —	$ 23,348

Concentrations of Credit Risk

Financial instruments that potentially subject the Company to credit risk primarily consist of cash and cash equivalents, marketable securities and accounts receivable. The Company maintains deposits in highly-rated, federally-insured financial institutions in excess of federally insured limits. The Company's investment strategy is focused on capital preservation. The Company invests in instruments that meet the high credit quality standards outlined in the Company's investment policy. This policy also limits the amount of credit exposure to any one issue or type of instrument.

The Company's accounts receivable primarily consists of amounts due to the Company from licensees and collaborators. The Company has not experienced any material losses related to accounts receivable from individual licensees or collaborators.

Fair Value Measurements

The fair value of the Company's financial assets and liabilities reflects the Company's estimate of amounts that it would have received in connection with the sale of the assets or paid in connection with the transfer of the liabilities in an orderly transaction between market participants at the measurement date. In connection with measuring the fair value of its assets and liabilities, the Company seeks to maximize the use of observable inputs (market data obtained from sources independent from the Company) and to minimize the use of unobservable inputs (the Company's assumptions about how market participants would price assets and liabilities). The following fair value hierarchy is used to classify assets and liabilities based on the observable inputs and unobservable inputs used in order to value the assets and liabilities:

Level 1: Quoted prices in active markets for identical assets or liabilities. An active market for an asset or liability is a market in which transactions for the asset or liability occur with sufficient frequency and volume to provide pricing information on an ongoing basis.

Level 2: Observable inputs other than Level 1 inputs. Examples of Level 2 inputs include quoted prices in active markets for similar assets or liabilities and quoted prices for identical assets or liabilities in markets that are not active.

Level 3: Unobservable inputs based on the Company's assessment of the assumptions that market participants would use in pricing the asset or liability.

Financial assets and liabilities are classified in their entirety within the fair value hierarchy based on the lowest level of input that is significant to the fair value measurement. The Company measures the fair value of its marketable securities by taking into consideration valuations obtained from third-party pricing sources. The pricing services utilize industry standard valuation models, including both income and market based approaches, for which all significant inputs are observable, either directly or indirectly, to estimate fair value. These inputs include reported trades of and broker-dealer quotes on the same or similar securities, issuer credit spreads, benchmark securities and other observable inputs.

As of December 31, 2017, the Company's financial assets valued based on Level 1 inputs consisted of cash and cash equivalents in a U.S. government money market fund and in addition, for 2016, high-grade corporate debt securities, including commercial paper, and its financial assets valued based on Level 2 inputs consisted of high-grade corporate debt securities, including commercial paper, and in addition, for 2017, U.S. government agency securities. During the years ended December 31, 2017 and 2016, the Company did not have any transfers of financial assets between Levels 1 and 2.

As of December 31, 2017, the Company's financial liabilities that were recorded at fair value consisted of warrant liabilities, including the PIPE warrant liability and the estimated fair value of the Settlement Warrants.

The fair value of the Company's loans payable at December 31, 2017 approximates its carrying value, computed pursuant to a discounted cash flow technique using a market interest rate and is considered a Level 3 fair value measurement. The effective interest rate, which reflects the current market rate, considers the fair value of the warrants issued in connection with the loan, loan issuance costs and the deferred financing charge.

The following table summarizes the assets and liabilities measured at fair value on a recurring basis at December 31, 2017 and December 31, 2016:

	Fair Value Measurements as of December 31, 2017			
	Level 1	Level 2	Level 3	Total
	(in thousands)			
Financial assets carried at fair value:				
Cash and money market funds	$14,949	$—	$—	$14,949
Corporate debt securities	—	—	—	—
Total cash and cash equivalents	$14,949	$—	$—	$14,949
Marketable securities:				
Corporate debt securities due within 1 year	$—	$17,070	$—	$17,070
US government agency securities due within 1 year	—	1,506	—	1,506
Total marketable securities	$—	$18,576	$—	$18,576
Total cash, cash equivalents and marketable securities	$14,949	$18,576	$—	$33,525
Financial liabilities carried at fair value:				
PIPE warrant liability	$—	$—	$37,746	$37,746
Settlement warrant liability	—	—	2,073	2,073
Total warrant liabilities	$—	$—	$39,819	$39,819

	Fair Value Measurements as of December 31, 2016			
	Level 1	Level 2	Level 3	Total
	(in thousands)			
Financial assets carried at fair value:				
Cash and money market funds	$14,091	$—	$—	$14,091
Corporate debt securities	—	1,005	—	1,005
Total cash and cash equivalents	$14,091	$1,005	$—	$15,096
Marketable securities:				
Corporate debt securities due within 1 year	—	$8,252	—	$8,252
Total marketable securities	$—	$8,252	$—	$8,252
Total cash, cash equivalents and marketable securities	$14,091	$9,257	$—	$23,348
Financial liabilities carried at fair value:				
PIPE warrant liability	$—	$—	$4,593	$4,593
Total warrant liability	$—	$—	$4,593	$4,593

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. Depreciation expense for the years ended December 31, 2017, 2016 and 2015 was $0, $30 thousand and $9.6 million, respectively. In September 2014, the Company entered into a Lease Termination Agreement (refer to Note 12). As a result, the Company revised the estimated useful life of its leasehold improvements related to this space. 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.

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, $0 and $0.2 million of impairment losses during the years ended December 31, 2017, 2016 and 2015, respectively, primarily related to leasehold improvements.

Basic and Diluted Loss per Common Share

Basic net loss per share is computed using the weighted average number of common shares outstanding during the period, excluding restricted stock that has been issued but is not yet vested. Diluted net loss per common share is computed using the weighted average number of common shares outstanding and the weighted average dilutive potential common shares outstanding using the treasury stock method. However, for the years ended December 31, 2017, 2016 and 2015, diluted net loss per share is the same as basic net loss per share as the inclusion of weighted average shares of unvested restricted common stock and common stock issuable upon the exercise of stock options and warrants would be anti-dilutive.

The following table summarizes outstanding securities not included in the computation of diluted net loss per common share as their inclusion would be anti-dilutive for the years ended December 31, 2017, 2016 and 2015, respectively:

	Years Ended December 31,		
	2017	2016	2015
Outstanding stock options	7,537,958	4,858,678	4,796,005
Outstanding warrants	17,383,415	19,453,295	608,696
Unvested restricted stock	—	—	42,750
Total	24,921,373	24,311,973	5,447,451

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 Accounting Standards

Codification (“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 Company uses the Black-Scholes option pricing model to value its stock option awards without market conditions, which require the Company to make certain assumptions regarding the expected volatility its common stock price, the expected term of the option grants, the risk-free interest rate and the dividend yield with respect to its common stock. In 2016, the Company began calculating volatility using its historical data. Previously, the Company did not have sufficient history to support a calculation of volatility using only its historical data. As such, prior to 2016, the Company 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 the lack of the Company's own historical data, the Company elected to use the "simplified" method for "plain vanilla" options to estimate the expected term of the Company's 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. The Company utilizes a dividend yield of zero based on the fact that the Company has never paid cash dividends and has no present intention to pay cash dividends.

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, 2017, 2016 and 2015, the Company recorded the following stock-based compensation expense:

	Years Ended December 31,		
	2017	2016	2015
	(in thousands)		
Research and development	$290	$293	$298
General and administrative	799	706	765
Restructuring	—	—	69
Total stock-based compensation expense	$1,089	$999	$1,132

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. Expenses recognized in connection with the modification of awards in connection with the Company's strategic restructurings are allocated to restructuring expense. No related tax benefits of the stock-based compensation expense have been recognized.

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. The Company calculates its provision for income taxes on ordinary income based on its projected annual tax rate for the year. 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.

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, 2017 and 2016, the Company has $0 and $0.8 million, respectively, of net assets located in the United Kingdom.

Use of Estimates

The preparation of financial statements in conformity with GAAP requires management to make estimates and assumptions that affect certain reported amounts of assets and liabilities, disclosure of contingent assets and liabilities at the date of the financial statements, and the reported amounts of revenues and expenses during the reporting periods. Significant items subject to such estimates and assumptions include revenue recognition, contract research accruals, measurement of the PIPE warrant liability, estimated settlement liabilities and measurement of stock-based compensation. The Company bases its estimates on historical experience and various other assumptions that management believes to be reasonable under the circumstances. Changes in estimates are recorded in the period in which they become known. Actual results could differ from those estimates.

Recent Accounting Pronouncements

In May 2014, the FASB issued ASU No. 2014-09, Revenue from Contracts with Customers (Topic 606), ("ASU 2014-09") that will supersede nearly all existing revenue recognition guidance under 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 by one year and will now be effective for annual and interim periods beginning after December 15, 2017. ASU 2014-09 also permits two methods of adoption: retrospectively to each prior reporting period presented (full retrospective method), or retrospectively with the cumulative effect of initially applying the guidance recognized at the date of initial application (the modified retrospective method). The Company will adopt ASU 2014-09 on January 1, 2018 using the modified retrospective method. The Company is in the process of completing its analysis with respect to its active revenue arrangements, including those with CANbridge Life Sciences Ltd. ("CANbridge"), EUSA, and Novartis, as well as identifying any appropriate changes to its revenue recognition policies and internal controls.

Under ASU 2014-09, an entity recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration which the entity expects to receive in exchange for those goods or services. To determine revenue recognition for arrangements that an entity determines are within the scope of ASU 2014-09, the entity performs the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) the entity satisfies a performance obligation. ASU 2014-09 also impacts certain other areas, such as the accounting for costs to obtain or fulfill a contract. The standard also requires disclosure of the nature, amount, timing, and uncertainty of revenue and cash flows arising from contracts with customers. To date, the Company has identified the following differences in accounting treatment for its collaboration agreements under ASU 2014-09:

- The Company expects the accounting for contingent milestone payments under its collaboration agreements to change under ASU 2014-09. Under ASC 605, the Company generally considers non-refundable preclinical research and development, clinical development and regulatory milestones that the Company expects to be achieved as a result of the Company's efforts during the period of the Company's performance obligations under its collaboration and license agreements to be substantive and recognizes them as revenue upon the achievement of the milestone, assuming all other revenue recognition criteria are met. ASU 2014-09 does not contain guidance specific to milestone payments, thereby requiring contingent milestone payments to be considered in accordance with the overall model of ASU 2014-09. Revenue from contingent milestone payments may be recognized earlier under ASU 2014-09 than under ASC 605, based on an assessment of the probability of achievement of the milestone event and the likelihood of a significant reversal of such milestone revenue at each reporting date. This assessment may result in the recognition of revenue related to a contingent milestone payment before the milestone event has been achieved.
- ASU 2014-09 requires more robust disclosures than required by previous guidance, including disclosures related to disaggregation of revenue into appropriate categories, performance obligations, the judgments made in revenue recognition determinations, adjustments to revenue which relate to activities from previous quarters or years, any significant reversals of revenue, and costs to obtain or fulfill contracts.

The Company has not yet completed its assessment of the impact the adoption of this standard may have on its consolidated financial statements and internal control. With regard to the arrangements with CANbridge and Novartis, the Company currently does not expect the impact of adoption of this standard to be material. The Company is continuing to evaluate the effects of the adoption of the standard on its arrangement with EUSA. Expected impacts from the adoption of this standard could differ upon the final adoption and implementation of the standard. In connection with the adoption of this standard, the Company is implementing several new internal controls, including controls to monitor the probability of achievement of contingent milestone payments.

In February 2016, the FASB issued ASU 2016-02, Leases (Topic 842), which requires lessees to recognize a right-of-use asset and lease liability for most lease arrangements. The new standard is effective for annual reporting periods beginning after December 15, 2018 with early adoption permitted. The Company will not early adopt this standard and is currently evaluating the potential changes from this ASU.

In August 2016, the FASB issued ASU 2016-15, Statement of Cash Flows (Topic 230): Classification of Certain Cash Receipts and Cash Payments. The new standard clarifies certain aspects of the statement of cash flows, including the classification of debt prepayment or debt extinguishment costs, settlement of zero-coupon debt instruments or other debt instruments with coupon interest rates that are insignificant in relation to the effective interest rate of the borrowing, contingent consideration payments made after a business combination, proceeds from the settlement of insurance claims, proceeds from the settlement of corporate-owned life insurance policies, distributions received from equity method investees and beneficial interests in securitization transactions. The new standard also clarifies that an entity should determine each separately identifiable source or use within the cash receipts and cash payments on the basis of the nature of the underlying cash flows. In situations in which cash receipts and payments have aspects of more than one class of cash flows and cannot be separated by source or use, the appropriate classification should depend on the activity that is likely to be the predominant source or use of cash flows for the item. The new standard will be effective for the Company on January 1, 2018. The adoption of this standard is not expected to have a material impact on the Company’s consolidated statements of cash flows.

In May 2017, the FASB issued ASU 2017-09, Compensation-Stock Compensation (Topic 718): Scope of Modification Accounting, which clarifies when to account for a change to the terms or conditions of a share-based payment award as a modification. The new standard does not change the accounting for modifications but clarifies that modification accounting guidance should only be applied if the fair value, vesting conditions, or classification of the award changes as a result of the change in terms or conditions. The new standard is effective for fiscal years, and interim periods within, beginning after December 15, 2017. Early adoption is permitted. A reporting entity must apply the amendments in the ASU prospectively to an award modified on or after the adoption date. The adoption of ASU 2017-09 is not expected to have a material effect on the Company's consolidated financial statements or disclosures.

Recently Adopted Accounting Pronouncements

In March 2016, the FASB issued ASU No. 2016-09, Compensation—Stock Compensation (Topic 718): Improvements to Employee Share-Based Payment Accounting. The standard revised the accounting for share-based compensation arrangements, including the accounting for income taxes, forfeitures, and statutory tax withholding requirements, as well as classification in the statement of cash flows. The adoption of ASU 2016-09 did not have a material impact in the Company's financial statements.

(4) Collaborations and License Agreements

Out-License Agreements

CANbridge

In March 2016, the Company entered into a collaboration and license agreement (the "CANbridge Agreement") with CANbridge Life Sciences Ltd. ("CANbridge"). Under the terms of the CANbridge Agreement, the Company granted CANbridge the exclusive right to develop, manufacture and commercialize AV-203, the Company's proprietary ErbB3 (HER3) inhibitory antibody, for the diagnosis, treatment and prevention of disease in humans and animals in all countries other than the United States, Canada and Mexico (the "CANbridge Licensed Territory"). The effective date of the CANbridge Agreement is March 16, 2016 (the "Effective Date").

Pursuant to the CANbridge Agreement, CANbridge made an upfront payment to the Company of $1.0 million in April 2016, net of $0.1 million in foreign withholding taxes. CANbridge agreed to reimburse the Company $1.0 million for certain manufacturing costs and expenses incurred by the Company prior to the Effective Date with respect to AV-203. CANbridge paid this manufacturing reimbursement in two installments of $0.5 million each, including one in March 2017 and one in September 2017, net of $0.1 million in foreign withholding taxes. The Company is also eligible to receive up to $42.0 million in potential development and regulatory milestone payments and up to $90.0 million in potential sales based milestone payments based on annual net sales of licensed products. In December 2017, CANbridge filed an IND with the China Food and Drug Administration for a Phase 1b / III clinical study of AV-203 in esophageal squamous cell cancer. Upon commercialization, the Company is eligible to receive a tiered royalty, with a percentage range in the low double-digits, on net sales of approved licensed products. CANbridge's obligation to pay royalties for each licensed product expires on a country-by-country basis on the later of the expiration of patent rights covering such licensed product in such country, the expiration of regulatory data exclusivity

in such country and ten years after the first commercial sale of such licensed product in such country. No development and regulatory milestone payments have been earned as of December 31, 2017.

CANbridge is obligated to use commercially reasonable efforts to develop and commercialize AV-203 in each of China, Japan, the United Kingdom, France, Italy, Spain, and Germany. CANbridge has responsibility for all activities and costs associated with the further development, manufacture, regulatory filings and commercialization of AV-203 in the CANbridge Licensed Territory.

A percentage of any milestone and royalty payments received by the Company, excluding upfront and reimbursement payments, are due to Biogen Idec International GmbH ("Biogen") as a sublicensing fee under the option and license agreement between the Company and Biogen dated March 18, 2009, as amended.

Activities under the CANbridge Agreement were evaluated under ASC 605-25 Revenue Recognition—Multiple Element Arrangements ("ASC 605-25") to determine whether such activities represented a multiple element revenue arrangement. The CANbridge Agreement includes the following non-contingent deliverables: (i) the Company's grant of an exclusive license to develop and commercialize AV-203 in the CANbridge Licensed Territory, (ii) the Company's obligation to transfer all technical knowledge and data useful in the development and manufacture of AV-203 and (iii) the Company's obligation to participate on a joint steering committee during the proof-of-concept development period. The relative selling price of the Company's joint steering committee participation had de minimis value. The Company determined that the delivered license and know-how did have stand-alone value from the undelivered element and have accounted for these items as separate deliverables. The Company allocated the upfront consideration of $1.0 million to the units of accounting and recognized the $1.0 million attributed to the delivered license and know how as revenue during the year ended December 31, 2016.

The Company believes the development and regulatory milestones that may be achieved under the CANbridge Agreement are consistent with the definition of a milestone included in ASC 605-28, 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.

The Company recognized the two $0.5 million payments by CANbridge for the reimbursement of manufacturing development activities conducted by the Company prior to the Effective Date as revenue during each of the three months ended March 31, 2017 and September 30, 2017, respectively, as the amounts were fixed and determinable and non-refundable. In addition, the Company has no further performance obligations.

EUSA

In December 2015, the Company entered into a license agreement with EUSA Pharma (UK) Limited (“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 “EUSA Licensed Territories”) for all diseases and conditions in humans, excluding non-oncologic diseases or conditions of the eye.

Under the license agreement, EUSA made research and development reimbursement payments to the Company of $2.5 million upon the execution of the license agreement during the year ended December 31, 2015 and $4.0 million in September 2017 upon its receipt of marketing approval from the EMA for tivozanib (FOTIVDA) for the treatment of RCC. In September 2017, EUSA elected to opt-in to co-develop the ongoing TiNivo trial. As a result of exercising its opt-in right, EUSA made an additional research and development reimbursement payment to the Company of $2.0 million. This $2.0 million payment was received in October 2017, in advance of the completion of the TiNivo trial, and represents EUSA’s approximate 50% share of the total estimated costs of the TiNivo trial. The Company is also eligible to receive an additional research and development reimbursement payment from EUSA of fifty percent (50%) of the total costs for the Company’s TIVO-3 phase 3 study in third-line RCC, up to $20.0 million, if EUSA elects to opt-in to that study.

The Company is entitled to receive milestone payments of $2.0 million per country upon reimbursement approval for RCC, if any, in each of France, Germany, Italy, Spain and the United Kingdom, and an additional $2.0 million for the grant of marketing approval, if any, in three of the five following countries: Argentina, Australia, Brazil, South Africa and Venezuela. In February 2018, EUSA obtained reimbursement approval from the NICE in the UK in first line RCC. Accordingly, the Company earned a $2.0 million milestone payment that was received in March 2018. The Company is also eligible to receive a payment of $2.0 million in connection with a filing by EUSA with the EMA for marketing approval, if any, 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 is also eligible to receive tiered double-digit royalties on net sales, if any, of licensed products in the EUSA Licensed Territories ranging from a low double digit up to mid-twenty percent depending on the level of annual net sales.

The research and development reimbursement payments under the EUSA license agreement are not subject to the 30% sublicensing payment to KHK, subject to certain limitations. The Company, however, would owe KHK 30% of other, non-research and development payments it may receive from EUSA pursuant to the EUSA license agreement, including EU reimbursement approval milestones in up to five specified EU countries, EU marketing approvals for up to three additional indications beyond RCC, marketing approvals in up to three specified licensed territories outside of the EU, sales-based milestones and royalties, as set forth above. The $2.0 million milestone the Company earned in February 2018 upon EUSA’s reimbursement approval from the NICE in the UK in first line RCC is subject to the 30%

KHK sub-license fee, or $0.6 million.

EUSA is obligated to use commercially reasonable efforts to seek regulatory approval for and commercialize tivozanib throughout the EUSA Licensed Territories in RCC. With the exception of certain support provided by the Company in connection with the application for 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 EUSA Licensed Territories.

Activities under the agreement were evaluated under 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 tivozanib in the EUSA 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 EUSA 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 EUSA 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 the upfront consideration of $2.5 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 $0.4 million, $0.4 million and $14 thousand as revenue during each of the years ended December 31, 2017, 2016 and 2015, respectively, related to the previously deferred upfront consideration.

The Company believes the regulatory milestones that may be achieved under the EUSA agreement are consistent with the definition of a milestone included in ASC 605-28, 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.

In August 2017, the European Commission ("EC") approved tivozanib (FOTIVDA) for the treatment of adult patients with aRCC, as described above. Accordingly, the Company earned a $4.0 million research and development reimbursement payment upon the EMA approval in RCC that was paid by EUSA in September 2017. In accordance with ASC 605-28, Revenue Recognition—Milestone Method, the Company recognized the $4.0 million received from EUSA upon achievement of EMA approval as revenue as the underlying milestone was considered to be substantive. In November 2017, EUSA commenced the first commercial launch of tivozanib (FOTIVDA) with the initiation of product sales in Germany. Accordingly, the Company began earning sales royalties and recognized approximately $19 thousand in revenue in the three months ended December 31, 2017.

In September 2017, EUSA elected to opt-in to co-develop the TiNivo trial. As a result of EUSA's exercise of its opt-in right, it became an active participant in the ongoing conduct of the TiNivo trial and is able to utilize the resulting data from the TiNivo trial for regulatory and commercial purposes in its Licensed Territories. Upon exercise of its opt-in right, EUSA became responsible for funding 50% of the total estimated costs of the TiNivo trial, up to $2.0 million. EUSA's opt-in rights were identified as a contingent deliverable at the inception of the arrangement and, because they did not contain a significant incremental discount, were not considered as a deliverable in connection with the Company's initial accounting for the EUSA arrangement. Accordingly, the Company evaluated EUSA's exercise of its opt-in rights as a separate arrangement. The Company is accounting for the joint development activities relative to the TiNivo trial as a joint risk-sharing collaboration in accordance with ASC 808, Collaborative Arrangements because EUSA is an active participant in the ongoing TiNivo trial and is exposed to significant risk and rewards in connection with the activity. Payments from EUSA with respect to its share of TiNivo trial development costs incurred by the Company pursuant to a joint development plan are recorded as a reduction in research and development expenses due to the joint risk-sharing nature of the activities. In the year ended December 31, 2017, the Company recognized an approximate $0.9 million reduction in research and development expenses related to EUSA's approximate 50% share of the cumulative study-to-date costs incurred through that date as the TiNivo trial was ongoing at the time EUSA made its opt-in election and EUSA paid the $2.0 million maximum amount of cost sharing per the license agreement in advance. The remaining $1.1 million in prepaid cost sharing was classified as deferred research and development reimbursements as of December 31, 2017 and will continue to be recognized as a reduction in research and development expenses as the related TiNivo trial costs are incurred over the duration of the trial. .

Novartis

In August 2015, the Company entered into a license agreement with Novartis. Under the license agreement, the Company 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 in September 2015. Novartis also 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. As of December 31, 2017, the Company is eligible to receive up to $51.2 million in potential clinical and development milestone payments, 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 up to $150.0 million in potential commercial milestone payments based on annual net sales of such products. If the product is commercialized, the Company would be eligible to receive tiered royalties on net sales of approved products ranging from the high single digits to the low double-digits.

Certain milestones achieved by Novartis or timelines associated with the development plan would trigger milestone payment obligations from the Company to St. Vincent's Hospital Sydney Limited ("St. Vincent's") under the Company's amended and restated license agreement with St. Vincent's. In addition, specified royalties on approved products, if any, will be payable to St. Vincent's, and the Company and Novartis will share that obligation equally.

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 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 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 the upfront consideration of $15.0 million to the delivered license and technical knowledge and recognized this amount as revenue during the year ended December 31, 2015. The relative selling price of the undelivered cooperation had de minimis value.

The Company received a cash payment of $3.5 million related to the delivery of its inventory of clinical quality drug substance to Novartis during the three months ended March 31, 2016.

In February 2017, Novartis paid the Company $1.8 million out of its future payment obligations under the license agreement. The funds were used to satisfy a $1.8 million time-based milestone obligation that the Company owed to St. Vincent's in March 2017. Novartis will reduce any subsequent payment obligations to the Company, if any, by the $1.8 million. The Company recognized the $1.8 million of consideration as revenue during the three months ended March 31, 2017, as the amount was fixed and determinable and non-refundable, and the Company does not have any further performance obligations to Novartis in connection with the license agreement. This payment reduces the aggregate future amounts potentially payable by Novartis to the Company, if any, under the license agreement by the $1.8 million, but does not amend any other terms of the Novartis license agreement. No milestone payments have been earned as of December 31, 2017.

Pharmstandard

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 granted to Pharmstandard the right to develop, manufacture and commercialize tivozanib in the territories of Russia, Ukraine and the Commonwealth of Independent States for all diseases and conditions in humans, excluding non-oncologic ocular conditions.

In June 2016, following unsuccessful efforts to renegotiate certain terms of the Pharmstandard license agreement, Pharmstandard notified the Company that due to economic and market changes in Russia it was exercising its right to terminate the license agreement effective September 9, 2016.

Upon the effective date of the termination, the remaining deferred revenue of approximately $0.9 million was recognized. The Company recognized approximately $0, $0.9 million and $61 thousand as revenue during the years ended December 31, 2017, 2016 and 2015, respectively.

Ophthotech

In November 2014, the Company entered into a research and exclusive option agreement (the "Option Agreement"), with Ophthotech Corporation ("Ophthotech") 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 tivozanib outside of Asia and the Middle East for the potential diagnosis, prevention and treatment of non-oncologic diseases or conditions of the eye in humans. Ophthotech paid the Company $0.5 million in consideration for the grant of the option. In January 2017, Ophthotech formally notified the Company that it would not be able to develop tivozanib and exercised its right to terminate the Option Agreement effective April 3, 2017.

Under the Option Agreement, the Company received a cash payment of $0.5 million during the year ended December 31, 2014. The Company deferred the payment and was recording the deferred revenue over the Company's period of performance, which was estimated to be through December 2017. Upon the effective date of the termination, the remaining deferred revenue of approximately $0.1 million was recognized. The Company recorded approximately $0.1 million, $0.1 million and $0.2 million of revenue during the years ended December 31, 2017, 2016 and 2015, respectively.

Biodesix

In April 2014, the Company entered into a worldwide co-development and collaboration agreement with Biodesix (the "Biodesix Agreement") to develop and commercialize ficlatuzumab, the Company's HGF inhibitory antibody. Under the Biodesix 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 VeriStrat®, Biodesix's proprietary companion diagnostic test. Biodesix granted the Company perpetual, non-exclusive rights to certain intellectual property, including diagnostic data related to VeriStrat, 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 September 2016, the Company and Biodesix announced the termination of a phase 2 proof-of-concept clinical study of ficlatuzumab in which VeriStrat® was used to select clinical trial subjects (the "FOCAL" trial).

Under the Biodesix Agreement, with the exception of the costs incurred for the FOCAL trial, the Company and Biodesix are each required to contribute 50% of all clinical, regulatory, manufacturing and other costs to develop ficlatuzumab. Pursuant to the Biodesix Agreement, Biodesix was obligated to fund all costs of the FOCAL trial up to a cap of $15 million, following which all costs of the FOCAL trial would be shared equally. In connection with the discontinuation of the FOCAL trial on October 14, 2016, the Company and Biodesix amended the Biodesix Agreement. Under the amendment, the Company agreed to share 50% of the shutdown costs for the FOCAL trial after August 1, 2016. In return for bearing these shutdown costs, the Company will be entitled to recover an agreed multiple of the additional costs borne by the Company out of any income Biodesix receives from the partnership in connection with the licensing or commercialization of ficlatuzumab. Following such recovery, the payment structure under the original Biodesix Agreement, which generally provides that the parties share equally in any costs and revenue, will resume without such modification.

In addition, the Company and Biodesix are funding investigator-sponsored clinical trials, including ficlatuzumab in combination with ERBITUX® (cetuximab) in squamous cell carcinoma of the head and neck, ficlatuzumab in combination with Cytosar (cytarabine) in acute myeloid leukemia and ficlatuzumab in combination with nab-paclitaxel and gemcitabine in pancreatic cancer.

Pending marketing approval or the sublicense of ficlatuzumab, and subject to the negotiation of a commercialization agreement, each party would share equally in commercialization profits and losses, subject to the Company's right to be the lead commercialization party.

Prior to the first commercial sale of ficlatuzumab, 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. 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. 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.

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 Biodesix Agreement were evaluated under ASC 605-25 to determine whether such activities represented a multiple element revenue arrangement. The Biodesix Agreement includes the following non-contingent deliverables: (i) the Company's obligation to deliver perpetual, non-exclusive rights to certain intellectual property including clinical and biomarker data related to ficlatuzumab for use in developing and commercializing VeriStrat; (ii) the Company's obligation to participate in the joint steering committee; and (iii) the Company's obligation to provide its existing supply of ficlatuzumab for development purposes. The Company concluded that any deliverables that would be delivered after the FOCAL trial is complete were contingent deliverables because these services are contingent upon the results of the FOCAL trial. As these deliverables were 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, 2017, no contingent deliverables had been provided by the Company.

The Company determined that the perpetual, non-exclusive rights to certain intellectual property for use in developing and commercializing VeriStrat 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 recorded the consideration earned in connection with the FOCAL trial, which consisted of reimbursements from Biodesix for expenses related to the trial, as a reduction to research and development expense during the period that reimbursable expenses were incurred. As a result of the cost sharing provisions in the Biodesix Agreement, the Company reduced research and development expenses by approximately $0.1 million, $2.5 million and $3.5 million during the years ended December 31, 2017, 2016 and 2015, respectively. The amount due to the Company from Biodesix pursuant to the cost-sharing provision was approximately $0.1 million and $0.8 million at December 31, 2017 and 2016, respectively. The Company received cash payments related to cost reimbursements of approximately $0.8 million and $2.8 million during the years ended December 31, 2017 and 2016, respectively.

Astellas Pharma

In February 2011, the Company, together with its wholly-owned subsidiary AVEO Pharma Limited, entered into a collaboration and license agreement (the “Astellas Agreement”) with Astellas Pharma Inc. and certain of its subsidiaries (together, “Astellas”), pursuant to which the Company and Astellas intended to develop and commercialize tivozanib for the treatment of a broad range of cancers. Astellas elected to terminate the agreement effective on August 11, 2014, at which time the tivozanib rights were returned to the Company. In accordance with the Astellas Agreement, committed development costs, including the costs of completing certain tivozanib clinical development activities, continue to be shared equally.

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. 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 decreased research and development expenses by $0.2 million, $0.3 million and $0.7 million during the years ended December 31, 2017, 2016 and 2015, respectively. The net amount due to the Company from Astellas pursuant to the cost-sharing provisions was $0.2 million and $0.1 million at December 31, 2017 and 2016, respectively.

Under the agreement, the Company received cash payments related to reimbursable payments and milestone payments of $0 and $0.3 million during the years ended December 31, 2017 and 2016, respectively.

Biogen Idec International GmbH

In March 2009, the Company entered into an exclusive option and license agreement with Biogen regarding the development and commercialization of the Company’s discovery-stage ErbB3-targeted antibodies, AV-203, for the potential treatment and diagnosis of cancer and other diseases outside of North America. Under the agreement, the Company was 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 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, the Company was obligated to use reasonable efforts to seek a collaboration partner for the purpose of funding further development and commercialization of ErbB3 targeted antibodies. The Company 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 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 agreement, as amended. 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 nor 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 was recognized on a straight-line basis over the period of performance, or through March 2016, when the Company executed its agreement with CANbridge.

Under the agreement, the Company recorded revenue of $0, $38 thousand and $0.3 million during the years ended December 31, 2017, 2016 and 2015, respectively.

In March 2016, the Company entered into a collaboration and license agreement for AV-203 with CANbridge. See "—CANbridge" herein for a further description of that arrangement.

In-License Agreements

St. Vincent's

In July 2012, the Company entered into a license agreement with St. Vincent's, under which the Company obtained an exclusive, worldwide license to research, develop, manufacture and commercialize products for human therapeutic, preventative and palliative applications that benefit from inhibition or decreased expression or activity of GDF15, which is also referred to as MIC-1. Under the agreement, the Company has the right to grant sublicenses subject to certain restrictions. Under the license agreement, St. Vincent's also granted the Company non-exclusive rights for certain related diagnostic products and research tools.

In order to sublicense certain necessary intellectual property rights to Novartis in August 2015, the Company and St. Vincent's amended and restated the license agreement (the "Amended St. Vincent's Agreement"). Under the Amended St. Vincent's Agreement, the Company was required to make an upfront payment to St. Vincent's of $1.5 million. St. Vincent's is also eligible to receive up to approximately $16.7 million in connection with development and regulatory milestones and /or defined timelines under the Amended St. Vincent's Agreement. 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. 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.

During the year ended December 31, 2016, the Company recognized approximately $0.4 million in research and development expense in connection with a milestone obligation due to St. Vincent's related to the selection of a development candidate.

During the year ended December 31, 2017, the Company recognized $1.8 million in research and development expense in connection with a time-based milestone obligation due to St. Vincent's.

Kyowa Hakko Kirin (KHK)

In December 2006, the Company entered into a license agreement with KHK under which it 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 in all potential indications. Its exclusive license covers all territories in the world except for Asia and the Middle East, where KHK has retained the rights to tivozanib. Under the license agreement, the Company obtained exclusive rights in its 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. The Company 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, the Company is obligated to use commercially reasonable efforts to develop and commercialize tivozanib in its territory. Prior to the first anniversary of the first post-marketing approval sale of tivozanib in its territory, neither the Company nor any of its 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 a VEGF receptor.

The Company has upfront, milestone and royalty payment obligations to KHK under the license agreement. Upon entering into the license agreement with KHK, the Company made an upfront payment in the amount of $5.0 million. In March 2010, the Company made a milestone payment to KHK in the amount of $10.0 million in connection with the dosing of the first patient in the Company's first phase 3 clinical trial of tivozanib (TIVO-1). In December 2012, the Company made a $12.0 million milestone payment to KHK in connection with the acceptance by the US Food and Drug Administration ("FDA") of the Company's 2012 New Drug Application ("NDA") filing for tivozanib. Each milestone under the KHK agreement is a one-time only payment obligation, accordingly, the Company did not owe KHK another milestone payment in connection with the dosing of the first patient in the Company's TIVO-3 trial, and would not owe a milestone payment to KHK if the Company files an NDA with the FDA following the completion of the

TIVO-3 clinical trial. If the Company obtains approval for tivozanib in the U.S., the Company would owe KHK a one-time milestone payment of $18.0 million, provided that the Company does not sublicense U.S. rights for tivozanib prior to obtaining a U.S. regulatory approval. If the Company were to sublicense the U.S. rights, the associated U.S. regulatory milestone would be replaced by a specified percentage of sublicensing revenue, as set forth below.

If the Company sublicenses any of its rights to tivozanib to a third party, as it has done with EUSA, the sublicense defines the payment obligations of the sublicensee, which may vary from the milestone and royalty payment obligations under the KHK license relating to rights the Company retains. The Company is required to pay KHK a fixed 30% of amounts the Company receives from its sublicensees, including upfront license fees, milestone payments and royalties, but excluding amounts the Company receives in respect of research and development reimbursement payments or equity investments, subject to certain limitations. Certain research and development reimbursement payments by EUSA, including the $2.5 million upfront payment in December 2015, the $4.0 million payment in September 2017 upon the approval from the EMA of tivozanib (FOTIVDA) and the $2.0 million payment upon EUSA's election in September 2017 to opt-in to co-develop the TiNivo trial were not subject to sublicense revenue payments to KHK. In addition, if EUSA elects to opt-in to the TIVO-3 trial, the additional research and development reimbursement payment from EUSA of fifty percent (50%) of the total trial costs, up to $20.0 million, would also not be subject to a sublicense revenue payment to KHK, subject to certain limitations. The Company would, however, owe KHK 30% of other, non-R&D reimbursement payments the Company may receive from EUSA pursuant to the EUSA agreement, including EU reimbursement approval milestones in up to five specified EU countries, EU marketing approvals for up to three additional indications beyond RCC, marketing approvals in up to three specified licensed territories outside of the EU, sales-based milestones and royalties. The $2.0 million milestone the Company earned in February 2018 upon EUSA's reimbursement approval from the NICE in the UK in first line RCC is subject to the 30% KHK sub-license fee, or $0.6 million.

The Company is also required to pay tiered royalty payments on net sales it makes of tivozanib in its North American 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. The Company's royalty payment obligations in a particular country in its territory begin on the date of the first commercial sale of tivozanib in that country, and end on the later of 12 years after the date of first commercial sale of tivozanib in that country or the date of the last to expire of the patents covering tivozanib that have been issued in that country.

The license agreement will remain in effect until the expiration of all of the Company's royalty and sublicense revenue obligations to KHK, determined on a product-by-product and country-by-country basis, unless the Company elects to terminate the license agreement earlier. If the Company fails to meet its obligations under the agreement and is 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 the Company may have in tivozanib, including its regulatory filings, regulatory approvals, patents and trademarks for tivozanib.

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, 2017, 2016 and 2015. The Company has not paid any royalties to date.

(5) Other Accrued Liabilities

Other accrued expenses consisted of the following:

	December 31, 2017	December 31, 2016
	(in thousands)	
Professional fees	$844	$ 464
Compensation and benefits	1,325	891
Other	289	176
Total	$2,458	$ 1,531

(6) Loans Payable

On May 28, 2010, the Company entered into a loan and security agreement with Hercules (the "First Loan Agreement"). The First Loan Agreement was subsequently amended in March 2012 (the "2012 Amendment"), September 2014 (the "2014 Amendment"), May 2016 (the "2016 Amendment") and December 2017 (the "2017 Loan Agreement"). Amounts borrowed under the 2012 Amendment were repaid in full in 2015.

Pursuant to the 2014 Amendment, the Company received additional loan proceeds from Hercules in the amount of $10.0 million and was not required to commence principal payments until May 1, 2016, with the last principal payment due on January 1, 2018. An end-of-term payment of approximately $0.5 million continued to be due on January 1, 2018 and was paid on the first business day of 2018. The Company incurred approximately $0.2 million in loan issuance costs paid directly to Hercules, which were offset against the loan proceeds and are accounted for as a loan discount. The 2014 Amendment was accounted for as a loan modification in accordance with ASC 470-50, Debt—Modifications and Extinguishments ("ASC 470-50").

In connection with the 2014 Amendment, 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. The Company recorded the 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. In July 2017, Hercules exercised all 608,696 warrants. Pursuant to the terms of the warrant, Hercules, at their election, exercised the warrants via a non-cash "net share issuance." The Company issued Hercules 369,297 shares of its common stock and did not receive any cash proceeds in connection with the warrant exercise.

In May 2016, pursuant to the 2016 Amendment, the Company received additional loan proceeds from Hercules in the amount of $5.0 million, which increased the aggregate outstanding principal balance under the First Loan Agreement to $15.0 million. The Company was not required to commence principal payments on the $15 million loan until July 1, 2017, at which time the Company would have been required to make 30 equal monthly payments of principal and interest through December 2019. An end-of-term payment of approximately $0.2 million is due on December 1, 2019. The Company incurred approximately $0.1 million in loan issuance costs paid directly to Hercules, which were offset against the loan proceeds and are accounted for as a loan discount. The 2016 Amendment was accounted for as a loan modification in accordance with ASC 470-50. The 2016 Amendment included a financial covenant that required the Company to maintain an unrestricted cash position (defined as cash and liquid cash, including marketable securities) greater than or equal to $10.0 million through the date of completion of the Company's TIVO-3 trial, with results that were satisfactory to Hercules.

Under the 2016 Amendment, from March 1, 2017 through June 30, 2017, the Company could draw down an additional $5.0 million in funding upon confirmation by Hercules, in its reasonable discretion, that the Company had achieved the following conditions: (i) satisfactory developmental progression on a minimum of two (2) clinical programs (other than the TIVO-3 trial) that are either managed directly by the Company or funded, in whole or in part, by the Company and (ii) having an unrestricted cash position greater than or equal to $25.0 million on the date of the draw down request. If the Company drew down the additional $5.0 million in funding, the commencement of principal payments on the aggregate $20.0 million loan balance would be deferred by six months from July 1, 2017 until January 1, 2018.

In June 2017, pursuant to the 2016 Amendment, the Company received the additional $5.0 million in loan proceeds from Hercules, which increased the aggregate outstanding principal balance under the First Loan Agreement to $20.0 million and resulted in a six-month deferral in the commencement of principal payments. There was no change in the

loan maturity date of December 2019. The Company was not required to commence principal payments on the $20.0 million loan until January 1, 2018, at which time the Company would have been required to make 23 equal monthly payments of principal and interest, in the approximate amount of $0.8 million, through November 2019 and an approximate $5.3 million payment of principal and interest in December 2019, which represented approximately 26% of the entire $20.0 million loan. An additional end-of-term payment of approximately $0.1 million is due on December 1, 2019, which increased the total end-of-term payments under the 2016 Amendment to $0.3 million.

In connection with the 2016 Amendment, the Company issued warrants to Hercules to purchase up to 1,202,117 shares of the Company's common stock at an exercise price equal to $0.87 per share. The Company recorded the fair value of the warrants of approximately $0.7 million as a component of 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. In July 2017, Hercules exercised all 1,202,117 warrants. Pursuant to the terms of the warrant, Hercules, at their election, exercised the warrants via a non-cash "net share issuance." The Company issued Hercules 846,496 shares of its common stock and did not receive any cash proceeds in connection with the warrant exercise.

As part of the 2016 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.

In connection with the Company's May 2016 private placement (refer to Note 7), Hercules purchased 259,067 units for cash proceeds of $0.2 million to the Company. This purchase was separate from the $2.0 million equity purchase option under the 2016 Amendment. Each unit in the May 2016 private placement included one share of the Company's common stock and a PIPE Warrant to purchase one share of the Company's common stock at an exercise price of $1.00 per share. In July 2017, Hercules exercised its PIPE Warrants with respect to all 259,067 shares of common stock underlying such PIPE Warrants. The Company issued Hercules 259,067 shares of its common stock and received approximately $0.3 million in cash proceeds.

In December 2017, the Company entered into an amended and restated loan and security agreement with Hercules to refinance the $20.0 million First Loan Agreement (the "2017 Loan Agreement). The proceeds of the new loan facility were used to retire the existing $20.0 million in secured debt outstanding under the First Loan Agreement. Per the terms of the 2017 Loan Agreement, the new loan facility has a 42-month maturity from closing, no financial covenants, a lower interest rate and an interest-only period of no less than 12 months, which could be extended up to a maximum of 24 months, assuming the achievement of specified milestones relating to the development of tivozanib. Per the 2017 Loan Agreement, Hercules did not receive any additional warrants to purchase shares of the Company's common stock and no longer has the option, subject to the Company's written consent, to participate in its future equity financings up to $2.0 million through the purchase of the Company's common stock either with cash or through the conversion of outstanding principal under the loan.

The loan maturity date has been revised from December 2019 to July 2021. The Company is not required to make principal payments until February 1, 2019, at which time the Company will be required to make 29 equal monthly payments of principal and interest, in the approximate amount of $0.8 million, through July 2021. An additional end-of-term payment of approximately $0.8 million is due on July 1, 2021, which increases the total end-of-term payments under the 2014 Amendment, 2016 Amendment and 2017 Loan Agreement to approximately $1.6 million. The end-of-term payments under the 2014 Amendment, in the approximate amount of $0.5 million, and the 2016 Amendment, in the amount of $0.3 million, continue to be due on their original due dates of January 1, 2018 and December 1, 2019, respectively. The financial covenant per the 2016 Amendment to maintain an unrestricted cash position greater than or equal to $10.0 million through the date of completion of our TIVO-3 trial with results that are satisfactory to Hercules has been removed. Per the 2017 Loan Agreement, the current interest rate has been decreased from 11.9% to 9.45%. The Company incurred approximately $0.1 million in loan issuance costs paid directly to Hercules, which are accounted for as a loan discount. The 2017 Loan Agreement was accounted for as a loan modification in accordance with ASC 470-50.

The interest-only period could be extended by two 6-month deferrals upon the achievement of specified milestones relating to the development of tizozanib, including (i) on or prior to September 30, 2018, the Company has received positive data with respect to its TIVO-3 trial for the treatment of RCC for patients in the third-line setting which positive data supports the filing for a new drug application with the FDA, subject to confirmation by Hercules at its reasonable discretion, and (ii) on or prior to June 28, 2019, the Company has received approval from the FDA for its tivozanib product for the treatment of RCC for patients in the third-line setting, subject to confirmation by Hercules at its reasonable discretion.

The unamortized discount to be recognized over the remainder of the loan period was approximately $1.5 million and $1.0 million as of December 31, 2017 and 2016, respectively.

The Company must make interest payments on the loan balance each month it remains outstanding. Per annum interest is payable on the principal balance of the loan each month it remains outstanding at the greater of 9.45% and

an amount equal to 9.45% plus the prime rate minus 4.75% as determined daily, provided however, that the per annum interest rate shall not exceed 15.0% (9.45% as of December 31, 2017).

The loans are secured by a lien on all the Company's personal property (other than intellectual property), whether owned or acquired after the date of the First Loan Agreement. The 2017 Loan Agreement define 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 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 2017 Loan Agreement, the related liens or the priority thereof. As of December 31, 2017, the Company was in compliance with all loan covenants, 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 2017 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, 2017 are as follows (amounts in thousands):

Year Ending December 31:	
2018	$2,493
2019	8,725
2020	9,013
2021	6,087
	26,318
Less amount representing interest	(4,688)
Less unamortized discount	(1,523)
Less deferred charges	(1,630)
Less loans payable current, net of discount	—
Loans payable, net of current portion and discount	$18,477

(7) Common Stock

As of December 31, 2017, the Company had 250,000,000 authorized shares of common stock, $0.001 par value, of which 118,325,396 shares were issued and outstanding.

In June 2017, the Company amended its certificate of incorporation, which increased the number of authorized shares of common stock, $0.001 par value, by 50,000,000 from 200,000,000 shares to 250,000,000 shares. The amendment was adopted by the Board of Directors in April 2017 and approved by stockholders at the Annual Meeting of Stockholders held on June 21, 2017

ATM Sales Agreement with Leerink

In February 2018, the Company entered into an at-the-market issuance sales agreement (the “Leerink Sales Agreement”), with Leerink Partners LLC (“Leerink”) pursuant to which the Company could issue and sell shares of its common stock from time to time up to an aggregate amount of $50 million, at its option, through Leerink as its sales agent, with any sales of common stock through Leerink being 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 (the “Securities Act”)

pursuant to an effective shelf registration statement on Form S-3. The Company agreed to pay Leerink a commission of up to 3% of the gross proceeds of any sales of common stock pursuant to the Leerink Sales Agreement. At the time of issuance of these financial statements, no shares of our common stock have been sold under the Leerink Sales Agreement.

On November 30, 2017, the Company filed a shelf registration statement on Form S-3 with the Securities and Exchange Commission (the "SEC"), which covers the offering, issuance and sale of up to $200.0 million of its common stock, preferred stock, debt securities, warrants and/or units (the "2017 Shelf"). The 2017 Shelf (file No. 333-221873) was declared effective by the SEC on December 15, 2017 and was filed to replace the Company's then existing 2015 Shelf, which was terminated.

Public Offering

On March 31, 2017, the Company closed an underwritten public offering of 34,500,000 shares of its common stock, including the exercise in full by the underwriter of its option to purchase 4,500,000 shares, at the public offering price of $0.50 per share for gross proceeds of approximately $17.3 million. Certain of the Company's executive officers and a director purchased an aggregate of 420,000 shares and an entity affiliated with New Enterprise Associates, a greater than 5% stockholder of the Company, purchased 6,000,000 shares in this offering at the same public offering price per share as the other investors. The net offering proceeds to the Company were approximately $15.4 million after deducting underwriting discounts and estimated offering expenses payable by the Company. The Company sold these shares pursuant to the 2015 Shelf (as defined below).

Private Placement / PIPE Warrants

In May 2016, the Company entered into a securities purchase agreement with a select group of qualified institutional buyers, institutional accredited investors and accredited investors pursuant to which the Company sold 17,642,482 units, at a price of $0.965 per unit, for gross proceeds of approximately $17.0 million. Each unit consisted of one share of the Company's common stock and a warrant to purchase one share of the Company's common stock (the "PIPE Warrants"). The PIPE Warrants have an exercise price of $1.00 per share and are exercisable for a period of five years from the date of issuance. Certain of the Company's directors and executive officers purchased an aggregate of 544,039 units in this offering at the same price as the other investors. The net offering proceeds to the Company were approximately $15.4 million after deducting placement agent fees and other offering expenses payable by the Company. In July 2017, Hercules exercised its PIPE Warrants with respect to all 259,067 shares of common stock underlying such PIPE Warrants, and the Company issued Hercules 259,067 shares of its common stock and received approximately $0.3 million in cash proceeds. As of December 31, 2017, there were PIPE Warrants outstanding and exercisable for 17,383,415 shares of common stock.

ATM Sales Agreement with FBR

In February 2015, the Company entered into an at-the-market issuance sales agreement (the "FBR Sales Agreement") with FBR & Co. and MLV & Co. (together "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, with any sales of common stock through FBR being made by any method that is deemed an "at-the-market" offering as defined in Rule 415 promulgated under the Securities Act pursuant to an effective shelf registration statement on Form S-3. The Company agreed to pay FBR a commission of up to 3% of the gross proceeds of any sales of common stock pursuant to the FBR Sales Agreement.

On May 7, 2015, the Company filed a shelf registration statement on Form S-3 with the SEC, which covered 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 also amended its FBR Sales Agreement 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. Through August 2015, the Company sold approximately 5.9 million shares pursuant to the FBR Sales Agreement, as amended, resulting in proceeds of approximately $10.2 million, net of commissions and issuance costs. In June 2017, the Company sold approximately 6.5 million shares pursuant to the FBR Sales Agreement, as amended, resulting in proceeds of approximately $8.8 million, net of commissions and issuance costs. No shares were sold between August 2015 and June 2017, and between July 2017 and December 15, 2017 under the FBR Sales Agreement. The FBR Sales Agreement has expired.

(8) Stock-based Compensation

Stock Incentive Plan

The Company maintains the 2010 Stock Incentive Plan (the “Plan”) for employees, consultants, advisors, and directors, as amended in March 2013, June 2014 and June 2017. The Plan provides for the grant of equity awards such as stock options and restricted stock. In June 2017, the Company amended the Plan to increase the total number of shares reserved under the Plan by 3,500,000 from 8,500,000 shares to 12,000,000 shares. The amendment was adopted by the Board of Directors in February 2017 and approved by stockholders at the Annual Meeting of Stockholders held on June 21, 2017. 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. As of December 31, 2017, there were 3,549,657 shares of common stock available for future issuance under the Plan.

The following table summarizes stock option activity during the year ended December 31, 2017:

	Options	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term	Aggregate Intrinsic Value
Outstanding at January 1, 2017	4,858,678	$ 2.31		
Granted	3,455,135	$ 1.40		
Exercised	(17,576)	$ 0.87		
Forfeited	(758,279)	$ 1.03		
Outstanding at December 31, 2017	7,537,958	$ 2.00	7.49	$10,709,000
Exercisable at December 31, 2017	3,582,756	$ 2.67	6.06	$5,075,000

Stock options to purchase 178,564 shares of common stock contain performance-based milestone conditions, which were not deemed probable of vesting at December 31, 2017.

The aggregate intrinsic value is based upon the Company's closing stock price of $2.79 on December 29, 2017, the last trading day of the year.

The fair value of stock options subject only to service or performance conditions that are granted to employees 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,		
	2017	2016	2015
Volatility factor	71.82% - 80.15%	72.18% - 75.47%	73.04% - 78.70%
Expected term (in years)	5.50 - 6.25	3.00 - 6.25	5.50 - 6.25
Risk-free interest rates	1.84% - 2.22%	1.07% - 2.01%	1.54% - 1.93%
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.

In July 2016, the Company began calculating volatility using its historical data. Previously, the Company did not have sufficient history to support a calculation of volatility using only its historical data. As such, prior to July 2016, the Company 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. Based upon these assumptions, the weighted-average grant date fair value of stock options granted during the years ended December 31, 2017, 2016 and 2015 was $0.97, $0.65 and $0.75, respectively.

On January 1, 2017, the Company adopted ASU No. 2016-09, Compensation–Stock Compensation (Topic 718): Improvements to Employee Share-Based Payment Accounting and elected to account for forfeitures as they occur. Prior to 2017, the Company included an estimate of the value of the awards that would be forfeited in calculating compensation costs, which the Company estimated based upon actual historical forfeitures. The forfeiture estimates were recognized over the requisite service period of the awards on a straight-line basis. The Company used a forfeiture rate of 0%, 76% and 71% during years ended December 31, 2017, 2016 and 2015, respectively.

As of December 31, 2017, there was $3.4 million of total unrecognized stock-based compensation expense related to stock options granted to employees under the Plan. The expense is expected to be recognized over a weighted-average period of 2.6 years. The intrinsic value of options exercised during the years ended December 31, 2017, 2016 and 2015 was $46,000, $6,000 and $58,000, respectively.

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 fair value of restricted stock awards that vested was $0 in the year ended December 31, 2017, and $0.1 million in each of the years ended December 31, 2016 and 2015.

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, as amended in March 2013. 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 Company has reserved 764,000 shares of common stock under the ESPP. As of December 31, 2017, there were 307,282 shares available for future issuance under the ESPP.

Pursuant to the ESPP, the Company did not sell any shares of common stock during the years ended December 31, 2017 and December 31, 2016. For the year ended December 31, 2015, the Company sold a total of 7,138 shares of common stock 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. The total stock-based compensation expense recorded as a result of the ESPP was approximately $3 thousand, $2 thousand and $27 thousand during the years ended December 31, 2017, 2016 and 2015, respectively.

(9) 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 $0.6 million, $0.6 million and $(9.1) million for the years ended December 31, 2017, 2016 and 2015, respectively. The net rent credit for the year ended December 31, 2015 was recorded within operating expenses and allocated to research and development and general and administrative expense based upon the use of the underlying facility space. Refer to the following paragraphs and Note 12 for further discussion of the net rent credit recognized in 2015.

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 Note 12 for further discussion regarding the termination of this lease. The Company recognized rent expense of approximately ($9.5) and $4.3 million related to the lease during the years ended December 31, 2015 and 2014, respectively. The expense recognized during the years ended December 31, 2015 and 2014 included 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 Note 15 for further discussion of legal contingencies.

(10) Income Taxes

The Company accounts for income taxes under the provisions of ASC 740. The Company recorded a $0.1 million tax provision for foreign withholding taxes in each of the years ended December 31, 2017 and 2016 in connection with the $1.0 million in reimbursement payments in 2017 related to manufacturing development activities conducted by the Company prior to the Effective Date and the $1.0 million upfront payment by CANbridge in March 2016 upon the execution of the collaboration and license agreement. For the year ended December 31, 2015, 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, 2017, 2016 and 2015:

	Years Ended December 31,		
	2017	2016	2015
Income tax computed at federal statutory tax rate	34.0%	34.0%	34.0%
State taxes, net of federal benefit	5.3%	5.2%	5.3%
Research and development credits	0.4%	1.4%	2.0%
Other permanent differences	(20.8)%	6.1%	(2.0)%
Foreign rate differential	0.0%	(0.1)%	(0.1)%
Foreign withholding taxes	(0.2)%	(0.4)%	—
SEC settlement liability	0.0%	—	(9.1)%
Excess benefit stock compensation	0.0%	—	—
Tax reform - rate change	(97.5)%	—	—
Other	0.1%	(6.6)%	(3.8)%
Change in valuation allowance	78.7%	(39.6)%	(26.3)%
Total	—	—	—

With limited exceptions, the Company has incurred net operating losses from inception. At December 31, 2017, the Company had domestic federal, state, and United Kingdom (UK) net operating loss carryforwards of approximately $503.6 million, $394.3 million, and $6.0 million respectively, available to reduce future taxable income. The federal net operating loss carryforwards expire beginning in 2022 through 2037 and the state loss carryforwards begin to expire in 2030 and continue through 2037 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 $10.5 million and $4.3 million, respectively, available to reduce future tax liabilities and which expire at various dates. The federal credits expire beginning in 2022 through 2037 and the state credits expire beginning in 2019 through 2032. 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, 2017 and 2016 are as follows (in thousands):

	2017	2016
Deferred tax assets:		
NOL carryforwards	$131,683	$182,433
Research and development credits	13,913	13,060
Deferred revenue and R&D reimbursements	770	867
Estimated settlement liability	4,664	—
Other temporary differences	4,420	4,570
Total deferred tax assets:	155,450	200,930
Deferred tax liabilities:		
Insurance recovery	(4,098)	—
Total deferred tax liabilities:	(4,098)	—
Valuation allowance	(151,352)	(200,930)
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 decreased by $49.6 million as of December 31, 2017 which was primarily related to the "Tax Cuts and Jobs Act", which reduced the federal tax rate from 35% to 21%. The valuation allowance increased $10.6 million and $3.9 million during the years ended December 31, 2016 and 2015, respectively, primarily due to the generation of net operating loss carryforwards.

As of December 31, 2016, the Company had federal and state net operating losses of approximately $4.1 million related to excess tax deductions that had been excluded from the above table. The benefit of these net operating losses would have been recognized as an increase in additional paid in capital when it resulted in a reduction of taxes payable. In January 2017, the Company adopted ASU 2016-09, Improvements to Employee Share-Based Payment Accounting. As part of the adoption, the Company recorded through retained earnings these additional deferred tax assets of $4.1 million related to previously unrecognized tax losses with an equal and offsetting adjustment to the Company's valuation allowance. The net impact of the adoption on the Company's deferred tax assets was $0.

On December 22, 2017, President Trump signed into law The Tax Cuts and Jobs Act ("the Act"). The Act, among other things, contains significant changes to corporate taxation, including reduction of the corporate tax rate from a top marginal rate of 35% to a flat rate of 21%, limitation of the tax deduction for interest expense to 30% of adjusted earnings (except for certain small businesses), limitation of the deduction for net operating losses to 80% of current year taxable income and elimination of net operating loss carrybacks, one time taxation of offshore earnings at reduced rates regardless of whether they are repatriated, elimination of U.S. tax on foreign earnings (subject to certain important exceptions), immediate deductions for certain new investments instead of deductions for depreciation expense over time, and modifying or repealing many business deductions and credits.

On December 22, 2017, the SEC issued guidance under Staff Accounting Bulletin No. 118, Income Tax Accounting Implications of the Tax Cuts and Jobs Act directing taxpayers to consider the impact of the U.S. legislation as "provisional" when it does not have the necessary information available, prepared or analyzed (including computations) in reasonable detail to complete its accounting for the change in tax law.

The Company recognizes the changes in tax law, including the Act, in the period the law is enacted. Accordingly, the effects of the Act have been recognized in the financial statements for the year ended December 31, 2017. As a result of the change in law, the Company recorded a reduction to its deferred tax assets of $63.3 million and a corresponding reduction to its valuation allowance. As a result, there was no impact to the Company's income statement due to the reduction in the U.S. corporate tax rate.

At December 31, 2017, the Company has not completed its accounting for the tax effects of enactment of the Act; however in certain cases the Company has made a reasonable estimate of the effects of the Act. For the items for which we were able to determine a reasonable estimate and thus are considered provisional, we recorded a $63.3 million reduction to deferred tax assets. The Company's preliminary estimate of the effects Act, including the remeasurement of deferred tax assets and liabilities, is subject to the finalization of management's analysis related to certain matters, such as developing interpretations of the provisions of the Act and the filing of the Company's tax returns. U.S. Treasury regulations, administrative interpretations or court decisions interpreting the Act may require further adjustments and changes in estimates. The final determination of the effects of the Act will be completed as additional information becomes available, but no later than one year from the enactment of the Act. In all cases, the Company will continue to make and refine its calculations as additional analysis is completed. In addition, the Company's estimates may also be affected as it gains a more thorough understanding of the tax law.

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 2014 through 2017. 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, 2017, 2016 and 2015:

	Years Ended December 31,		
	2017	2016	2015
	(in thousands)		
Amount established upon adoption	$1,200	$1,200	$1,200
Additions for current year tax provisions	—	—	—
Additions for prior year tax provisions	—	—	—
Reductions of prior year tax provisions	—	—	—
Balance as of end of year	$1,200	$1,200	$1,200

(11) Strategic Restructuring

On January 6, 2015, the Board of the Company approved a 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 amounts accrued at December 31, 2016	Restructuring expense incurred during the year ended December 31, 2017	Restructuring amounts paid during the year ended December 31, 2017	Restructuring amounts accrued at December 31, 2017
Employee severance, benefits and related costs.	$—	$ —	$ —	$ —
	Restructuring	Restructuring	Restructuring	Restructuring

	amounts at December 31, 2015	expense incurred during the year ended December 31, 2016	amounts paid during the year ended December 31, 2016	amounts accrued at December 31, 2016
Employee severance, benefits and related costs.	$357	$ —	$ (357)	$ —

(12) Facility Lease Exit

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 had 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.

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. 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 six months ended June 30, 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 six months ended June 30, 2015. Upon the surrender of the remaining space, the Company had no further rights or obligations with respect to the lease. The Company secured office space appropriate for its current needs under a cancellable arrangement that began in May 2015. The Company recognized rent expense of approximately ($9.5) million and $4.3 million related to the lease during the years ended December 31, 2015 and 2014, respectively. The net rent credit for the year ended December 31, 2015 and December 31, 2014 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. 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.

The following table summarizes the components of the Company's lease exit activity recorded in current liabilities at December 31, 2015:

	Lease Exit 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
Lease exit costs	$4,981	224	$ (5,477)	$ 272	$ —

No costs were incurred during the year ended December 31, 2016 or 2017.

(13) Employee Benefit Plan

In 2002, the Company established the AVEO Pharmaceuticals, Inc. 401(k) Plan (the "401(k) Plan") for its employees, which is designed to be qualified under Section 401(k) of the Internal Revenue Code. Eligible employees are permitted to contribute to the 401(k) Plan within statutory and 401(k) Plan limits. The Company makes matching contributions of 50% of the first 5% of employee contributions. The Company made matching contributions of $0.1 million for each of the years ended December 31, 2017, 2016 and 2015.

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(14) Quarterly Results (Unaudited)

	Three Month Ended March 31, 2017	June 30, 2017	September 30, 2017	December 31, 2017
	(in thousands, expect per share data) (unaudited)			
Collaboration and licensing revenue	$2,532	$351	$4,614	$82
Operating expenses	10,287	9,183	6,767	10,153
Loss from operations	(7,755)	(8,832)	(2,153)	(10,071)
Change in fair value of PIPE warrant liability	(484)	(23,925)	(23,538)	14,207
Other expense, net	(551)	(530)	(655)	(637)
Provision for income taxes	(50)	—	(51)	—
Net income (loss)	$(8,840)	$(33,287)	$(26,397)	$3,499
Basic net income (loss) per share				
Net income (loss) per share	$(0.12)	$(0.30)	$(0.22)	$0.03
Weighted average number of common shares outstanding	76,246	110,550	118,006	118,323
Dilutive net income (loss) per share				
Net income (loss) per share	$(0.12)	$(0.30)	$(0.22)	$(0.08)
Weighted average number of common shares and dilutive common share equivalents outstanding	76,246	110,550	118,006	130,108

	Three Month Ended March 31, 2016	June 30, 2016	September 30, 2016	December 31, 2016
	(in thousands, expect per share data) (unaudited)			
Collaboration and licensing revenue	$1,203	$193	$992	$127
Operating expenses	8,435	7,335	6,585	9,553
Loss from operations	(7,232)	(7,142)	(5,593)	(9,426)
Change in fair value of PIPE warrant liability	—	(996)	1,178	4,569
Other expense, net	(377)	(468)	(551)	(748)
Provision for income taxes	(101)	—	—	—
Net loss	$(7,710)	$(8,606)	$(4,966)	$(5,605)
Net loss per share - basic and diluted	$(0.13)	$(0.13)	$(0.07)	$(0.07)
Weighted average number of common shares outstanding	58,166	66,917	75,861	75,863

(15) Legal Proceedings

Two class action lawsuits have been filed against the Company and certain of its former officers and 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 stockholders who purchased the Company's common stock between January 3, 2012 and May 1, 2013 (the "Class"). This consolidated amended complaint was dismissed without prejudice on March 20, 2015, and the lead plaintiffs then filed a second amended complaint bringing similar allegations, and which no longer named Mr. DePinho as a defendant. The Company moved to dismiss again, and after a second round of briefing and oral argument, the District Court ruled in the Company's favor and dismissed the second amended complaint with prejudice on November 18, 2015. The lead plaintiffs appealed the District Court's decision to the United States Court of Appeals for the First Circuit. They also filed a motion to vacate and reconsider the District Court's judgment, which the Company opposed. On January 3, 2017, the District Court granted the plaintiffs' motion to vacate the dismissal and judgment, and the plaintiffs filed a motion to dismiss their appeal on February 8, 2017. On February 2, 2017, the plaintiffs filed a third amended complaint, on behalf of stockholders who purchased common stock between May 16, 2012 and May 1, 2013, alleging claims similar to those alleged in the prior complaints, namely that the Company and certain of the Company's former officers and directors

violated Sections 10(b) and/or 20(a) of the Securities Exchange Act of 1934, as amended (the "Exchange Act") 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 clinical trial in an effort to lead investors to believe that the drug would receive approval from the FDA. On March 2, 2017, the Company filed an answer to the third amended complaint, and the parties initiated discovery. On June 29, 2017, the plaintiffs filed a motion for class certification and on July 27, 2017, the Company filed its response. On July 18, 2017, the District Court entered an order referring the case to alternative dispute resolution. The parties mediated on September 12 and 13, 2017. On December 26, 2017, the parties entered into a binding Memorandum of Understanding (the "MOU") regarding the settlement of the lawsuit. On January 29, 2018, the parties entered into a Stipulation of Settlement (the "Stipulation"), which was filed with District Court on February 2, 2018. Under the terms of the MOU and Stipulation, AVEO agreed with counsel for the lead plaintiffs to cause certain of AVEO's and the Individual Defendants' insurance carriers to provide the Class with a cash payment of $15.0 million, which includes the cash amount of any attorneys' fees or litigation expenses that the District Court may award lead plaintiffs' counsel and costs lead plaintiffs incur in administering and providing notice of the settlement. Additionally, AVEO agreed to issue to the Class the Settlement Warrants for the purchase of 2.0 million shares of AVEO common stock exercisable from the date of issue until the expiration of a one-year period after the date of issue at an exercise price equal to the closing price on December 22, 2017, the trading day prior to the execution of the MOU, which was $3.00 ("the "Settlement Warrants"). On February 8, 2018, the District Court issued an order preliminarily approving the terms of the Stipulation. The Stipulation is subject to final approval by the District Court. The District Court set a Final Approval Hearing for May 30, 2018. The Company has agreed to use its best efforts to issue and deliver the Settlement Warrants within ten business days following the effective date of the final approval of the Stipulation.

The Company evaluates developments in legal proceedings on a quarterly basis. The Company records an accrual for loss contingencies to the extent that the Company concludes that it is probable that a liability has been incurred and the amount of the related loss can be reasonably estimated. In December 2017, upon entering into the MOU, this settlement became estimable and probable. Accordingly, the Company recorded an estimated $17.1 million contingent liability, including $15.0 million for the cash portion of the settlement with a corresponding insurance recovery for the 100% portion to be paid directly by certain of the Company's insurance carriers, and an approximate $2.1 million estimate for the warrant portion of the settlement with a corresponding non-cash charge to the Statement of Operations as a component of operating expenses. In February 2018, the insurance carriers funded the settlement escrow account for the $15.0 million cash settlement. Refer to Note 3, "Potential Class Action Settlement" for further discussion of the warrants.

On July 3, 2013, the staff, or SEC Staff, of the SEC served a subpoena on the Company for documents and information concerning tivozanib, including related communications with the FDA, investors and others. In September 2015, the SEC Staff invited the Company to discuss the settlement of potential claims asserting that the Company violated federal securities laws by omitting to disclose to investors the recommendation by the staff of the FDA on May 11, 2012, that the Company conduct an additional clinical trial with respect to tivozanib. On March 29, 2016, the SEC filed a complaint against the Company and three of its former officers in the U.S. District Court for the District of Massachusetts alleging that the Company misled investors about its efforts to obtain FDA approval for tivozanib. Without admitting or denying the allegations in the SEC's complaint, the Company consented to the entry of a final judgment pursuant to which the Company paid the SEC a $4.0 million civil penalty to settle the SEC's claims against it. As this settlement was probable and estimable as of December 31, 2015, the Company recorded an estimated settlement liability of $4.0 million and recorded a corresponding loss in the Statement of Operations as a component of operating expenses. On March 31, 2016, the District Court entered a final judgment which (i) approved the settlement; (ii) permanently enjoined the Company from violating Section 17(a) of the Securities Act of 1933, as amended, Sections 10(b) and 13(a) of the Securities Exchange Act of 1934, as amended, and rules 10b-5, 12b-20,

13a-1, 13a-11 and 13a-13 promulgated thereunder; and (iii) ordered the Company to pay the agreed-to civil penalty. On September 15, 2017 and October 31, 2017, respectively, two of the Company's former officers consented to entry of final judgment to settle the SEC's claims against them. The Company is not a party to the litigation between the SEC and the remaining former officer, and the Company can make no assurance regarding the outcome of that action or the SEC's claims against that individual.

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 defined in Rules 13a-15(e) and 15d-15(e) promulgated under the Exchange Act) as of December 31, 2017. 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 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, 2017. 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, 2017, 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

To the Stockholders and the Board of Directors of AVEO Pharmaceuticals, Inc.

Opinion on Internal Control over Financial Reporting

We have audited AVEO Pharmaceuticals, Inc.'s internal control over financial reporting as of December 31, 2017, 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). In our opinion, AVEO Pharmaceuticals, Inc. (the Company) maintained, in all material respects, effective internal control over financial reporting as of December 31, 2017, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the consolidated balance sheets of the Company as of December 31, 2017 and 2016, the related consolidated statements of operations, comprehensive loss, stockholders' equity (deficit), and cash flows for each of the three years in the period ended December 31, 2017, and the related notes and our report dated March 13, 2018 expressed an unqualified opinion thereon that included an explanatory paragraph regarding the Company's ability to continue as a going concern.

Basis for Opinion

The Company's management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting included in the accompanying Management's Report on Internal Control Over Financial Reporting. Our responsibility is to express an opinion on the Company's internal control over financial reporting based on our audit. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audit in accordance with the standards of the PCAOB. 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.

Definition and Limitations of Internal Control Over Financial Reporting

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.

/s/ Ernst & Young LLP

Boston, Massachusetts

March 13, 2018

Changes in Internal Control Over Financial Reporting

There have been no changes in our internal control over financial reporting, as such term is defined in Rules 13a-15(f) and 15(d)-15(f) promulgated under the Securities Exchange Act of 1934, during the fourth quarter of 2017 that have materially affected, or is 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 2018 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 of the Registrant” 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 2018 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 2018 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 2018 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 2018 Annual Meeting of Stockholders and is incorporated by reference herein.

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PART IV

ITEM 15. Exhibits, 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' (Deficit) 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.

ITEM 16. Form 10-K Summary

None.

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	Certificate of Amendment of Restated Certificate of Incorporation of the Registrant	10-Q	001-34655	08/09/2017	3.1	
3.4	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	
4.2	Registration Rights Agreement, dated May 13, 2016, by and among the Company and the Investors named therein	8-K	001-34655	05/13/2016	10.3	
	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	Second Amended and Restated 2010 Stock Incentive Plan	8-K	001-34655	06/27/2017	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	Offer Letter by the Registrant to Michael Needle, dated January 8, 2015	10-Q	001-34655	05/07/2015	10.4
10.15	Severance Agreement, dated September 13, 2010, by and between the Registrant and Michael Bailey	10-Q	001-34655	11/05/2010	10.1
10.16	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

Exhibit Number	Description of Exhibit	Incorporated by Reference Form	File Number	Date of Filing	Exhibit Number	Filed Herewith
10.17	Offer Letter by and between the Registrant and Keith Ehrlich, dated April 21, 2015	10-K	001-34655	03/15/2016	10.19	
10.18	Transition Retirement and Release of Claims Agreement, dated as of May 3, 2017, by and between the Registrant and Keith Ehrlich	10-Q	001-34655	08/09/2017	10.1	
10.19	Offer Letter by and between the Registrant and Matthew Dallas, dated May 8, 2017	8-K	001-34655	05/17/2017	10.1	
10.20	Severance and Change in Control Agreement, dated November 20, 2017, by and between the Registrant and Matthew Dallas	8-K	001-34655	11/20/2017	10.1	
10.21	Offer Letter by and between the Registrant and Nikhil Mehta, dated November 10, 2017					X
10.22	Severance and Change in Control Agreement, dated November 20, 2017, by and between the Registrant and Nikhil Mehta					X
	Material Contracts—Financing Agreements					
10.23	Securities Purchase Agreement, dated May 13, 2016, by and among the Company and the Investors named therein	8-K	001-34655	05/13/2016	10.1	
10.24	Form of Warrant to Purchase Common Stock	8-K	001-34655	05/13/2016	10.2	
10.25	Amended and Restated Loan and Security Agreement, dated December 28, 2017, by and among the Registrant and the parties named therein.	8-K	001-34655	01/02/2018	10.1	
10.26	Sales Agreement dated February 16, 2018, by and between the Company and Leerink Partners LLC	8-K	001-34655	02/16/2018	1.1	
	Material Contracts—License and Strategic Partnership Agreements					
10.27†	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	
10.28†	Option and License Agreement, dated as of March 18, 2009, by and between the Registrant and Biogen Idec International GmbH	S-1	333-163778	12/16/2009	10.26	
10.29†		10-Q	001-34655	05/07/2014	10.1	

	Amendment No. 1 to Option and License Agreement, dated as of March 18, 2014 by and between the Registrant and Biogen Idec MA Inc.				
10.30†	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
10.31	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
10.32	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
10.33†	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
10.34†	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
10.35†	License Agreement, dated December 18, 2015, by and between the Registrant and EUSA Pharma (UK) Limited	10-K	001-34655	03/15/2016	10.42

Exhibit Number	Description of Exhibit	Incorporated by Reference Form	File Number	Date of Filing	Exhibit Number	Filed Herewith
10.36†	Collaboration and License Agreement, dated March 17, 2016, by and between the Registrant and CANbridge Life Sciences Ltd.	10-Q	001-34655	05/10/2016	10.1	
10.37†	First Amendment, dated October 14, 2016, to Co-Development and Collaboration Agreement, dated April 9, 2014, by and between the Company and Biodesix, Inc.	10-Q	001-34655	11/04/2016	10.1	
	Additional Exhibits					
10.38	Memorandum of Understanding, dated December 26, 2017, by and among the Company and the parties named therein	8-K	001-34655	12/26/2017	10.1	
21.1	Subsidiaries of the Registrant					
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

X

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

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 13, 2018 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 13, 2018
/s/ MATTHEW DALLAS Matthew Dallas	Chief Financial Officer Principal Financial and Accounting Officer	March 13, 2018
/s/ Kenneth M. Bate Kenneth M. Bate	Director	March 13, 2018
/s/ Anthony B. Evnin Anthony B. Evnin	Director	March 13, 2018
/s/ ROBERT C. YOUNG Robert C. Young	Director	March 13, 2018
/s/ JOHN H. JOHNSON John H. Johnson	Director	March 13, 2018